Questionnaire

Summary of the main activities of a research institute of the Slovak Academy of Sciences

Period: January 1, 2016 - December 31, 2021

1. Basic information on the institute:

1.1. Legal name and address

Centre of Biosciences Slovak Academy of Sciences Dúbravská cesta 9 SK-840 05 Bratislava Slovakia

1.2. URL of the institute web site

http://www.cbv.sav.sk

1.3. Executive body of the institute and its composition

Directoriat	Name	Year of birth	Years in the position, from - to
Director	lng. Zdena Sulová, DrSc.	1957	2015 - present
Deputy director	Prof. MVDr. Štefan Faix, DrSc.	1958	2018 - present
	RNDr. Ľubor Košťál, CSc.	1956	2017 - present
Scientific secretary	RNDr. Jana Antalíková, PhD.	1966	2009 - present
	RNDr. Viera Boháčová, CSc.	1964	2011 - present
	RNDr. Štefan Čikoš, DrSc.	1963	2018 - present

Add more rows for any changes during the evaluation period

1.4. Head of the Scientific Board

Mgr. Martin Valachovič, PhD.

1.4.1 Composition of the International Advisory Board

Prof. Matthias Sipiczki - University of Debrecen, Hungary, gecela@post.sk

Prof. Adam Cieslak - Poznan University of Life Sciences, Poland, adam.cieslak@up.poznan.pl

Prof. Ulrike Stein - Max-Delbrück-Center for Molecular Medicine (MDC), Germany, ustein@mdc-berlin.de

Dr. Peter Jedlicka - Goethe University Frankfurt, Germany, <u>jedlicka@em.unifrankfurt.de</u>

Prof. Jan Vondracek - Institute of Biophysics of CAS, Czech Republic, vondracek@ibp.cz

1.5. Basic information on the research personnel

1.5.1. Fulltime equivalent work capacity of all employees (FTE all), FTE of employees with university degrees engaged in research projects (FTE researchers)

	2016	6 2017		2018		20	19	20	20	20	21	2016-2021		
FTE all	FTE	FTE all	FTE researchers	FTE all	FTE researchers	FTE all	FTE researchers	FTE all	FTE	FTE all	FTE	average FTE all per year	average FTE researchers per year	
110.13	66.93	106.91	79.57	100.79	76.23	96.86	68.96	100.51	71.81	105.69	75.52	103.48	73.17	

1.5.2. If applicable, add also a short information on the merger of the institute in the evaluation period. You can also add rows in the above table corresponding to the founding institutes

On January 1, 2017, merged the Institute of Animal Biochemistry and Genetics in Ivanka pri Dunaji (in the same year relocated to Bratislava) and the Institute of Molecular Physiology and Genetics in Bratislava into the Centre of Biosciences of the Slovak Academy of Sciences.

On January 1, 2018, the Institute of Animal Physiology in Košice merged with the Centre of Biosciences of the Slovak Academy of Sciences.

1.6. Basic information on the funding of the institute

1.6.1. Institutional salary budget, other salary budget¹, non-salary budget²

Salary budget	2016	2017	2018	2019	2020	2021	average
Institutional salary budget [millions of EUR]	1.693	1.790	1.773	1.971	2.220	2.191	1.940
Other salary budget [millions of EUR]	0.164	0.191	0.160	0.146	0.133	0.150	0.157
Total salary budget [millions of EUR]	1.857	1.981	1.933	2.117	2.353	2.341	2.097
Non-salary budget [millions of EUR]	0.816	0.868	0.925	0.919	0.991	0.984	0.917

1.7. Mission Statement of the Institute as presented in the Foundation Charter indicating the years when it was adopted and revised

- 1. The Centre of Biosciences of the Slovak Academy of Sciences (hereafter referred to as CBs SAS) is a scientific research organization of the Slovak Academy of Sciences focused on basic and applied research on chemical, physical, genetic, and physiological processes in animals and microorganisms. The research activities of the CBs SAS are interdisciplinary in nature, and their focus falls mainly into the following scientific fields (according to the Directive on the Code of Branches of Science and Technology No. 27/2006-R issued by the Ministry of Education and Science of the Slovak Republic): biophysics, biochemistry, ethology, animal physiology, genetics, immunology, microbiology, molecular biology, neuroscience, normal and pathological physiology, and other disciplines of the veterinary sciences.
- 2. CBs SAS carries out scientific research activities through the following three organizational units:

2

¹ Salary budget originating outside the regular budgetary resources of the organization, e.g. from the project funding.

² Includes Goods and Services and PhD fellowships

- a. Institute of Animal Physiology
- b. Institute of Animal Biochemistry and Genetics
- c. Institute of Molecular Physiology and Genetics
- 3. CBs SAS carries out doctoral studies as an external educational institution in accredited fields of science in accordance with the legislation in force.
- 4. CBs SAS and its organizational units cooperate with academic and research institutions working in related scientific fields at home and abroad.
- 5. CBs SAS and its organizational units publish and disseminate the results of their research activities via the periodical and non-periodical press and other information media.
- 6. CBs SAS publishes the international journal General Physiology & Biophysics in the English language.
- 7. CBs SAS and its organizational units provide consulting and expert services related to the main activities of the Centre.
- 1.8. Summary of R&D activity pursued by the institute during the evaluation period in both national and international contexts. Describe the scientific importance and societal impact of each important result/discovery. Explain on general level the information should be understandable for a non-specialist (recommended 5 pages, max. 10 pages for larger institutes with more than 50 average FTE researchers per year as per Table 1.5.1.)

The formation of the Centre of Biosciences through the gradual integration of three formerly independent organizations resulted in the creation of a new entity with a broad research focus. Currently, the activities of all research groups within the Centre fall under two main research areas, Cell Biology and Integrative Animal Physiology.

- **1. Cell Biology** is focused on genetics, biochemistry, toxicology, cytochemistry, biophysics, electrophysiology, and lipid metabolism using cell models of normal and tumor-transformed mammalian cells as well as microbial eukaryotic cells.
- **2. Integrative Animal Physiology** is focused on reproductive biology, neurophysiology and behavior, and physiology of the digestive tract in laboratory and farm animals

We study the mechanisms underlying physiological and pathological processes across the spectrum of biological organization, including subcellular, cellular, tissue, organ, and the whole organism processes as well as whole organism behaviors.

The summary of R&D activity pursued by the Centre during the evaluation period is presented according to the thematic affiliation to the two abovementioned scientific fields.

Cell Biology

Apart from the large differences in the function and homeostasis of microbial eukaryotes and animal cells, which we currently use in our research, there are some major similarities, such those in the structure and function of biological membranes, the response of cells to toxic substances, in DNA repair and removal of damaged bio(macro)molecules, in the mitotic division and cell cycle, and similarities of meiotic division, that allow comparison of these models.

Regulation of RNA splicing

We are interested in identifying the molecular mechanisms responsible for genetic susceptibility to complex genetic diseases at the level of pre-mRNA splicing. Understanding how common and disease-predisposing variants interact with gene expression machinery along with molecular insights into the mechanisms governing RNA-based regulation of gene expression is fundamentally important for understanding neurobiology, neurological disorders and cancers and is key for the development of successful future therapies.

In our latest studies, we identified human PUF60 (poly U binding splicing factor 60)-regulated exons and provided new insights into the regulation of exon usage by the 3' splice site organization. PUF60, as a splicing factor, binds uridine (U)-rich sequences, and our results revealed that germline mutation heterogeneity in PUF60 can enhance phenotypic variability associated with PUF60 deficiency (10.1093/nar/gky389). Hereby, we identified functional cancer-associated somatic mutations in genes encoding PUF60 and U2AF (Auxiliary factor of U2 small nuclear ribonucleoprotein) and suggested the existence of a shared oncogenic pathway initiated by impaired recognition of 3' splice sites that enhance mRNA isoform diversity (10.3390/cancers12071865) (Fig. 1 left panel).

We have further determined the molecular mechanism regulating the expression of Ca2+-insensitive and -sensitive subunits of the 2-oxoglutarate dehydrogenase complex (OGDHC) that in turn regulate tissue-specific NADH and ATP supply by means of mutually exclusive OGDH exons 4a and 4b. Moreover, we hypothesized that OGDH alternative splicing may have facilitated the evolution of endothermy (10.1093/nar/gkab046) (Fig. 1 right panel).

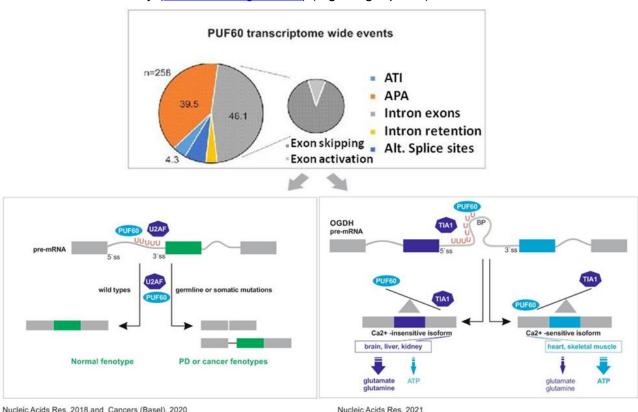


Fig. 1 Graphical summary of the regulation of RNA splicing

Molecular basis of electrical signaling in excitable cells

The research focused on the molecular basis of electrical signaling in excitable cells is bringing together experts in the field of in vivo and in vitro electrophysiology of excitable cells, neurons and cardiac cells. Synergies between smaller research units are being spontaneously created to better respond to scientific challenges in the field of neuronal and cardiac physiology and pathophysiology.

Various aspects of neuronal signaling implicated in pathologies such as chronic pain and mood disorders have been characterized at several functional levels. We analyzed the activity of voltage-gated $Ca_V2.2\ Ca^{2+}$ channels responsible for the synaptic transmission of a pain signal to advance understanding of their regulation. We identified six new interaction partners of $Ca_V2.2\ Ca^{2+}$ channels, each having a unique modulatory role. Of these proteins, the transmembrane protein Grina/TMBIM3 is of greatest interest because its modulatory action is reminiscent of that of G-proteins activated by agonist binding to opioid receptors, i.e., it mimics modulation of the $Ca_V2.2$ channels by morphins.

The Grina/TMBIM3 pathway may represent an alternative to opioids for pain therapy (10.1016/j.ceca.2019.04.002), as the effectiveness of opioids is outweighed by their side effects. We have demonstrated that an agonist of delta opioid receptors enhanced hippocampal excitability and modulated voltage-dependent Na⁺, K⁺, and Ca²⁺ channels, and the observed changes may contribute to behavioral changes accompanying the use of these opioids (10.4149/gpb 2018009, 10.1007/s43440-020-00183-2). Pathophysiological changes in neuronal signaling have been characterized with in vivo electrophysiological analysis. We used the assessment of the excitability of individual neurons in vivo (10.3390/ijms222413626) as a tool for early preclinical testing of novel drugs for the treatment of central nervous system disorders.

In the heart, intracellular ion channels play a critical role in maintaining ion homeostasis as well as intracellular ion-based signaling. Ca2+ release from the sarcoplasmic reticulum (SR) mediated by ryanodine receptors (RYR2) is fundamental to cardiac contraction. In addition to RYR2 activation by cytosolic Ca²⁺ there is accumulating evidence for a regulatory role for luminal Ca²⁺ inside the SR lumen. The molecular identity of a luminal Ca2+ sensor is under debate because impairment of this regulatory pathway has been implicated in cardiac arrhythmias. To provide the first structural insight, we examined various functional aspects of RYR2 luminal regulation at the single-channel level, considering the strong function-structure relationship. In combination with bioinformatics, we suggest that two distinct luminal Ca²⁺ sites mediate RYR2 luminal regulation. One site, facing the lumen and having the potential EF-hand structure (10.1016/j.bioelechem.2016.01.002), regulates channel responsiveness to cytosolic ligands, while the other site, presumably positioned in the channel pore, governs how the channel opens and closes (10.1016/j.bioelechem.2019.107449). Impaired mitochondrial bioenergetics, also implicated in the genesis of cardiac arrhythmias, has been related to the dysfunction of mitochondrial chloride channels. To advance knowledge about their molecular composition we analyzed a gating (opening and closing) pattern that is highly likely to reflect a synchronized gating of four-channel subunits (10.1002/1873-3468.12721).

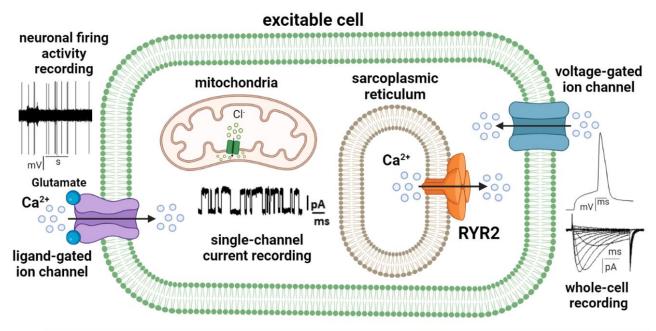


Fig. 2 Electrophysiological approaches employed to study the molecular basis of electrical signaling in excitable cells.

To monitor molecular interactions implicated in the regulation of ion channels, we are currently testing the quartz crystal microbalance method with the mass-based detection principle. This label-free method has been recently used for the development of biosensors based on sensing with DNA aptamers for detecting specific plasmalemma proteins (10.1007/s00216-017-0238-5) and for rapid and selective monitoring of hazardous contaminants in milk (10.1016/j.snb.2015.09.143, 10.1016/j.foodcont.2020.107774).

Phospholipid metabolism

Defects in phospholipid biosynthesis, transport, remodeling and turnover have a profound effect on cellular pathophysiology. In particular, some myopathies and neuropathies are the result of derailed metabolism in a typical mitochondrial phospholipid, cardiolipin (CL). We suggest that phosphatidylglycerol (PG), a CL precursor, performs some of the functions originally attributed to CL. In our work, we showed for the first time the coexistence of two separate pools of PG in the yeast *Saccharomyces cerevisiae*. One of the pools is controlled by the Pgc1 protein through an effective mechanism capable of fast, wide-ranging, and bidirectional PG regulation (10.1093/femsyr/foz045), while the second is used for direct CL synthesis. Deletion of *PGC1* leads to a nonspecific accumulation of PG with adverse effects on mitochondrial fusion and respiration (10.1016/j.bbabio.2015.10.004). We have studied phospholipid metabolism in another widely used yeast model, *Schizosaccharomyces pombe*. We showed that CL synthase is essential in this yeast, in contrast to *S. cerevisiae*, and that this enzyme is part of a fusion mitochondrial protein with a unique regulation (10.1016/j.bbalip.2018.06.019).

In addition to mitochondrial phospholipid metabolism, we explored lipid transfer proteins (LTPs) (10.1016/j.bbalip.2021.158990). These proteins are interesting not only from the point of understanding how lipids move between membranes but also from the point of development of new ways to combat infections caused by eukaryotic pathogens. In this respect, we have characterized Pdr17 (pleiotropic drug resistance protein 17), an LTP that, together with Pdr16, contributes to the resistance of yeast to azole antimycotics. We showed that Pdr17 binds sterol molecules as second ligands in addition to phosphatidylinositol (10.1016/j.bbalip.2019.07.005).

Neutral lipid metabolism and production of value-added lipids

Long-neglected organelles, lipid droplets (LDs), are currently comprehensively studied cellular compartments due to their involvement in various metabolic processes and intensive interactions with other cellular organelles. In addition to their involvement in energy storage, they provide important protection against excess lipid toxicity. We showed that accumulation of a specific sterol biosynthesis intermediate squalene results in lipotoxicity in cells without LDs. In a simple eukaryotic model organism, the yeast S. cerevisiae, we demonstrated that excessive accumulation of this ergosterol precursor compromised cellular membrane properties such as permeability and impaired maintenance of plasma membrane potential (10.1002/yea.3454). In wild-type cells, squalene lipotoxicity is prevented by its sequestration to LDs (10.1016/j.bbrc.2015.12.050). In addition, understanding squalene toxicity provides valuable knowledge for squalene production in microorganisms. Microorganisms have shown great promise in the production of value-added compounds. In collaboration with the University of Alberta, we have focused on the production of punicic acid (PuA). PuA is the main component of pomegranate seed oil. It is a conjugated linolenic acid with a wide range of nutraceutical effects, with the potential to reduce the incidence of a number of health disorders including diabetes, obesity, and cancer. We showed that metabolic engineering of PuA in the yeast S. pombe results in the production of PuA at the highest level reported to date for heterologous expression (10.1007/s00253-017-8498-8). By employing S. cerevisiae, we created an effective "push-pull" approach to increase PuA content (10.1021/acs.jafc.1c03256). In addition, we used yeast mutants to better understand the mechanism of the enrichment of flax seed oil with α-linolenic acid (10.1042/BCJ20170910), and we engineered long-chain acyl-CoA synthetase 9 variants with enhanced enzyme activity (10.1042/BCJ20180787). Our findings are important for future efforts to produce value-added lipids in recombinant oleaginous organisms.

Multidrug resistance of neoplastic cells

The real barrier against effective chemotherapy in malignancies is cellular resistance to a wide range of anticancer drugs (multidrug resistance - MDR). Overexpression of ABC family transporters, particularly ABCB1, ABCC1-3 and ABCG2, alone or in combination, leads to typical forms of MDR to defined groups of substances. These transporters effectively eliminate their substrates from cells

and may cooperate with enzymes oxidizing enzymes (such as cytochromes P450 – CYP) and conjugating enzymes (such as glutathione S-transferases – GST). For example, significant overexpression of CYP2J6 and GSTP1 has been detected in two sublines of mouse leukemic cells L1210 expressing the ABCB1 transporter compared with parental cells (10.3390/molecules25112517).

We further have highlighted the interplay between ABCB1-mediated MDR and the cellular response to poorly assembled protein accumulation and subsequent endoplasmic reticulum stress (ERS, 10.3390/molecules23020337). This association appears to be induced by significant overexpression of the GRP78/BiP protein in ABCB1-positive cells (10.3390/cells9040890). GRP78/BiP regulates the cellular response to ERS by binding to ER stress receptors (PERK, IRE1 and ATF6). When misfolded proteins accumulate in cells, GRP78/BiP binds them and detaches from PERK, IRE1, and ATF6, which begin to mediate the ER stress response. More GRP78/BiP in ABCB1-positive cells allows its simultaneous binding to misfolded proteins as well as ER stress receptors, leading to a less pronounced response to ERS. Interestingly, p21 (a CDK1 and 2 inhibitor) is expressed in ABCB1-positive cells from an alternative transcript variant, in contrast to ABCB1-negative cells, which express this protein from a common variant (10.3390/ijms22115504).

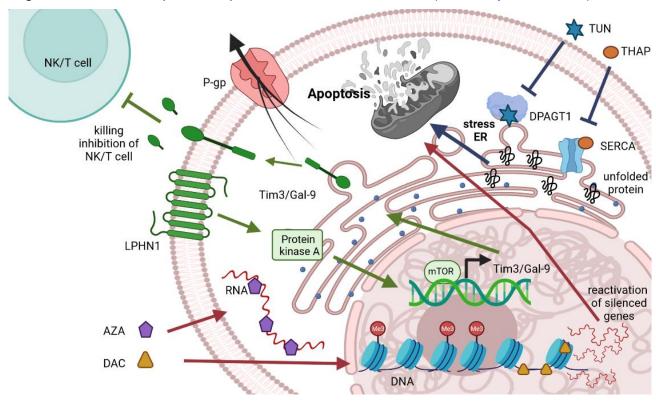


Fig. 3 Graphical summary of results. AZA and DAC are incorporated into DNA or RNA and induce methylation changes. Tunicamycin (TUN) or thapsigargin (THAP) causes the accumulation of unfolded proteins and ERS, leading to apoptosis. Latrophilin-1 (LPHN1) induces the expression/secretion of Tim-3/galectin-9, which protects cells from killing lymphocytes.

By adapting cells to vincristine, 5-azacytidine (AZA) and 2'-deoxy-5-azacytidine (DAC), we prepared variants of human leukemic SKM-1 and MOLM-13 cells resistant to these substances. Both vincristine-adapted variants express the ABCB1 transporter (10.4149/gpb 2018008), in contrast to cells adapted to AZA and DAC, in which expression of this transporter was not detected (10.3390/ijms22042076). We used AZA- and DAC-resistant cell variants of MOLM-13 to further characterize the development of resistance to DNA demethylation therapy.

The G protein-coupled plasma membrane receptor latrophilin 1, also known as the α -latrotoxin receptor, is specifically expressed in myeloid leukemia blasts but not in healthy white blood cells. We also confirmed this finding in SKM-1 and MOLM-13 cells as well as in samples from patients with

myelodysplastic syndrome (10.3390/cancers13143629). However, we have shown that latrophilin expression levels in myeloid blasts decrease when ABCB1 or ABCC1 expression is induced, even in patient samples. Latrophilin can activate a pathway that allows cells to escape the immune system through the expression and secretion of TIM-3 and galectin-9. In the case of galectin-9, we have shown that it occurs in AML cells in 8 protein isoforms that correspond to 8 mRNA splice variants, and their amount varies depending on the expression of ABCB1. We were the first to experimentally confirm all predicted Galectin 9 variants (10.3390/cancers13143629).

Chorioallantoic membrane - in vivo model for cancer diagnosis and treatment

Avian embryos can serve as a replacement for mammalian models in some research fields. A dense capillary network in the chorioallantoic membrane (CAM) is suitable for the study in various fields of biomedical research. Japanese quail (*Cotumix japonica*) ex ovo and turkey (*Meleagris gallopavo*) in ovo CAM models were used in our research (10.3390/biology10040301). Our studies focused on angiogenesis research as well as on the development of drug delivery systems and the use of photodynamically active drugs for cancer diagnosis and treatment. The photosensitizer hypericin, a natural substance extracted from the plant *Hypericum perforatum*, has shown promising results. In addition to its virucidal activity and antiproliferative and cytotoxic effects on tumor cells in the presence of light, hypericin also showed an antiangiogenic effect. Drug delivery was significantly improved using nanoparticles as a transport system for hydrophobic drugs such as hypericin (10.1016/j.pdpdt.2018.12.013).

Integrative Animal Physiology

Reproductive and Developmental Biology

Our research has focused on the study of gamete development, fertilization, and subsequent early embryonic development.

Identification of new proteins and molecular mechanisms required for faithful chromosome segregation

The duplication, organization, and maintenance of the genome is one of the most fundamental processes in reproduction and development. Meiosis is a specialized cell division that generates gametes (such as eggs and sperm) and the fission yeast *Schizosaccharomyces pombe* is one of the best model organisms for studying the regulatory mechanisms involved. We have used *S. pombe* to study yet uncharacterized proteins involved in cell division. To identify new proteins required for faithful meiotic chromosome segregation, we screened an *S. pombe* deletion mutant library. We have identified 25 new genes that have not yet been implicated in meiosis. The functional analysis of three of these proteins, Dbl2, Mal3, and Mto1, has been previously published (10.1371/journal.pgen.1006102, 10.4161/cc.26815). Our latest research reveals that repression of many genes requires interplay between DNA repair and the HIRA histone chaperone complex (10.1093/nar/gkab027). The HIRA complex is known to be involved in the regulation of gene expression and in activating the immune response against various types of viruses. Therefore, understanding the interconnection of DNA repair, gene expression, and the HIRA histone chaperone at the molecular level will have broad implications for the field of sexual reproduction and viral pathogenesis.

The role of tetraspanins in gamete development, maturation, and fertilization

Fertilization (fusion of male and female gametes) is well described in mammals; however, the involved molecules and their exact roles are not fully known. Therefore, the characterization of previously unidentified molecules is significant not only in terms of basic research in reproductive biology but also for understanding pathological changes at the molecular level.

Tetraspanins participate in many fundamental cellular processes. They are mostly known as organizers of molecular complexes, which form the tetraspanin web at specific sites of cell membranes, tetraspanin-enriched microdomains. To understand the mechanism of tetraspanin web action it is necessary to know the location and dynamics of its members during maturation and the mutual contact of gametes (10.1007/s00430-020-00676-0, 10.3390/ijms21207568). We described the presence and distribution of several tetraspanins (CD9, CD81, CD151) and other proteins in reproductive tissues, gametes, and embryos using cattle as the model organism (Fig. 4 A, B). Collaboration with the Laboratory of Reproductive Biology of the Institute of Biotechnology, Czech Academy of Sciences enabled us to perform comparative studies involving several species, including mice, pigs, and humans, that confirmed the species-specific expression of tetraspanins and their behavior (10.1530/REP-16-0304, 10.1016/j.ijbiomac.2018.11.161, 10.1038/s41598-020-61334-2, 10.3390/ijms19041236). These results suggest the existence of unique species-dependent mechanisms in mammalian reproduction.

The result of successful fertilization is the formation of a single-cell embryo (zygote), which further divides and differentiates into a stage called the blastocyst, which can implant into the uterine wall and continue further development. However, a damaged blastocyst will either fail to implant or will have impaired subsequent embryonic development, and some consequences of impaired preimplantation development may even affect the health of the offspring in adulthood. We have focused on the development of the preimplantation embryo in an altered maternal environment and the relevant molecular mechanisms involved in embryo-maternal communication.

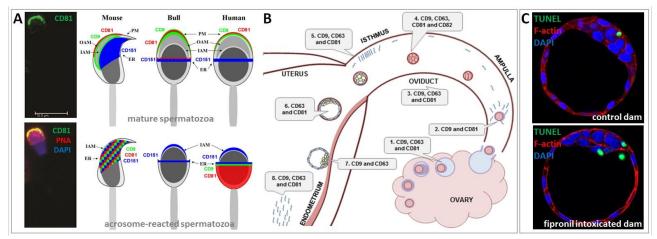


Fig. 4 Expression and localization of tetraspanins during maturation of sperm (A) and development of the early embryo (B); Illustrative microphotographs showing increased incidence of cell death in mouse blastocysts originating from dams exposed to insecticide (C).

Embryotoxic potential of selected insecticides

Despite their declared minimal danger to mammalian cells and organs, some insecticides can adversely affect the mammalian reproductive system. We analyzed the sensitivity of early embryonic cells (mouse and/or rabbit models were used) to three widely used types of insecticides (pyrethroids, neonicotinoids, and phenyl-pyrazoles) and found significant embryotoxic effects of these insecticides (Fig. 4 C). Interestingly, the presence of some secondary components of commercial preparations in the environment of developing embryos significantly increased the detrimental effect of their active components (10.1016/j.tox.2017.10.011, 10.1016/j.tox.2018.08.008, 10.1016/j.tiv.2019.03.009). Our results indicate that insecticides can negatively affect early pregnancy in pets, livestock and wild-living animals, which are frequently exposed to them either at high single doses (veterinary pest control) or at low doses repeated over a long time (consumption of vegetables, fruits or crops contaminated with residues).

Cell receptors in embryo-maternal communication

Stress and obesity are considered important reasons for the fertility decline in humans and animals. We investigated cell receptors potentially mediating the effects of maternal stress and obesity on the early embryo. Our results show that several glucocorticoid receptor (GR) subtypes are expressed in oocytes and preimplantation embryos and can mediate different effects of natural and synthetic glucocorticoids (corticosterone, an endogenous glucocorticoid elevated in stress, vs. dexamethasone, a synthetic glucocorticoid widely used for therapeutic purposes) on early embryonic development (10.1093/biolre/ioy196). In our research on the effects of adipose tissue cytokines on early embryos, we demonstrated that blastocysts express adiponectin receptors and glucose transporters that increase glucose uptake in adiponectin-stimulated embryos. These results suggest that adiponectin can maintain the glucose supply for early embryos under hypoinsulinemic conditions, for example, in mothers suffering from type 1 diabetes mellitus (10.1530/REP-19-0251). Our results, obtained using an intergenerational model of obesity, show that elevated body fat deposits in female mice negatively affect early embryonic development. Furthermore, the origin of embryos (from obese vs. control dams) significantly altered their overall metabolic activity in vitro, i.e., their metabolomic profile (10.1016/j.repbio.2016.02.002), and their response to leptin and insulin during development in vitro (10.3389/fendo.2017.00233, 10.1262/jrd.2020-096).

Neurobiology and Behavior

We applied a combination of molecular, electrophysiological, and behavioral methods to understand the pathophysiology of stress-related disorders, brain regeneration, learning, and behavior related to animal welfare.

Among **stress-related disorders**, depression and posttraumatic stress disorder are intensively studied. We found that the interactions between brain monoamines and between corticosteroids and monoamines in rodents are of particular importance in the pathophysiology of these disorders (10.1016/j.euroneuro.2020.12.002, 10.1007/s43440-022-00366-z).

Songbirds learn their vocalizations similarly to the way humans learn speech. During a study of **brain regeneration following injury**, we found that injury within the basal ganglia of the brain (responsible for song **learning**) causes increased expression of dopamine D3 receptors in the neurogenic zone. In turn, activation of D3 receptors leads to the acceleration of striatal regeneration (10.1016/j.neuroscience.2016.06.032). We began utilizing magnetic resonance imaging (MRI) of the songbird brain for longitudinal structural and functional studies, one of the few laboratories in the world to do so. We used the diffusion tensor imaging technique to track the changes in brain structure relative to the time after striatal injury. The analyses revealed the existence of a human-like cerebello-thalamic-basal ganglia pathway capable of modifying vocal motor output (Fig. 5, 10.1016/j.neuroimage.2018.07.010). Using between- and within-species comparisons we showed that the higher incorporation of newborn neurons in the adult brain is associated with plastic song and thus that neurogenesis might facilitate the variability of birdsong (10.1098/rspb.2018.2872).

The increasing societal concern over the **welfare of farm animals** is accompanied by fast growth in animal welfare science. In collaboration with the Norwegian School of Veterinary Science, we tested possible methods of environmental enrichment for broiler chickens to increase their level of activity and reduce leg problems (10.1016/j.applanim.2015.11.007). We validated the use of infrared cameras for the assessment of feather cover damage in laying hens and demonstrated greater feather damage in cages than in deep litter pens (10.1017/S1751731116001981). We studied the effects of different housing systems utilizing the interaction between cognition and emotions (judgment bias) in Japanese quail and laying hens (10.1016/j.applanim.2016.09.007, 10.1093/jas/skaa039). Together with Wageningen University, we showed that a high feather pecking line of laying hens manifested more optimistic judgment bias than hens of a low feather pecking line, which may reflect their higher impulsiveness (10.1016/j.applanim.2021.105305). We actively

participated in the work of two European networks (COST) focused on poultry welfare and published the results of the mapping of farm animal welfare research in an enlarged Europe (10.1007/s11192-017-2505-9).

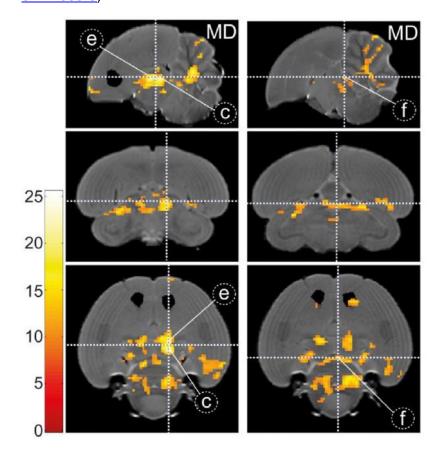


Fig. 5 MRI diffusion tensor imaging detects microstructural remodeling in the cerebello-thalamo-basal ganglia pathway.

Digestive Tract Physiology

Our research addresses nutritional modulation of digestive processes and gastrointestinal microbiota in animals to optimize gastrointestinal (GIT) functionality and health. The keynote of our research is "functional GIT – safe food – environment" (Fig. 6).

We investigated innovative methods to reduce the spread of antibiotic resistance genes among beneficial (and pathogenic or spoilage) microbiota of food-producing and companion animals. Our basic research is focused on the isolation and characterization of bacteriocin-producing beneficial bacteria and testing **natural compounds** with antimicrobial and antibiofilm activities. To develop therapeutic strategies to overcome **antibiotic resistance**, we also carry out applied research in which we investigate the applicability of substances we have identified in veterinary and human medicine. In addition, we investigated nutritional modulation of GIT functionality in monogastric animals and ruminants with endoparasites, and used alternative feed additives (phytogenic and mineral additives, biosurfactants, organic acids) to improve animal health (mineral and antioxidant status), performance and welfare to **reduce environmental pollution** (methane emissions, heavy metal pollution).

We screened, selected and characterized beneficial, bacteriocin-producing bacterial strains and their bacteriocins to maintain the healthy status of food-producing and companion animals (10.1016/j.lwt.2018.03.033; 10.1007/s00253-019-09847-3; 10.1007/s12223-019-00703-5). We also examined their application potential in the dairy industry for functional food production. Beneficial strains producing antimicrobial substances, such as bacteriocins (*E. mundtii* EM2/2, *E. durans* ED26E/7), were assessed as safe, and their use in dairy products prolonged their stability (10.3390/ijerph17249504). *Lactiplantibacillus plantarum* LP17L/1 and *Lactococcus lactis* MK1/3 (isolated from stored ewe cheese and raw goat milk) producing the enzyme β-galactosidase are

important for the production of dairy products intended for lactose-intolerant people and are in the process of being patented. These strains will be included in dairy starter cultures and/or as an additive in milk drinks produced in Slovakia. Moreover, a bacteriocin produced by *Lactiplantibacillus plantarum* LP17L/1 showed antilisterial and antistaphylococcal activity, and LP17L/1 significantly reduced larval migration of *Trichinella spiralis* (in mice infected with *T. spiralis*). The strains were assessed as safe according to EFSA rules; they were sequenced, documented in GenBank and deposited in the Czech Culture Collection-CCM.



Fig. 6 Multidisciplinary research optimizing the GIT health of animals and humans with respect to the environment.

We showed beneficial effects (broad antimicrobial spectrum, stimulation of phagocytic activity) of a new type of enterocin - Enterocin M (produced by *E. faecium* AL41=CCM 8558 strain, isolated and characterized in our laboratory) in horses, poultry, and broiler rabbits (10.1007/s12602-020-09655-6; 10.3390/ani10010115). Moreover, enterocins inhibited the growth of the human strain *Str. pneumoniae* and *Str. pyogenes* from otitis media, important for children when erythromycin therapy is not effective.

In other studies, we characterized antibiotic resistance and virulence factors of pathogenic *E. coli* (from food, wild, companion and food-producing animals) as potential sources of distribution of multidrug-resistant and virulent bacteria in the environment, posing a risk to human and animal health (10.3390/microorganisms9091808, 10.1080/03601234.2019.1608103). Looking for innovative strategies for combating multidrug-resistant bacterial biofilm-associated infections, we found that bone marrow mesenchymal stem cell conditioned media can control pathogenic bacteria through quorum sensing inhibitory compounds that block the bacterial communication system (10.3390/microorganisms8101478).

Exploring the usability of natural substances, we demonstrated the positive effects of selected medicinal plants (MPs) containing bioactive compounds on rumen metabolism and the microbial population of lambs in vitro and in vivo (10.17221/17/2016-CJAS, 10.1111/jpn.13349). Administration of MP and organic Zn helped to modulate the fermentation properties in lambs (10.1111/jpn.12940) but did not negatively affect trace mineral absorption in the GIT lambs and rabbits (10.3390/antiox9121172, 10.3389/fvets.2021.740658). A combination of both feed additives

(MP, Zn) in the diets of lambs infected with endoparasites showed strong anthelmintic activity (10.1186/s12917-018-1405-4) and attenuated the adverse effects of parasite infection by stimulating endogenous antioxidant defense systems. Phenolic compounds of plant additives improved the gut health of rabbits by stimulating the growth of beneficial bacteria and enterocytes in the small intestine and by preventing intestinal colonization by spoilage bacteria (doi.org/10.3390/ani11092595). Moreover, they improved the fatty acid profile and oxidative stability of meat in poultry and rabbits (10.1080/00071668.2019.1631445, 10.3390/ani10081248).

Our results show that MP feed supplementation help to slow the dynamics of endoparasitic infection in lambs (10.1016/j.smallrumres.2017.04.023, 10.1186/s12917-019-2050-2) and affect antioxidant parameters by reducing oxidative stress in the abomasal mucosa, thus helping to trigger local immune responses (10.3390/ani11020462). Adequate trace mineral supplementation is an effective way of reducing enteric methane from high-yielding dairy cows and lambs (10.3389/fvets.2021.630971; 10.1186/s12917-021-02984-w).

2. Partial indicators of main activities:

2.1. Research output

2.1.1. Principal types of research output of the institute: basic research/applied research, international/regional (in percentage)

Peer reviewed papers in impacted journals, monographs, chapters in monographs basic research/applied research - 98 % / 2 % international/regional - 98 % / 2 %

- 2.1.2 List of selected publications documenting the most important results of basic research. The total number of publications should not exceed the number of average FTE researchers per year. The principal research outputs (max. 10% of the total number of selected publications, including Digital Object Identifier DOI if available) should be underlined. Authors from the evaluated organizations should be underlined.
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2.1.3 List of monographs/books published abroad

none

2.1.4. List of monographs/books published in Slovakia

<u>STROMPFOVÁ, Viola</u> - <u>KUBAŠOVÁ, Ivana</u>. Mikrobiota čreva zvierat a spôsoby jej prospešnej modulácie. [Intestinal microbiota in animals and ways of its beneficial modulation] Rec. Radomíra Nemcová, Marcela Capcarová. Bratislava: VEDA, publisher SAS, 2020. 88 s. ISBN 978-80-224-1823-2

2.1.5. List of other scientific outputs specifically important for the institute, max. 10 items for institute with less than 50 average FTE researchers per year, 20 for institutes with 50 – 100 average FTE researchers per year and so on

FRAQUEZA, Maria Joao - PATARATA, L. - <u>LAUKOVÁ, Andrea</u>. Protective starter cultures and bacteriocins in fermented meats. In Fermented meat products: health aspects. - CRC Press Taylor a. Francis group, 2016, p. 228-269. ISBN 9781498733045. www.amazon.com/Fermented-meat-products-aspects-biology/dp/1498733042

<u>CAGALINEC, Michal</u>. Nanoparticles Targeting Mitochondria in Neurodegenerative Diseases: Toxicity and Challenge for Nanotherapeutics. In Nanomedicine and Neurosciences: Advantages, Limitations and Safety Aspects. - Sharjah: Bentham Science Publishers, 2017, chap. 2, p. 61-100. ISBN 978-1-68108-493-0. https://doi.org/10.2174/9781681084930117020005

ČERTÍK, Milan - KLEMPOVÁ, Tatiana - <u>JALČ, Dušan</u> - <u>VÁRADYOVÁ, Zora</u> - MARCINČÁK, Slavomír. Biotechnologically enriched cereals with PUFAs in ruminant and chicken nutrition. In AKOH, Casimir C. Food lipids - chemistry, nutrition, and biotechnology. - Boca Raton (FL): Taylor and Francis Group, LLC, 2017, p. 765-778. ISBN 978-1-4987-4485-0.

BÁBELOVÁ, Lenka - SLABÝ, Cyril - BIZIK, Jozef - RÁZUS, Martin - EBNER, Andreas - HIANIK, Tibor. Advances in diagnosis of leukemia by aptamer based biosensors. In Horizons in Cancer Research: Volume 77. - New York: Nova Science Publishers, Inc, 2020, p. 1-38. ISBN 978-1-53618-717-5.

2.1.6. List of patents, patent applications, and other intellectual property rights registered abroad

- In 2018 the environmental bacteriocin-producing strain Enterococcus faecium AL41 producing a new type of bacteriocin-enterocin M (isolated and characterized in the Laboratory of Animal Microbiology) was deposited into the Czech Culture Collection in Brno, Czech Republic (CCM), according to the Budapest treaty on the International Recognition of the Deposit of Microorganisms for the purposes of patent procedure under no. CCM8558.
- The autochthonous fecal probiotic strain Enterococcus faecium D7 (isolated from healthy dog) was deposited in DSMZ-Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (German Culture Collection) under the number DSM 32820
- In 2021 two strains were deposited as a component of the Utility model into the Czech Culture Collection in Brno, Czech Republic (CCM) according to the Budapest treaty on the International Recognition of the Deposit of Microorganisms for the purposes of patent procedure under no. CCM9208 for Lactiplantibacillus plantarum LP17L/1 and CCM 9209 for Lactococcus lactis MK1/3.
- The strains CCM 9208 Lactiplantibacillus plantarum (LP17L/1) and CCM 9209 Lactococcus lactis MK1/3 were sequenced and their nucleotide sequences were registered in the GenBank under the accession numbers SUB11246785 Seq ON114094 and SUB11246790 Seq1 ON114093, respectively.
- Enterococcus faecium EF34E5 isolated from the traditional Slovak dairy drink (ewes fermented milk žinčica was requested for deposition in the Czech Culture Collection in Brno CCM under the number CCM 8969, www.sci.muni.cz/ccm

2.1.7. List of patents, patent applications, and other intellectual property rights registered in Slovakia

Utility model:

Title of Utility model:

Strains of lactic acid bacteria

Lactococcus lactis subsp. lactis MK1/3 (CCM 9209), Lactiplantibacillus plantarum LP 17L/1 (CCM 9208),

use of indicated strains, way of fermented goat milk production, a product manufactured in this

Number of UM: PUV50094-2021

Date of submission: 14.12.2021

Property/co-property of UM: Centre of Biosciences of the Slovak Academy of Sciences,

Košice

Authors of UM: Lauková Andrea, Kološta Miroslav

2.1.8. Narrative on the most important research outputs of the institute – especially focused on their importance for society (3-5 pages)

Cell Biology

Multidrug resistance of leukemia cells

In addition to investigating the mechanisms responsible for the reduced sensitivity of leukemia cells to antileukemic chemotherapy, the MDR research team is focused on finding and describing the cytotoxic effects of various natural, semisynthetic and synthetic substances, as well as environmental pollutants, on leukemia cells in the context of MDR development. During the reporting period, we investigated and published the effects of the following substances:

- plant alkaloids derived from cryptopleurin (10.3390/molecules24112127)
- plant aliphatic isothiocyanates (10.3390/molecules25092093)
- organotin derivatives (10.3390/molecules23051053)
- tunicamycin as an endoplasmic reticulum (ER) stressor (10.3390/cells9040890)
- bortezomib as a proteasome inhibitor (10.3390/ijms22115504)

Although such results are not directly applied in socially significant directions, they may provide an impetus for state and nonstate medical treatment facilities to supplement treatment protocols. Our following experience may serve as an example. We previously demonstrated and published that pentoxifylline and its derivatives can reverse drug resistance provided by the ABCB1 transporter. We published our last paper on this topic in 2012 (10.3390/ijms13010369). This work inspired Dr. Daniel Thomas and his colleagues at Healthy and Strong (344 S. Highland St., Mount Dora, FL 32757, USA) to create the "Comprehensive and potent cancer treatment protocol", which among other things uses pentoxifylline to promote chemosensitivity and chemoprotection and inhibit multidrug resistance, with reference to our work

(https://www.healthyandstrong.com/our-approach/)

Neutral lipid metabolism and production of value-added lipids in microorganisms

Many lipidic substances have been shown to have positive effects on human health and are often used as food supplements. Among these, **squalene and punicic acid** are two lipids we intensively investigated. **In addition to the food industry, they have vast applications in cosmetics and pharmaceuticals (e.g., squalene as a vaccine adjuvant).** Previously, we designed *S. cerevisiae* and *Kluyveromyces lactis* yeast strains for high production of squalene (10.1111/1567-1364.12107, 10.1111/lam.12425). To further enhance its production, we studied the lipotoxicity of squalene, a biotechnologically relevant issue (10.1016/j.bbrc.2015.12.050). Similarly, we created an effective "push-pull" approach to increase punicic acid content in yeast (10.1021/acs.jafc.1c03256) and described the lipotoxic effect of punicic acid on dividing cells (10.1007/s00253-017-8498-8). **Microorganisms are promising sources of high-value lipids, thus protecting natural sources.** This is substantial advantage, for instance, in the case of squalene, for which the main source is deep-sea shark livers.

Integrative Animal Physiology

Reproductive and Developmental Biology

Lifestyle disorders such as obesity and stress are thought to be one of the causes of declining fertility in humans, and these factors can negatively influence reproductive performance in animals. To investigate the possible impact of maternal obesity on the "metabolic programming" of germ cells, early embryos obtained from control and obese female mice (using an intergenerational model of obesity) were exposed to insulin in vitro. Insulin usually acts as a beneficial proliferation-stimulating and anti-apoptotic factor. However, contrary to effects seen in the control embryos, the presence of insulin in the culture medium had no effect on cell numbers, cell differentiation, or apoptosis rates in blastocysts developed from embryos originating

from obese dams. The lower sensitivity of such embryos suggests that they show some kind of "insulin resistance". In untreated blastocysts isolated from obese dams an increased amount of insulin receptor (Insr) and facilitated glucose transporter 4 (Slc2a4, GLUT4) transcripts were recorded, indicating activation of a compensatory mechanism for impaired signaling from insulin receptors in embryonic cells originating from obese individuals (10.3389/fendo.2017.00233, 10.1262/jrd.2020-096). In accordance with the developmental origin of health and disease theory, a lowered insulin sensitivity in early conceptus might have long-term consequences and negatively impact the health of the offspring.

To investigate the molecular mechanisms involved in the effects of maternal stress on early embryos, we analyzed glucocorticoid receptor (GR) expression and activity in mouse preimplantation embryos. GR can bind endogenous glucocorticoids (such as corticosterone and cortisol) released during the stress response or therapeutically administered glucocorticoids (such as dexamethasone, widely used in human and veterinary medicine). Our results show that GRa and GRy transcripts are relatively highly expressed in mouse oocytes, and both transcripts are present in lower amounts in preimplantation embryos. We also detected low expression of two other splice variants, GRβ and a transcript orthologous to the human GR-P subtype, mainly at the blastocyst stage. Using western blot analysis, we detected several GR protein bands that differed in size between oocytes and preimplantation embryos. To compare the effects of corticosterone and dexamethasone on early embryos, we cultured mouse preimplantation embryos in the presence of these glucocorticoids. Corticosterone showed a strong inhibitory effect on embryo development, without a significant influence on apoptosis incidence. On the other hand, dexamethasone induced apoptosis in early embryo cells, and its effect on embryo development was less detrimental than that found with the same dose of corticosterone. In summary, our results showed that different GR subtypes are expressed in mouse oocytes and preimplantation embryos and that their activation can significantly impair early embryonic development. Moreover, we found significant differences in the effects of the two glucocorticoids on early embryonic development, which might be associated with the activation of different GR subtypes (10.1093/biolre/iov196).

Although many factors are known to cause infertility or fertility disorders in humans and animals, such as hormonal diseases, obesity, and urogenital infections, the molecular background is largely unknown. For successful fertilization the correct molecular arrangement of the gametes that is configured during their development and maturation is critical. Here, we studied gamete membrane proteins as potential markers for fertility/infertility. Since there are ethical limitations on research with human gametes, at least for eggs, and because human biological material is difficult to obtain, the use of animal models such as cattle in our case appears to be advantageous. Our research has preferentially focused on studying the tetraspanin family proteins and their partners in cattle. In addition, we have performed cross-species comparative studies addressing species-specific expression patterns of tetraspanins (CD9, CD81, and CD151) and their partners in gametes and reproductive tissues of pigs, humans, and) mice (10.1530/REP-16-0304. 10.1016/j.ijbiomac.2018.11.161, 10.3390/ijms19041236, 10.1038/s41598-020-61334-2. We have also described the presence of estrogen receptors in bovine testicular and epididymal tissues and sperm (10.3390/cells9010183), important for understanding the negative effect of environmental estrogens (endocrine disruptors) on processes leading to fertilization. The results obtained on the expression, dynamics, and role of the molecular complexes on gametes and tissues of the reproductive tract during the decisive events related to fertilization not only contribute to the understanding of these processes in mammals but could also help to identify novel male and female fertility/infertility markers that could be applied in reproductive biotechnologies in animal husbandry and potentially in assisted reproductive technologies in humans.

Neurobiology and Behavior

Only three groups of mammals (humans, cetaceans (whales and dolphins), and bats) and three groups of birds (parrots, hummingbirds, and songbirds) learn to vocalize. Human speech is undoubtedly much more complex than the song of songbirds. Nevertheless, they show remarkable parallels on the neural level (brain anatomy, connectivity), gene expression, and behavior (learning based on auditory feedback). Similar to human speech, bird song is controlled by several pathways, including a cortico-basal ganglia-thalamo-cortical (C-BG-T-C) loop. Neurotoxic disengagement of the basal ganglia component, i.e., Area X, induces long-term changes in song performance, while most of the lesioned area regenerates within the first months. Importantly, however, the timing and spatial extent of structural neuroplastic events potentially affecting other constituents of the C-BG-T-C loop is not clear. We designed a longitudinal MRI study in which changes in brain structure were evaluated relative to the time after neurotoxic lesioning or to vocal performance. By acquiring both diffusion tensor imaging and 3-dimensional anatomical scans we were able to track alterations in intrinsic tissue properties and local volume. We described structural remodeling remote to the lesion, i.e., in the thalamus and, surprisingly, the cerebellum, both peaking within the first two months after lesioning Area X. Correlations between song performance and MRI parameters uncover intriguing brain-behavior relationships in several brain areas pertaining to the C-BG-T-C loop supervising vocal motor control. Our results clearly point to structural neuroplasticity in the cerebellum induced by basal ganglia (striatal) damage and may point to the existence of a human-like cerebello-thalamiccapable basal ganglia pathway modifying vocal output of motor (10.1016/j.neuroimage.2018.07.010).

Our Centre has unique position within the institutions belonging to the Slovak Academy of Sciences since two of our organizational units are running **approved animal facilities**, enabling us to perform **basic research on farm animal species** (poultry, sheep). This includes research on **farm animal physiology**, **behavior and welfare**.

We participated in the mapping of farm animal welfare science in an enlarged Europe (10.1007/s11192-017-2505-9). Based on questionnaires sent out to a wide researcher network in regions of an enlarged Europe, we found differences with regard to 'input factors' such as human resources, animal and laboratory facilities and national and international research funding and 'output factors' such as inter/national collaboration, participation in EU-funded projects related to farm animal welfare and the number of publications. A pronounced difference was found in funding, as 35% of respondents in the Eastern EU region stated that they lack funded farm animal welfare projects compared to 4% in the Western EU region. In general, respondents from the Western EU region were significantly more involved in EU-funded schemes such as the EU framework programs or ERA-NET, and there was an association between the scientific output in this field and economic ranking.

Stimulation of foraging behavior during the first weeks of life by **increasing environmental complexity** may represent a way to prevent leg disorders, reduce fear, and, in general, **improve the welfare of broiler chickens**. We found that various forms of food-related enrichment such as the scattering of whole wheat or wood shavings did not increase the locomotor or foraging activity of broilers. Interestingly, the **scattering of mealworms in the litter**, considered a highly valued food by broilers, **increased activity levels**. However, the effect was only transient. To prolong the effects of food-based enrichment, more frequent feeding with smaller amounts would be necessary, as well as the development of specific feeding systems for distribution under practical conditions (10.1016/j.applanim.2015.11.007).

Plumage damage represents one of the **animal-based measures of laying hen welfare**. Damage occurs predominantly due to age, the environment and damaging pecking. Due to its noninvasiveness, objectivity and repeatability, infrared thermography is a promising alternative to feather damage scoring systems such as the system included in the Welfare Quality^R assessment

protocol for poultry. Feather scoring revealed higher damage in enriched cages than in deep litter pens. The **infrared thermography assessment of feather damage** revealed differences between hens kept in different housing systems in agreement with feather scoring. It was demonstrated that infrared thermography is a useful tool for the assessment of poultry feather cover quality that is **not biased by the subjective component** and provides a higher precision than feather damage scoring (10.1017/S1751731116001981).

Digestive Tract Physiology

Disruption of intestinal microbiota equilibrium (dysbiosis) and the immune system play crucial roles in the majority of currently diagnosed medical conditions in dogs. Improving gut health through the use of probiotic microorganisms has become an area of research activity in both human and animal nutrition. The present review evaluates and compares the effects achieved after application of the canine-derived strain Lactobacillus fermentum CCM 7421 (selected in our laboratory) to healthy dogs as well as to dogs suffering from gastrointestinal disorders. The experiments involved varying durations of application (4 days-14 days), dosages (107-109 CFU), forms of application (fresh culture or lyophilized) or combinations with natural substances (chlorophyl, alginite, Eleutherococcus senticosus, inulin). The results from nine independent studies show the ability of probiotic strains to establish themselves in the canine gastrointestinal tract, alter the composition of intestinal microbiota (increase of lactic acid bacteria, decrease of coliforms, clostridia) and metabolites (organic acids), and modulate the physiology (serum biochemical parameters) and immunity parameters (stimulation of cellular immunity parameters) in dogs. Almost all observed effects were irrespective of the dose or duration of probiotic administration. Among the combinations used with natural substances, the addition of chlorophyll at a dose of 60 mg/dog to a probiotic strain showed the best effects in relation to microbiota modulation and stimulation of immunity (doi: 10.1007/s00253-017-8425-z).

Trace elements are integral components of various antioxidant enzymes and play an essential role as components of antioxidant defense against free radical-induced tissue damage. Selenium is an essential trace element in animal nutrition required for multiple actions related to health, performance and disease prevention. The main biological form of Se is represented by the amino acid selenocysteine, which is an integral component of the active sites of specific selenoproteins responsible for the biological effects of this trace element. Glutathione peroxidase (GPx) and thioredoxin reductase are the most abundant antioxidant selenoenzymes protecting cells from oxidative damage. Dietary selenium supplementation at a level of 0.4 mg Se/kg DM is an effective means of increasing selenium levels in the blood and tissues of sheep. Furthermore, our results confirm the beneficial effect of long-term Se supplementation on the parameters of antioxidant status and innate immunity in sheep. The presented findings suggest that selenium, whether from organic or inorganic dietary sources, can be accumulated in the bacterial and protozoal fractions of rumen content and subsequently increases the GPx activity in rumen microbiota (https://doi.org/10.1007/s12011-016-0794-0).

2.1.9. Table of research outputs

Papers from international collaborations in large-scale scientific projects (Dwarf team, ALICE Collaboration, ATLAS collaboration, CD Collaboration, H1 Collaboration, HADES Collaboration, and STAR Collaboration) have to be listed separately

		2016	ina S i		2017		,	2018			2019			2020			2021		total			
Scientific publications	number	No. / FTE researches	No. / one million total salary budget	number	No. / FTE researches	No. / one million total salary budget	number	No. / FTE researches	No. / one million total salary budget	number	No. / FTE researches	No. / one million total salary budget	number	No. / FTE researches	No. / one million total salary budget	number	No. / FTE researches	No. /1 million total salary budget	number	averaged number per year	av. No. / FTE researches	av. No. / one million total salary budget
Scientific monographs and monographic studies in journals and proceedings published abroad (AAA, ABA)	0	0,000	0,000	0	0,000	0,000	0	0,000	0,000	0	0,000	0,000	0	0,000	0,000	0	0,000	0,000	0	0,000	0,000	0,000
Scientific monographs and monographic studies in journals and proceedings published in Slovakia (AAB, ABB)	0	0,000	0,000	0	0,000	0,000	0	0,000	0,000	0	0,000	0,000	1	0,014	0,425	0	0,000	0,000	1	0,167	0,002	0,079
Chapters in scientific monographs published abroad (ABC)	2	0,030	1,077	2	0,025	1,010	1	0,013	0,517	0	0,000	0,000	1	0,014	0,425	0	0,000	0,000	6	1,000	0,014	0,477
Chapters in scientific monographs published in Slovakia (ABD)	0	0,000	0,000	0	0,000	0,000	0	0,000	0,000	0	0,000	0,000	0	0,000	0,000	0	0,000	0,000	0	0,000	0,000	0,000
Scientific papers published in journals registered in Current Contents Connect (ADCA, ADCB, ADDA, ADDB)	48	0,717	25,848	46	0,578	23,221	49	0,643	25,349	46	0,667	21,729	46	0,641	19,550	50	0,662	21,358	285	47,500	0,649	22,651
Scientific papers published in journals registered in Web of Science Core Collection and SCOPUS not listed above (ADMA, ADMB, ADNA, ADNB)	14	0,209	7,539	15	0,189	7,572	16	0,210	8,277	14	0,203	6,613	23	0,320	9,775	17	0,225	7,262	99	16,500	0,226	7,868
Scientific papers published in other foreign journals (not listed above) (ADEA, ADEB)	2	0,030	1,077	1	0,013	0,505	2	0,026	1,035	0	0,000	0,000	4	0,056	1,700	1	0,013	0,427	10	1,667	0,023	0,795
Scientific papers published in other domestic journals (not listed above) (ADFA, ADFB)	10	0,149	5,385	6	0,075	3,029	2	0,026	1,035	5	0,073	2,362	5	0,070	2,125	7	0,093	2,990	35	5,833	0,080	2,782
Scientific papers published in foreign peer- reviewed proceedings (AECA)	0	0,000	0,000	0	0,000	0,000	0	0,000	0,000	1	0,015	0,472	1	0,014	0,425	0	0,000	0,000	2	0,333	0,005	0,159
Scientific papers published in domestic peer- reviewed proceedings (AEDA)	1	0,015	0,539	2	0,025	1,010	1	0,013	0,517	1	0,015	0,472	0	0,000	0,000	0	0,000	0,000	5	0,833	0,011	0,397
Published papers (full text) from foreign scientific conferences (AFA, AFC)	13	0,194	7,001	1	0,013	0,505	5	0,066	2,587	4	0,058	1,889	2	0,028	0,850	0	0,000	0,000	25	4,167	0,057	1,987
Published papers (full text) from domestic scientific conferences (AFB, AFD)	23	0,344	12,386	15	0,189	7,572	40	0,525	20,693	23	0,334	10,864	28	0,390	11,900	25	0,331	10,679	154	25,667	0,351	12,240

2.2. Measures of research outputs (citations, etc.)

2.2.1. Table with citations per annum (without self-citations)

Citations of papers from international collaborations in large-scale scientific projects (Dwarf team, ALICE Collaboration, ATLAS collaboration, CD Collaboration, H1 Collaboration, HADES Collaboration, and STAR Collaboration) are listed separately

	2015		2016		2017		2018		2019		2020		total		
Citations, reviews	number	No. / FTE researchers	number	No. / FTE researchers	unuper	averaged number per year	av. No. / FTE researchers								
Citations in Web of Science Core Collection (1.1, 2.1)	1 109	16,57	1 165	14,64	1 338	17,55	1 325	19,21	1 394	19,41	1 672	22,14	8 003	1 333,83	18,23
Citations in SCOPUS (1.2, 2.2) if not listed above	264	3,94	229	2,88	163	2,14	163	2,36	110	1,53	135	1,79	1 064	177,33	2,42
Citations in other citation indexes and databases (not listed above) (3.2,4.2)	0	0,00	0	0,00	2	0,03	0	0,00	3	0,04	2	0,03	7	1,17	0,02
Other citations (not listed above) (3.1, 4.1)	35	0,52	17	0,21	15	0,20	24	0,35	22	0,31	1	0,01	114	19,00	0,26
Reviews (5,6)	0	0,00	0	0,00	0	0,00	0	0,00	0	0,00	0	0,00	0	0,00	0,00

- 2.2.2. List of 10 most-cited publications published any time with the address of the institute, with number of citations in the assessment period (2015 2020)
- 1. BEOPOULOS, A. MRÓZOVÁ, Zuzana THEVENIEAU, F. LE DALL, M.T. HAPALA, Ivan PAPANIKOAOU, S. CHARDOT, S. NICAUD, J.M. Control of Lipid Accumulation in the Yeast Yarrowia lipolytica. In *Applied and Environmental Microbiology*, 2008, vol. 74, no. 24, p. 7779-7789. (2007: 4.004 IF, Q1 JCR, 2.036 SJR, Q1 SJR, karentované CCC). (2008 Current Contents). ISSN 0099-2240, 10.1128/AEM.01412-08. Times cited: 138
- ČIKOŠ, Štefan BUKOVSKÁ, Alexandra KOPPEL, Juraj. Relative quantification of mRNA: comparison of methods currently used for real-time PCR data analysis. In BMC Molecular Biology [elektronický zdroj], 2007, vol.8, art. no.113. ISSN 1471-2199 (Electronic). 10.1186/1471-2199-8-113. Times cited: 127
- CASTILLO, Gabriela SPINELLA, Katia POTURNAYOVÁ, Alexandra ŠNEJDÁRKOVÁ, Maja MOSIELLO, Lucia HIANIK, Tibor. Detection of aflatoxin B-1 by aptamer-based biosensor using PAMAM dendrimers as immobilization platform. In Food Control, 2015, vol. 52, no., p. 9-18. (2014: 2.806 IF, Q1 JCR, 1.380 SJR, Q1 SJR, karentované CCC). (2015 Current Contents). ISSN 0956-7135, 10.1016/j.foodcont.2014.12.008. Times cited: 86
- 4. <u>BILČÍK, Boris</u> KEELING, Linda J. Changes in feather condition in relation to feather pecking and aggressive behaviour in laying hens. In *British Poultry Science*, 1999, vol. 40, no. 4, p. 444–451. ISSN 0007-1668, <u>10.1080/00071669987188</u>. **Times cited: 79**
- 5. BREIER, Albert GIBALOVÁ, Lenka ŠEREŠ, Mário BARANČÍK, Miroslav SULOVÁ, Zdena. New Insight into P-Glycoprotein as a Drug Target. In Anti-cancer Agents in Medicinal Chemistry, 2013, vol.13, no. 1., p. 159-170. (2012: 2.610 IF, Q2 JCR, 1.027 SJR, Q2 SJR). ISSN 1871-5206, 10.2174/187152013804487380. Times cited: 76
- 6. PLACHÁ, Iveta TAKÁČOVÁ, Jana RYZNER, Miroslav ČOBANOVÁ, Klaudia LAUKOVÁ, Andrea STROMPFOVÁ, Viola VENGLOVSKÁ, K. FAIX, Štefan. Effect of thyme essential oil and selenium on intestine integrity and antioxidant status of broilers. In British Poultry Science, 2014, vol. 55 no.1, p. 105-114. (2013: 0.782 IF, Q3 JCR, 0.551 SJR, karentované CCC). (2014 Current Contents). ISSN 0007-1668, 10.1080/00071668.2013.873772. Times cited: 62
- 7. RAJMAN, Marek JURÁNI, Marián LAMOŠOVÁ, Dalma MÁČAJOVÁ, Mariana SEDLAČKOVÁ, Monika KOŠŤÁL, Ľubor JEŽOVÁ, Daniela VÝBOH, Pavel. The effects of feed restriction on plasma biochemistry in growing meat type chickens (Gallus gallus). In Comparative biochemistry and physiology: Part A. Comparative physiology, 2006, vol. 145, no. 3, p. 363-371. (2005: 1.351 IF, Q2 JCR, 0.666 SJR, Q3 SJR). ISSN 1095-6433, 10.1016/j.cbpa.2006.07.004. Times cited: 44
- BARANČÍK, Miroslav <u>BOHÁČOVÁ, Viera</u> KVACKAJOVA, J. <u>HUDECOVÁ, Soňa</u> <u>KRIŽANOVÁ, Oľga BREIER, Albert</u>. SB203580, a specific inhibitor of p38-MAPK pathway, is a new reversal agent of P-glycoprotein-mediated multidrug resistance. In *European Journal of Pharmaceutical Sciences*, 2001, vol. 14, no. 1, p. 29-36. (2000: 1.212 IF). ISSN 0928-0987, 10.1016/S0928-0987(01)00139-7. Times cited: 43
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- KUBÍKOVÁ, L'ubica WADA, Kazuhiro JARVIS, Erich D. Dopamine receptors in a songbird brain. In *Journal of Comparative Neurology*, 2010, vol. 518, no. 6, p. 741-769. (2009: 3.718 -IF, Q2 - JCR, 2.970 - SJR, Q1 - SJR, karentované - CCC). (2010 - Current Contents). ISSN 0021-9967, 10.1002/cne.22255. Times cited: 37

- 2.2.3. List of 10 most-cited publications published any time with the address of the institute, with number of citations obtained until 2020
- ČIKOŠ, Štefan BUKOVSKÁ, Alexandra KOPPEL, Juraj. Relative quantification of mRNA: comparison of methods currently used for real-time PCR data analysis. In BMC Molecular Biology [elektronický zdroj], 2007, vol.8, art. no.113. ISSN 1471-2199 (Electronic). 10.1186/1471-2199-8-113. Times cited: 254
- MARX, S. O. <u>ONDRIAŠ, Karol</u> MARKS, A. R. Coupled gating between individual skeletal muscle Ca2+ release channels (ryanodine receptors). In *Science*, 1998, vol. 281, issue 5378, p. 818-821. (1997: 24.676 IF, Current Contents CCC). (1998 Current Contents). ISSN 0036-8075, 10.1126/science.281.5378.818. Times cited: 239
- 3. BEOPOULOS, A. MRÓZOVÁ, Zuzana THEVENIEAU, F. LE DALL, M.T. HAPALA, Ivan PAPANIKOAOU, S. CHARDOT, S. NICAUD, J.M. Control of Lipid Accumulation in the Yeast Yarrowia lipolytica. In *Applied and Environmental Microbiology*, 2008, vol. 74, no. 24, p. 7779-7789. (2007: 4.004 IF, Q1 JCR, 2.036 SJR, Q1 SJR, karentované CCC). (2008 Current Contents). ISSN 0099-2240, 10.1128/AEM.01412-08. Times cited: 209
- 4. <u>BILČÍK, Boris</u> KEELING, Linda J. Changes in feather condition in relation to feather pecking and aggressive behaviour in laying hens. In *British Poultry Science*, 1999, vol. 40, no. 4, p. 444–451. ISSN 0007-1668, 10.1080/00071669987188. **Times cited: 171**
- 5. <u>LACINOVÁ, L'ubica</u>. Voltage-dependent calcium channels. In *General Physiology and Biophysics*, 2005, vol. 24, suppl., p. 1-78. (2004: 0.694 IF, Current Contents CCC). (2005 Current Contents). ISSN 0231-5882. **Times cited: 124**
- BREIER, Albert GIBALOVÁ, Lenka ŠEREŠ, Mário BARANČÍK, Miroslav SULOVÁ, Zdena. New Insight into P-Glycoprotein as a Drug Target. In Anti-cancer Agents in Medicinal Chemistry, 2013, vol.13, no. 1., p. 159-170. (2012: 2.610 IF, Q2 JCR, 1.027 SJR, Q2 SJR). ISSN 1871-5206, 10.2174/187152013804487380. Times cited: 104
- BILČÍK, Boris KEELING, Linda J. Relationship between feather pecking and ground pecking in laying hens and the effect of group size. In *Applied animal behaviour science*. - Amsterdam, Netherlands: Elsevier, 2000, vol. 68, no. 1, p. 55–66. ISSN 0168-1591, 10.1016/S0168-1591(00)00089-7. Times cited: 96
- 8. <u>FABIAN, Dušan</u> SABOL, M. <u>HOROSOVÁ, Katarína</u> <u>BUJŇÁKOVÁ, Dobroslava</u>. Essential oils-their antimicrobial activity against Escherichia coli and effect on intestinal cell viability. In *Toxicology in vitro*, 2006, vol. 20, no. 8, p. 1435-1445. (2005: 1.754 IF, Q2 JCR, 0.644 SJR, Q1 SJR). ISSN 0887-2333, 10.1016/j.tiv.2006.06.012. **Times cited: 95**
- BARANČÍK, Miroslav <u>BOHÁČOVÁ, Viera</u> KVACKAJOVA, J. <u>HUDECOVÁ, Soňa KRIŽANOVÁ, Oľga BREIER, Albert</u>. SB203580, a specific inhibitor of p38-MAPK pathway, is a new reversal agent of P-glycoprotein-mediated multidrug resistance. In *European Journal of Pharmaceutical Sciences*, 2001, vol. 14, no. 1, p. 29-36. (2000: 1.212 IF). ISSN 0928-0987, 10.1016/S0928-0987(01)00139-7. Times cited: 92
- CASTILLO, Gabriela SPINELLA, Katia POTURNAYOVÁ, Alexandra ŠNEJDÁRKOVÁ, Maja MOSIELLO, Lucia HIANIK, Tibor. Detection of aflatoxin B-1 by aptamer-based biosensor using PAMAM dendrimers as immobilization platform. In Food Control, 2015, vol. 52, no., p. 9-18. (2014: 2.806 IF, Q1 JCR, 1.380 SJR, Q1 SJR, karentované CCC). (2015 Current Contents). ISSN 0956-7135, 10.1016/j.foodcont.2014.12.008. Times cited: 86

- 2.2.4. List of 10 most-cited publications published <u>during</u> the evaluation period (2016-2021) with the address of the Institute, with number of citations obtained until 2021
- ELEFANTOVÁ, Katarína LAKATOŠ, Boris KUBÍČKOVÁ, Jana <u>SULOVÁ, Zdena BREIER, Albert</u>. Detection of the Mitochondrial Membrane Potential by the Cationic Dye JC-1 in L1210 Cells with Massive Overexpression of the Plasma Membrane ABCB1 Drug Transporter. In *International Journal of Molecular Sciences*, 2018, vol. 19, art. no. 1985. (2017: 3.687 IF, Q2 JCR, 1.260 SJR, Q1 SJR, Current Contents CCC). (2018 Current Contents). ISSN 1422-0067, 10.3390/ijms19071985. Times cited: 32
- <u>ČOBANOVÁ, Klaudia</u> <u>FAIX, Štefan</u> <u>PLACHÁ, Iveta</u> <u>MIHALIKOVÁ, Katarína</u> <u>VÁRADYOVÁ, Zora</u> <u>KIŠIDAYOVÁ, Svetlana</u> <u>GREŠÁKOVÁ, Ľubomíra</u>. Effects of Different Dietary Selenium Sources on Antioxidant Status and Blood Phagocytic Activity in Sheep. In *Biological Trace Element Research*, 2017, vol. 175, no. 2, p. 339-346. (2016: 2.399 IF, Q3 JCR, 0.662 SJR, Q2 SJR, Current Contents CCC). (2017 Current Contents). ISSN 0163-4984, 10.1007/s12011-016-0794-0. Times cited: 26
- VALACHOVIČ, Martin GARAIOVÁ, Martina HOLIČ, Roman HAPALA, Ivan. Squalene is lipotoxic to yeast cells defective in lipid droplet biogenesis. In Biochemical and biophysical research communications, 2016, vol. 469, p. 1123-8. (2015: 2.371 IF, Q2 JCR, 1.180 SJR, Q1 SJR, Current Contents CCC). (2016 Current Contents). ISSN 0006-291X, 10.1016/j.bbrc.2015.12.050. Times cited: 24
- 4. SEDLAKOVA-KADUKOVA, J. KOPČÁKOVÁ, Anna GREŠÁKOVÁ, L'ubomíra GODANY, A. PRISTAŠ, Peter. Bioaccumulation and biosorption of zinc by a novel Streptomyces K11 strain isolated from highly alkaline aluminium brown mud disposal site. In Ecotoxicology and environmental safety, 2019, vol. 167, p. 204-211. (2018: 4.527 IF, Q1 JCR, 1.174 SJR, Q1 SJR, karentované CCC). (2019 Current Contents, WOS, SCOPUS). ISSN 0147-6513, 10.1016/j.ecoenv.2018.09.123. Times cited: 24
- HANO, Milan TOMÁŠOVÁ, Lenka ŠEREŠ, Mário PAVLÍKOVÁ, Lucia BREIER, Albert SULOVÁ, Zdena. Interplay between P-glycoprotein expression and resistance to endoplasmic reticulum stressors. In Molecules, 2018, vol. 23, no. 2, p. 337-357. (2017: 3.098 IF, Q2 JCR, 0.855 SJR, Q1 SJR, Current Contents CCC). (2018 Current Contents). ISSN 1420-3049, 10.3390/molecules23020337. Times cited: 22
- PICHOVÁ, Katarína NORDGREEN, Janicke LETTERIER, Christine KOŠŤÁL, Ľubor MOE, Randi Opperman. The effects of food-related environmental complexity on litter directed behaviour, fear and exploration of novel stimuli in young broiler chickens. In *Applied animal behaviour science*, 2016, vol. 174, p. 83-89. (2015: 1.795 IF, Q1 JCR, 1.040 SJR, Q1 SJR, Current Contents CCC). (2016 Current Contents). ISSN 0168-1591, 10.1016/j.applanim.2015.11.007. Times cited: 19
- POTURNAYOVÁ, Alexandra CASTILLO, Gabriela SUBJAKOVÁ, Veronika TATARKO, Marek ŠNEJDÁRKOVÁ, Maja HIANIK, Tibor. Optimization of cytochrome c detection by acoustic and electrochemical methods based on aptamer sensors. In Sensors and Actuators B: Chemical, 2017, vol. 238, p. 817-827. (2016: 5.401 IF, Q1 JCR, 1.343 SJR, Q1 SJR, Current Contents CCC). (2017 Current Contents). ISSN 0925-4005, 10.1016/j.snb.2016.07.113. Times cited: 18
- 8. BABEĽOVÁ, Janka ŠEFČÍKOVÁ, Zuzana ČIKOŠ, Štefan ŠPIRKOVÁ, Alexandra KOVAŘÍKOVÁ, Veronika KOPPEL, Juraj MAKAREVICH, A.V. CHRENEK, P. FABIAN, Dušan. Exposure to neonicotinoid insecticides induces embryotoxicity in mice and rabbits. In Toxicology, 2017, vol. 392, p. 71-80. (2016: 3.582 IF, Q1 JCR, 1.468 SJR, Q1 SJR, Current Contents CCC). (2017 Current Contents). ISSN 0300-483X, 10.1016/j.tox.2017.10.011. Times cited: 18
- POKORNÁ, Lucia ČERMÁKOVÁ, Petra HORVÁTH, Anton BAILE M. G., M. G. CLAYPOOL S. M., S. M. <u>GRIAČ, Peter</u> MALÍNSKÝ, Ján <u>BALÁŽOVÁ, Mária</u>. Specific degradation of phosphatidylglycerol is necessary for proper mitochondrial morphology and function. In *Biochimica et Biophysica Acta: bioenergetics*, 2016, vol. 1857, p. 34-45. (2015:

- 4.864 IF, Q1 JCR, 2.572 SJR, Q1 SJR, Current Contents CCC). (2016 Current Contents). ISSN 0005-2728, 10.1016/j.bbabio.2015.10.004. **Times cited: 16**
- 10. POTURNAYOVÁ, Alexandra DZUBINOVÁ, L'udmila BURÍKOVÁ, Monika BIZIK, Jozef HIANIK, Tibor. Detection of Breast Cancer Cells Using Acoustics Aptasensor Specific to HER2 Receptors. In *Biosensors*, 2019, vol. 9, no. 2, art. no. 72. (2018: 0.776 SJR, Q2 SJR, Current Contents CCC). (2019 Current Contents). ISSN 2079-6374, 10.3390/bios9020072. Times cited: 16
 - 2.2.5. List of most-cited authors from the Institute (at most 10 % of average FTE researchers per year) and their number of citations in the assessment period (2015–2020). The cited papers must bear the address of the institute

MVDr. Andrea Lauková, CSc. – 897 citations
 Prof. MVDr. Juraj Koppel, DrSc. – 551 citations
 Prof. Ing. Albert Breier, DrSc. – 506 citations
 MVDr. Iveta Plachá, PhD. – 473 citations
 Prof. RNDr. L'ubica Lacinová, DrSc. – 446 citations
 MVDr. Viola Strompfová, DrSc. – 431 citations
 RNDr. Štefan Čikoš, DrSc. – 411 citations

2.2.6. List of most-cited authors from the Institute (at most 10 % of average FTE researchers per year) and their number of citations obtained until 2020. The cited papers must bear the address of the Institute

MVDr. Andrea Lauková, CSc. – 2019 citations
 Prof. MVDr. Juraj Koppel, DrSc. – 1414 citations
 Prof. RNDr. L'ubica Lacinová, DrSc. – 1158 citations
 Prof. Ing. Albert Breier, DrSc. – 1006 citations
 RNDr. Štefan Čikoš, DrSc. – 822 citations
 MVDr. Viola Strompfová, DrSc. – 810 citations
 Prof. MVDr. Vladimír Kmeť, DrSc. – 780 citations

2.2.7. List of most-cited authors from the Institute (at most 10 % of average FTE researchers per year) and their number of citations obtained until 2021 of their papers published <u>during</u> the evaluation period (2016– 2021). The cited papers must bear the address of the Institute

1. MVDr. Andrea Lauková, CSc. 161 citations 2. MVDr. Iveta Plachá, PhD. - 141 citations 3. RNDr. Klaudia Čobanová. PhD. - 120 citations 4. MVDr. Ľubomíra Grešáková, PhD. - 103 citations - 87 citations 5. MVDr. Zora Váradyová, PhD. 6. Ing. Zdena Sulová, DrSc. 83 citations 7. Prof. Ing. Albert Breier, DrSc. - 79 citations 8. Ing. Alexandra Poturnayová, PhD. 79 citations

2.3. Research status of the institute in international and national context

- International/European position of the institute
 - 2.3.1. List of the most important research activities demonstrating the international relevance of the research performed by the institute, incl. major projects (details of projects should be supplied under Indicator 2.4). Max. 10 items for institute with less than 50 average FTE researchers per year, max. 20 for institutes with 50 100 average FTE researchers per year and so on

Among the most important research activities within bilateral projects, which are listed in section 2.4.6., was the DAAD-SAS exchange programme project "Characterisation of new interaction partners of the N-type calcium channel (Cav2.2)", in which L'ubica Lacinová collaborated with Albert-Ludwigs-Universität Freiburg, Germany, Within the project, students from Bratislava were trained in molecular biology methods in Freiburg and students from Freiburg were trained in electrophysiological methods in Bratislava. The project resulted in 2 publications and 1 invited review. The second successful project of the DAAD-SAS exchange programme was a project between CBv SAV and Martin Luther University, Halle-Wittenberg, Germany on "Hormonal dysregulation in diabetic pregnancy", whose principal investigator was Štefan Čikoš. It resulted in 2 joint publications in impacted journals. In the framework of the SAS-MOST cooperation scheme with Taiwan, Mária Balážová collaborated with Tunghai University in Taiwan on "Lipid metabolism as a crucial regulator of mitochondrial function". The project facilitated two 5-6 month stays of Taiwanese students in our laboratory and several short stays of our researchers in Taiwan. This collaboration resulted in 6 joint publications in impacted journals. Bacteriocins were the subject of two bilateral collaboration projects of Andrea Lauková, one with Portugal on "Bacteriocins and their benefits in reduction of spoilage, biofilm-producing bacteria from food products and food industry environment" and the other with Serbia on "Bacteriocins, a safe way to inhibit resistant bacteria from pigs for healthy farming." The first and the second resulted in 3 and 1 joint publication respectively. The bilateral project between the CBv SAS and the Institute of Biotechnology of the Czech Academy of Sciences on "Study of molecules involved in fertilization process of mammals" coordinated by Jana Jankovičová resulted in 6 CC publications.

COST is an important EU tool for addressing global challenges through networking. Its short-term scientific missions (STSMs) allow mainly early-stage researchers to visit cutting-edge laboratories within the networks. The training schools provide training in emerging research topics in the laboratories and organisations involved in the COST Action. In the evaluated period, our participation in COST networks increased to 10 from 7 in the previous evaluation (see **2.4.1.**)

The project "Epigenetics and periconception environment - Periconception environment as an epigenomic lever for optimising food production and health in livestock" (FA1201) coordinated by Juraj Koppel resulted in cooperation with University of Martin Luther, Halle-Wittenberg, Germany, resulted in 2 publications in CC Journals and 2 STSMs.

The project "Large-scale methane measurements on individual ruminants for genetic evaluations" (FA1302) coordinated by Zora Váradyová resulted in 2 publications in CC journals, participation at 3 STSMs and 2 training schools.

The project "European network on the factors affecting the gastro-intestinal microbial balance and the impact on the health status of pigs" (FA1401) coordinated by Andrea Lauková resulted in 4 publications in CC Journals, participation at 4 STSMs, 3 training schools and in collaboration with the Kielanowski Institute of Animal Physiology and Nutrition PAS, Jablonna, Poland, with which they submitted a bilateral project SK-PL-18-0017 (Prospects of mineral availability improvement in monogastric animals) - not funded.

The newly started project "Biosecurity enhanced through training evaluation and raising awareness" (CA20103) coordinated by Andrea Lauková resulted till now in one STSM.

The project "European network for optimization of veterinary antimicrobial treatment" (CA18217) coordinated by Dobroslava Bujňáková resulted in 1 CC publication.

The project "New diagnostic and therapeutic tools against multidrug resistant tumors" CA17104 coordinated by Lucia Messingerová resulted in attending 1 training school and in publication of 2 papers.

The project "Brillouin light scattering microspectroscopy for biological and biomedical research and applications" (CA16124) coordinated by Silvia Bágeľová Poláková resulted in 1 CC publication.

Th newly starte project "Pan-European network in lipidomics and epilipidomics" CA19105 is coordinated by Mária Balážová.

The project "Identifying causes and solutions of keel bone damage in laying hens" CA15224 coordinated by L'ubor Košťál and Boris Bilčík resulted in our participation at 4 training schools. As a part of the project dissemination, the principal coordinator of the project Dr. Michael Toscano from the University of Bern participated in 2018 at the conference of the Union of the Slovak Poultry Producers in Podbanské, as a part of our strategy to approach the industry.

The project "Synergy for preventing damaging behaviour in group housed pigs and chickens" (CA15134) coordinated by L'ubor Košt'ál and Boris Bilčík resulted in participation at two STSMs and 2 training schools. We have organized one training school in Bratislava with some world-leading scientists in the field (such as Larry Young from Emory University). Triggered by one of the STSMs was the longer stay of Katarína Pichová at Wageningen University & Research and resulting 1 CC publication.

Projects funded from private funds are described under 2.4.7.

Important non-project research activities:

The most important research activities that prove the international relevance of the Institute include extensive cooperation in the field of education, exchanges of student internships and related research between the Institute of Animal Physiology of CBs and the University of Science in Poznań, Poland (Department of Animal Nutrition). Three students from this university completed an internship (funded by EU funds: You study - You practice) at the Department of Digestive Tract Physiology in Košice. The internships were focused on f the use of plant secondary metabolites in ruminant nutrition, and the supervisor was Zora Váradyová. The students from the Department of Digestive Tract Physiology in Košice often visit the Department of Animal Nutrition at Poznań University as part of exchange internships, thus helping to create comprehensive, effective strategies for scientific communication and strong scientific cooperation between the Slovak and Polish working groups. In the accreditation period 2016-2021, they completed a one to two-month internship at the Department of Animal Nutrition of Poznan University. Based on the achieved results and several years of cooperation, the Dean of the Faculty of Veterinary Medicine and Animal Science of the University of Poznań and the Head of the Institute of Animal Physiology of the CBs in Košice signed a Memorandum of Cooperation (November 2019).

2.3.2. List of international conferences (co)organised by the institute

2nd conference of the Visegrád Group Society for Developmental Biology, Szeged, Hungary, September 2 – 5, 2021 (co-organizer, main organizer: Biological Research Centre, Szeged)

43rd Annual Conference on Yeasts, May 10 - 13, 2016, Slovakia, (co-organizer)

44th Annual Conference on Yeast, May 2 - 5, 2017, Slovakia (co-organizer)

45th Annual Conference on Yeast. May 15-18 2018, Slovakia, (co-organizer)

Animal Physiology 2016, Bořetice, Czech Republic, June 13 – 15, 2016 (co-organizer, main organizer: Mendel University in Brno)

Animal Physiology 2017, Stará Lesná, Slovakia, June 21 – 23, 2017 (main organizer)

Animal Physiology 2018, Cracow, Poland, June 13 – 15, 2018 (co-organizer, main organizer: Pedagogical University of Cracow)

Animal Physiology 2019, Vyhne, Slovakia, May 27 – 29, 2019 (co-organizer, main organizer: Slovak University of Agriculture in Nitra)

Animal Physiology 2021, Češkovice, Czech Republic, September 22 – 24, 2021 (co-organizer, main organizer: Mendel University in Brno)

Central European Genome Stability and Dynamics Meeting. September 26 - 27, 2019. Bratislava, Slovakia (co-organizer)

COST KeelBoneDamage Management Committee and Research Coordination Meeting, Hotel Saffron, January 25 - 26, 2018. Bratislava, (main organizer)

Visegrád Group Society for Developmental Biology: Inaugural Meeting, Brno, Czech Republic, September 07 – 09. 2018 (co-organizer, main organizer: Masaryk University in Brno)

2.3.3. List of edited proceedings from international scientific conferences

- **43rd Annual Conference on Yeast,** May 10-13, 2016, SAS Congress Centre, Smolenice, Slovakia: Program and Abstracts. Bratislava: Yeast Commissiom, Institute of Chemistry, Slovak Academy of Sciences, Institute of Animal Biochemistry and Genetics SAS, Faculty of Chemical and Food Technology SUT, 2016. ISBN 1336-4839.
- **44th Annual Conference on Yeast,** May 2-5, 2017, SAS Congress Centre, Smolenice, Slovakia. Bratislava: Institute of Chemistry SAS, Institute of Animal Biochemistry and Genetics, Centre of Biosciences SAS, 2017. ISSN 1336-4839.
- **45th Annual Conference on Yeast.** May 15-18 2018, SAS Congress Centre, Smolenice, Slovakia. Bratislava: Institute of Chemistry SAS, Institute of Animal Biochemistry and Genetics, Centre of Biosciences SAS, 2018. ISSN 1336-4839.
- **Animal Physiology 2017:** Book of abstracts from international conference. Eds. Fabian, D., Kišidayová, S., Babeľová, J. Košice: UFHZ-SAV, 2017. 89 s. ISBN 978-80-971428-4-1. https://sites.google.com/site/physiologyanimal2017/home
 - 2.3.4. List of journals edited/published by the institute and information on their indexing in WOS, SCOPUS, other database or no database, incl. impact factor and other metrics of journals in each year of the assessment period

Journal **General Physiology and Biophysics (GPB)** is an "Open Access", peer-reviewed scientific journal published by the Centre of Biosciences, SAS since 1982, 6 times per year in English language. **(ISSN 0231-5882 (print), eISSN 1338-4325 (online),** Web: www.gpb.sav.sk). Journal **GPB** is indexed in following databases: CC/Life Sciences, Science Citation Index, ISI/BIOMED, EMBASE, MEDLINE/PubMed, Web of Science Core Collection, Scopus, Crossref.

	2016	2017	2018	2019	2020	2021
Journal Impact Factor (WOS)	1.170	1.479	1.309	1.070	1.512	1.957
Category Quartile (WOS)	Q4	Q4	Q4	Q4	Q4	Q4
SJR (SCOPUS)	0.378	0.438	0.426	0.373	0.376	0.344
Category Quartile (SJR)	Q3	Q3	Q3	Q3	Q3	Q3

National position of the institute

2.3.5. List of selected activities of national importance

Cooperation with a commercial animal rendering plant (VAS, s.r.o., Mojšova Lúčka, Žilina), a partner for the implementation of applied research.

Cooperation in the investigation of pathogenicity and antibiotic resistance in animal *Escherichia coli* with the company VetServis, s.r.o., Nitra.

The International Probiotic Company (InProCo) s.r.o. produces probiotic products containing our probiotic and bacteriocin-producing strains *Lactobacillus fermentum* AD1-CCM7421 included in the preparation ProBioDog (for dogs) and rabbit strain *Enterococcus faecium* EF2019-CCM7420 included in the preparation ProRabbit (for rabbits and small rodents).

Cooperation with the human microbiology company HPL, s.r.o. We accomplished the PCR diagnostics of selected antibiotic resistance genes (e.g. betalactamase OXA-61, quinolone efflux cmeB and tetracycline genes) in *Campylobacters*.

2.3.6. List of journals (published only in the Slovak language) edited/published by the institute and information on their indexing in WOS, SCOPUS, other database or no database, incl. impact factor and other metrics of journals in each year of the assessment period

none

- Position of individual researchers in the international context
 - 2.3.7. List of invited/keynote presentations at international conferences, as documented by programme or invitation letter

BALÁŽOVÁ Mária. Subcellular distribution of phosphatidylglycerol is regulated by a lipid droplet protein. Prague Membrane Discusion. Praha 14.12. 2017

- **BARAN Vladimír:** Time-lapse imaging of oocytes and early embryos, 1st Advanced Microscopy Symposium, 15. 16. november 2016 Košice, Slovensko.
- BREIER Albert P-glykoproteín membránový transportér spôsobujúci viacliekovú rezistenciu nádorových tkanív. (Implikácie pre návrh efektívnych chemoterapeutík). [P-glycoprotein membrane transporter inducing multidrug resistance of tumor tissues. Impications for the design of effective chemotherapeutics]. In 68. Symposium Czech and Slovak Chemical Societes 2016, Praha, Czech Chemical Symposium Series, Vol. 14, no. 5, 2016, p. 165. ISSN 2336-7202.
- ČIKOŠ, Štefan ŠPIRKOVÁ, Alexandra KUBANDOVÁ Janka KOVAŘÍKOVÁ, Veronika ŠEFČÍKOVÁ, Zuzana FABIAN, Dušan KOPPEL, Juraj. Cell receptors mediating communication between preimplantation embryo and surrounding environment: clues from mouse and rabbit models. In Slovak J Anim Sci 2018, 50, p.174, ISSN 1337-9984; The 6th International Scientific Conference "Animal Biotechnology 2018", Nitra, December 6th, 2018
- DVOROŽŇÁKOVÁ, Emília BUCKOVÁ, Barbora HURNÍKOVÁ, Zuzana LAUKOVÁ, Andrea REVAJOVÁ, Viera. Protective effects of probiotic bacteria against experimental trichinellosis. In International Conference Theory and Practice of Struggle against Parasitic Diseases. May 15-17 2018, Moscow, Russia: proceedings. Kuročkin, K.G. (zost.) Moscow: All Russian Scientific Research Institute of Fundamental and Applied Parasitology of Animals and Plants named after K.I. Skryabin, 2018, s. 148-151. ISBN 978-5-904798-67-3.
- DVOROŽŇÁKOVÁ, Emília VARGOVÁ, Miroslava **LAUKOVÁ, Andrea** REVAJOVÁ, Viera. Modulatory effect of probiotic therapy on intestinal lymphocytes in mice infected with Trichinella spiralis. In Theory and Practice of Parasitic Disease Control: Collection of Scientific Articles adapted from the International Scientific Conference, 15–17 May 2019, Moscow. Indyuhova, F.N.M. (ed.). Moscow: All Russian Scientific Research Institute of Fundamental and Applied Parasitology of Animals and Plants, 2019, s. 741-745. ISBN 978-5-9902340-8.
- **KOŠŤÁL, Ľubor** SKALNÁ, Zuzana PICHOVÁ, Katarína. Studying affect induced judgement bias in birds. In Workshop: Cognitive affective biases from mechanisms to disease symptoms.Kraków, Poland, May 13-17, 2019.
- KOŠŤÁL, Ľubor SKALNÁ, Zuzana PICHOVÁ, Katarína. Using cognitive bias as a welfare tool in poultry. 17th International Conference on Production Diseases in Farm Animals (ICPD). Bern, Switzerland, June 27 - 29, 2019.
- LACINOVÁ, L'ubica JURKOVIČOVÁ-TARABOVÁ, Bohumila MORAVČÍKOVÁ, Lucia KARMAŽÍNOVÁ, Mária. Structural Determinants of the Regulation of T-type Calcium Channels by a Voltage. In SSB 2017. 10th International Conference Structure and Stability of Biomacromolecules: Book of contributions, September 4 7, 2017, Košice, Slovakia 2017, p. 28-29. ISBN 978-80-89656-19-6.
- LACINOVÁ, L'ubica ONDÁČOVÁ, Katarína LAPÍNOVÁ, Lucia JURKOVIČOVÁ, Dana. In vitro model of fibrotic scar differently modulates the excitability of hippocampal and cerebellar neurons. In 8th International Symposium on Experimental and Clinical Neurobiology: Program and Abstract Book. Košice: GAIA- Institute of Neurobiology SAS, 2017, p. 55. ISBN 978-80-972729-0-6.(International Symposium on Experimental and Clinical Neurobiology).
- **LAUKOVÁ Andrea**: Benefits of Enterocin-producing Enterococci and their Enterocins in Animals, Symposium: Power of Microbes in Industry and Environment 2016, 28.9.-1.10.2016, Krk, Croatia.
- LAUKOVÁ Andrea: Prospešnosť bakteriocín-produkujúcich, probiotických enterokokov a ich bakteriocínov pri odchove zvierat. [Benefits of bacteriocin-producing Enterococci and their enterocins in animal breeding]. Institute of Animal Science, Prague, Czech Republic, Conference: Aktuální poznatky ve výživě a zdraví zvířat a bezpečnosti produktu 2016 [Current knowledge in animal nutrition and health, and product safety] Book of abstract, 22.9.2016, Prague, Czech Republic. ISBN 978-80-7403-152-6.
- **LAUKOVÁ, Andrea** Use of non-autochthonous, bacteriocin-producing and probiotic strain Enterococcus durans ED26E/7 in broiler rabbits. In International Scientific Conference on Probiotics and Prebiotics IPC2017, June 20-22, 2017, Budapest, Hungary

- **LAUKOVÁ, Andrea**. Enterocins, beneficial additives in animals. In Symposium BAMP 2017-in the framework of International Scientific Conference on Probiotics and Prebiotics IPC2017, June 20-22, 2017, Budapest, Hungary.
- **LUKÁČOVÁ, Kristína_** HAMAIDE, Julie BACIAK Ladislav- VAN DER LINDEN Annemie L'ubica KUBÍKOVA NIEDEROVÁ. Beyond striatal injury of adult male zebra finches. In European birdsong meeting 2019. Capo Caccia, Sardinia, Italy May 5-7, 2019
- **MESSINGEROVÁ Lucia** Bunkové línie MOLM-13 a SKM-1 rezistentné na azacytidín vykazujú cross-rezistenciu k substrátom P-glykoproteínu. [Azacytidine-resistant cell lines MOLM-13 and SKM-1 show cross-resistance to P-glycoprotein substrates]. In XXV. Biochemical symposium Praha, august 2016, s. 221. ISBN 978-80-270-0331-0.
- **PLACHÁ**, **Iveta** OCEĽOVÁ, Vladimíra CHIZZOLA, Remigius BAČOVÁ, Kristína FAIX, Štefan: Effect of sustained dietary application of thyme oil on antioxidant parameters and thymol content in plasma and tissues of broilers. In 67th International Congress and Annual Meeting of the Society for Medicinal Plant and Natural Product Research (GA), p. 9-10, Innsbruck, Austria, September 1-5, 2019
- **POTURNAYOVÁ Alexandra**: Acoustics and AFM studies of protein cleavage by plasmin. International Workshop Acoustic and electrochemical methods in the study of affinity interactions at surfaces. Bratislava 20.6.2016
- **ZAHRADNÍKOVÁ Alexandra** Calcium wave generation in cardiac myocytes. In Regional Biophysics Conference (RBC2016): Book of Abstracts. Trieste, Italy, ISBN 978-88-8303-757-3, 978-88-8303-758-0. http://rbc2016.ge.ibf.cnr.it/congress/invited-speakers.html

2.3.8. List of researchers who served as members of the organising and/or programme committees

Bágeľová Poláková Slvia

- member of the programme/organising committee, Central European Genome Stability and Dynamics Meeting. Bratislava, Slovakia, 2019

Bilčík Boris, Pichová Katarína

- members of the organising committee, COST KeelBoneDamage Management Committee and Research Coordination Meeting, Bratislava, Slovakia 2018

Breier Albert

- member of the programme committee XXVI. Annual Congress of Czech and Slovak Societies for Biochemistry and Molecular Biology in cooperation the Austrian and German Biochemical Section: "Life is Biochemistry, Biochemistry is Life". České Budějovice, Czech Republic, 2021

Hapala Ivan

- head of the organising committee, member of the programme committee, 43rd Annual Conference on Yeast, Smolenice, Slovakia 2016
- head of the organising committee, member of the programme committee, 44th Annual Conference on Yeast, Smolenice, Slovakia 2017
- head of the organising committee, member of the programme committee, 45th Annual Conference on Yeasts, Smolenice, Slovakia 2018
- member of the programme committee, 13th Yeast Lipid Conference, Paris, France 2017

Čikoš Štefan

- head of the programme committee, Animal Physiology, High Tatras, Slovakia 2017

Fabian Dušan

- head of the organising committee, member of the programme committee, Animal Physiology, High Tatras, Slovakia 2017
- head of the programme/organising committee, Animal Physiology, Vyhne, Slovakia 2019

- member of the programme committee, 2nd conference of the Visegrád Group Society for Developmental Biology, Szeged, Hungary 2021

Faix Štefan

- member of the programme committee Animal Physiology, Cracow, Poland, 2018
- member of the programme committee, Animal Physiology, Češkovice, Czech Republic 2021

Košťál Ľubor

- head of the programme/organising committee, COST KeelBoneDamage Management Committee and Research Coordination Meeting, Bratislava, Slovakia 2018

Špirková Alexandra

- member of the organising committee, Animal Physiology, High Tatras, Slovakia 2017
- member of the organising committee, Animal Physiology, Češkovice, Czech Republic 2021

Valachovič Martin

- member of the programme committee, 14th Yeast Lipid Conference, Ljubljana, Slovenija 2019

Zahradníková Alexandra

- member of the programe committee, New Frontiers In Basic Cardiovascular Research, Chatenay-Malabry, France 2016

2.3.9. List of researchers who received an international scientific award

- Position of individual researchers in the national context
 - 2.3.10. List of invited/keynote presentations at national conferences, as documented by programme or invitation letter
- **PRISTAŠ, Peter**, RADAČOVSKÁ, N: O vode, čo sa mení na kameň. [The water that turns to stone]. XX. Okresné dni vody v Michalovciach [District water days in Michalovce], April 14 15, 2016, Hotel Vinnay, Vinné jazero, Slovakia.
- **GREŠÁKOVÁ, Ľubomíra**. Stopové prvky vo výžive zvierat. [Trace elements in animal nutrition]. Odborný seminár užívateľov prístrojov firmy Shimadzu [Technical seminar for the users of Shimadzu equipment], May 18 19. 2017, Mýto pod Ďumbierom, Slovakia.
- KMEŤ, Vladimír: Rezistencia na antibiotiká stafylokokov, laktobacilov a *Escherichia coli* v mlieku, u hydiny a u divožijúcich zvierat. [Antibiotic resistance in staphylococci, lactobacilli and Escherichia coli in milk, poultry and wild animals]. Vedecká konferencia: Krčméryho deň boja proti antibiotickej rezistencii [Krčméry's day in the action against antibiotic resistance], November 8, 2018, pri príležitosti Európskeho dňa zvyšovania povedomia o antibiotikách [European Antibiotic Awareness Day]. Aula Pazmaneum, FHCaSW, Trnava University
- **KRÁLOVIČOVÁ, Jana** BOROVSKÁ, Ivana VOŘECHOVSKÝ, Igor. Vplyv genomickej variability na reguláciu alternatívneho zostrihu RNA [Effect of genetic variability on regulation of alternative splicing]. In Biochemické dni 2019: Zborník abstraktov z konferencie [Biochemical Days 2019: Abstract Book from Conference]. Editor Gabriela Gavurníková. Bratislava, 2019, p. 40. ISBN 978-80-89965-27-4.

2.3.11. List of researchers who served as members of organising and programme committees of national conferences

Antalíková Jana, Griač Peter

 members of the organising committee, 9th Ivanka Days of Young Biologists, Ivanka pri Dunaji, Slovakia, 2016

Balážová Mária

- member of organising committee, Drobnica memorial (Conference of PhD students dedicated to prof. Drobnica memory), Stará Lesná, Slovakia, 2019
- member of organising committee, Drobnica memorial, Trenčín, Slovakia, 2021

Breier Albert, Sulová Zdena

- members of organising committee, Drobnica memorial (Conference of PhD students dedicated to prof. Drobnica memory), Danišovce, Slovakia, 2017
- members of organising committee, Drobnica memorial, Stará Lesná, Slovakia, 2019
- members of organising committee, Drobnica memorial, Trenčín, Slovakia, 2021

Breier Albert, Boháčová, Viera, Imrichová Denisa, Sulová Zdena

- members of programme/organising committee XXX. Xenobiochemical Symposium, Pezinok, Slovakia, 2019

Cagala Martin, Šereš Mário

- members of organising committee XXX. Xenobiochemical Symposium, Pezinok, Slovakia, 2019

Fabian Dušan

- head of the programme/organising committee, 11th memorial of Academician Bod'a (Conference of PhD students dedicated to prof. Bod'a memory), Košice, Slovakia 2016
- head of the programme/organising committee, 12th memorial of Academician Bod'a, Košice, Slovakia 2017
- head of the programme/organising committee, 13th memorial of Academician Boda, Košice, Slovakia 2018
- head of the programme/organising committee, 14th memorial of Academician Boda, Košice, Slovakia 2019
- head of the programme/organising committee, 15th memorial of Academician Bod'a, Košice, Slovakia 2020

Hamarová Ľudmila

- member of the organising committee, 13th memorial of Academician Boďa, Košice, Slovakia 2018

Imrichová Denisa

- member of organising committee, Drobnica memorial, Danišovce, Slovakia, 2017
- member of organising committee, Drobnica memorial, Stará Lesná, Slovakia, 2019

Kovaříková Veronika

- member of the organising committee, 15th memorial of Academician Boda, Košice, Slovakia 2020
- head of the programme/organising committee, 16th memorial of Academician Bod'a, Košice, Slovakia 2021

Lacinová Ľubica

- member of the programme/organising committee, 9th Slovak Biophysical Symposium, Trnava, Slovakia, 2020

Rusnák Andrej

- member of organising committee, Drobnica memorial, Danišovce, Slovakia, 2017

Valachovič Martin

- head of the programe/organising committee, 10th Ivanka Days of Young Biologists, Bratislava, Slovakia, 2018

Zahradníková Alexandra

- member of the programe committee, 7th Slovak Biophysical Symposium, Nový Smokovec, Slovakia, 2016

2.3.12. List of researchers who received a national scientific award

Bágeľová Poláková Slvia

- award of the Presidium of SAS to the authors of the top publication published in high-impacted journals. POLÁKOVÁ, Silvia MOLNÁROVÁ, Lucia HYPPA, Randy W. BENKO, Zsigmond MIŠOVÁ, Ivana SCHLEIFFER, Alexander SMITH, Gerald R. GREGAN, Juraj. Dbl2 Regulates Rad51 and DNA Joint Molecule Metabolism to Ensure Proper Meiotic Chromosome Segregation. In Plos Genetics, 2016, vol.12, no. 6, e1006102. PMID: 27304859. (6.661 IF2015).
- a national prize of Dr. Ludmila Sedlárová Rabanová for exceptional results in field of genetics, link: http://www.naturaoz.org/laureat2016.html, 2016

Balážová Mária

- honorable mention - competition L'Oréal – UNESCO "For Women in Science" 2020

Breier Albert

- medal of SAS for the support of science (award of SAS Presidium), 2017

Cagalinec Michal

award of SAS Presidium to a author of the top publication published in a high-impacted journals.
 CAGALINEC, Michal - LIIV, Mailis - HODUROVA, Zuzana - HICKEY, Miriam Ann - VAARMANN,
 Annika - MANDEL, Merle - ZEB, Akbar - CHOUBEY, Vinay - KUUM, Malle - SAFIULINA,
 Dzhamilja - VASAR, Eero - VEKSLER, Vladimir - KAASIK, Allen. Role of mitochondrial dynamics in neuronal development: Mechanism for Wolfram syndrome. In Plos Biology, 2016, vol. 14, p. e1002511. (8.668 - IF2015).

Faix Štefan

- medal of SAS for the support of science (award of SAS Presidium), 2018

Hapala Ivan

- medal of SAS for the support of science (award of SAS Presidium), 2019

Koppel Juraj

- medal of SAS for the support of science (award of SAS Presidium), 2019
- silver medal of Slovak Medical Association, 2020

Lacinová Ľubica

- medal of SAS for the support of science (award of SAS Presidium), 2019
- bronze medal of Slovak Medical Association, 2020

Lauková Andrea

- Medal of the SAS for contribution to science and research (award of SAS Presidium), 2018

Niederová Kubíková Ľubica

- Finalist of competition L'Oréal UNESCO "For Women in Science" 2018, 2019
- Award of SAS Presidium for publications included in the Nature index, 2020

Sulová Zdena

Honorary plaque of SAS Dionýz Ilkovič for merits in physico-chemical sciences (award of SAS Presidium), 2017

2.4. Research grants and other funding resources

(List type of project, title, grant number, duration, total funding and funding for the institute, responsible person in the institute and his/her status in the project, e.g. coordinator "C", work package leader "W", investigator "l". Add information on the projects which are interdisciplinary, and also on the joint projects with several participating SAS institutes)

International projects

2.4.1. List of major projects of Framework Programmes of the EU (which pilar), NATO, COST, etc.

Title	Grant number	Duration	Total funding	Funding for the institute	Responsible person	Status*
Epigenetics and Periconception Environment - Periconception environment as an epigenomic lever for optimising food production and health in livestock	COST Action FA1201	4.10.2012 - 3.10.2016	6 917.00	6 917.00	Juraj Koppel	W
Large-scale methane measurements on individual ruminants for genetic evaluations	COST Action FA1302	10.12.2013 - 9.12.2017	11 650.00	11 650.00	Zora Váradyová	MCm
European network on the factors affecting the gastro-intestinal microbial balance and the impact on the health status of pigs	COST Action FA1401	31.10.2014 - 30.10.2018	15 000.00	15 000.00	Andrea Lauková	MCm
Synergy for preventing damaging behaviour in group housed pigs and chickens	COST Action CA15134	2.3.2016 - 1.3.2020	15 204.00	15 204.00	Ľubor Košťál, Boris Bilčík	MCm
Identifying causes and solutions of keel bone damage in laying hens	COST Action CA15224	18.10.2016 - 17.10.2020	15 169.00	15 169.00	Ľubor Košťál, Boris Bilčík	MCm
Brillouin Light Scattering Microspectroscopy for Biological and Biomedical Research and Applications	COST Action CA16124	28.2.2017 - 27.2.2021	11 448.00	11 448.00	Silvia Bágeľová Poláková	MCm
New diagnostic and therapeutic tools against multidrug resistant tumors	COST Action Ca17104	11.9.2019 - 10.9.2022	9 045.00	9 045.00	Lucia Messingerová	W
European network for optimization of veterinary antimicrobial treatment	COST Action CA18217	15.11.2019 - 14.11.2023			Dobroslava Bujňáková	W
Pan-European Network in Lipidomics and Epilipidomics	COST Action CA19105	13.10.2020 - 12.10.2024	3 730.00	3 730.00	Mária Balážová	MCm
Biosecurity enhanced through training evaluation and raising awareness	COST Action CA20103	21.10.2021 - 20.10.2025	5 020.00	5 020.00	Andrea Lauková	MCm

^{* - &}quot;W" work package leader, "MCm" management committee member

Add information on your activities in international networks

In previous years, the Institute of Molecular Physiology and Genetics was successful in obtaining funds from international project schemes within the framework programs of the EU, NATO, Howard Hughes project and FIRCA project.

Unfortunately, this positive trend has not been maintained despite considerable efforts to engage in European project schemes. This is partly due to the increased focus of European project schemes on applied and translational research where, in addition to academic partners, commercial partners with a clear research focus and advanced infrastructure are needed. Unfortunately, there is a shortage of such partners in our research area. Another reason for not obtaining projects in Europe is the clear orientation towards basic research of the Institute of Molecular Physiology and Genetics, the Institute of Biochemistry and Animal Genetics and, to some extent, the Institute of Animal Physiology, which does not correspond to the current trend of European Commission support for European research.

To document the effort to obtain funds within the EU, we present a list of submitted applications in the years 2016-2021.

List of unsuccessful international grant applications 2021

- 1. Call: ERA-NET NEURON Call for Joint Transnational Research Projects 2021, No: NEURON_NDD-069, Acronym: NeuroMIA, Title: Neurodevelopmental abnormalities resulting from a maternal immune activation: pathophysiology and treatment and prevention strategies. Coordinator: Eliyahu Dremencov, Centre of Biosciences SAS, Status: not funded.
- 2. Call: Transnational Call (JTC) 2021 for "European Innovative Research & Technological Development Projects in Nanomedicine", Acronym: MULDEMON, Title: Multifunctional Precision Nanocarriers for Treatment of Motor Neuron Disease, Coordinator: Saak Ovsepian, Národní ústav duševního zdraví (National Institute of Mental Health), Klecany, Czech Republic, Status: successful application, withdrawn by the coordinator.
- 3. Call: EUREKA Eurostars, No: E509, Acronym: PreCNExuS, Title: A novel drug development tool for CNS disorders Coordinator: Carlos Cordeiro, ParaMedir B.V., Groningen, the Netherlands, Status: not funded.
- 4. Call: Visegrad Grants, No: 22030040 Title: Strategic Initiative Towards Prevention of Mental Illness Related Obesity and Comorbidities, Coordinator: Saak Ovsepian, Národní ústav duševního zdraví (National Institute of Mental Health), Klecany, Czech Republic, Status: Passed to the second phase, withdrawn by the coordinator.
- 5. Call: QuantERA II ERA-NET Cofund in Quantum Technologies 2021, QuantERA pre-proposal, Acronym: Titan-3D-Cell, Title: Optimization of the structure and post-production of the 3D-printed Ti6Al4V ELI titanium alloy materials for surgical applications using mouse, rabbit, and human stem cells, Coordinator: University of Science and Technology, Bydgoszcz, Poland, Status: not passed to the second stage.

2020

- 6. Call: EUREKA Eurostars, No: E115192, Acronym: PreCNExuS, Title: A novel drug development tool for CNS disorders, Coordinator: Carlos Cordeiro, ParaMedir B.V., Groningen, the Netherlands, Status: passed threshold, not short-listed for the funding.
- 7. Call: H2020-FETOPEN-2018-2019-2020-01, No: 22030040, Acronym: PREMOTOR, Title: Precision Guided Reinforcement of Motor Units to Prevent Muscle Paralysis and Neuronal Loss in Degenerative Diseases, Coordinator: Saak Ovsepian, Národní ústav duševního zdraví (National Institute of Mental Health), Klecany, Czech Republic, Status: successful application, withdrawn by the coordinator.

2019

8. Call: Euronanomed Joint Transnational Call For Proposals (2019) For European Innovative Research & Technological Development Projects In Nanomedicine, Acronym: SYNTETGENE, Title: Synergizing the superb retro-axonal transgene delivery by detoxified CS-TeTIM with RNA modifiers for extended survival and improved motor performance in ALS models, Coordinator:

Saak Ovsepian, Národní ústav duševního zdraví (National Institute of Mental Health), Klecany, Czech Republic

2018

- 9. Call: H2020 "Understanding causative mechanisms in co- and multimorbidities", Acronym: MAGiCS, Title: Shared Biology of Stress, Depression and Diabetes Drives Outcome in Metabolic Surgery, Coordinator: Enrico Ullmann, MD, University of Dresden, Status: not funded.
- 10. Call: BiodivERsA joint call (JTC 2018-2019) Biodiversity and its influence on animal, human and plant health, Proposal Reference: BiodivERsA2018-A-85, Acronym: DairyproSUS, Title: Sustainable milk production for biodiversity, Coordinator: Dublin Institute of Technology, School of Food Science and Environmental Health, Ireland, Status: not funded.

2017

- 11. Call: ERC-2017-COG, No: 771033, Acronym: NanoNeuro, Title: Using of cutting-edge nanotechnologies for the investigation of pathophysiology of depression. Coordinator: Eliyahu Dremencov, Centre of Biosciences SAS, Status: not funded.
- 12. Call: NATO SPS MYP, No: G5476, Acronym: NanoNeuro, Title: Health risks of psychological stress linked with ionizing irradiation. Coordinator: Eliyahu Dremencov, Centre of Biosciences SAS, Status: not funded.

2016

13. Call: NATO SPS MYP, No: G5476, Acronym: NanoNeuro, Title: Health risks of psychological stress linked with ionizing irradiation., Coordinator: Eliyahu Dremencov, Centre of Biosciences SAS, Status: not funded.

• National projects, incl. international projects with only national funding

2.4.2. List of ERA-NET projects funded from SAS budget none

2.4.3. List of projects of the Slovak Research and Development Agency, APVV

Title	Grant number	Duration	Total funding	Funding for the institute	Responsible person	Status*
Zinc in animal nutrition and consumer safety	APVV-0667-12	1.10.2013 - 30.9.2017	247 900.00	214 650.00	Klaudia Čobanová	С
Possible dual function of P-glycoprotein in leukemia cells: efflux pump and regulatory protein	APVV-14-0334	1.7.2015 - 30.6.2018	250 000.00	174 000.00	Zdena Sulová	С
Development of novel diagnostic method for clinical oncology based on the interaction of DNA aptamers with proteins	APVV-14-0267	1.7.2015 - 30.6.2019	216 541.00	57 125.00	Alexandra Poturnayová	W
Biochips and biosensors for glycorecognition, their development, preparation and application in cancer research	APVV-14-0753	1.7.2015 - 30.6.2019	250 000.00	26 000.00	Zdena Sulová	W
Xenobiotics and preimplantation embryo development	APVV-14-0763	1.7.2015 - 30.6.2019	249 470.00	228 898.00	Juraj Koppel	С
Small mammals as a potential source of zoonotic bacteria and resistance to antibiotics	APVV-14-0274	1.7.2015 - 30.6.2019	168 032.00	33 883.00	Vladimír Kmeť	W
Anthelmintic resistance of parasites – challenges, perspectives and solutions	APVV-14-0169	1.7.2015 - 30.6.2019	247 553.00	98 329.00	Zora Váradyová	W
Cytoarchitecture of calcium signalling of cardiac myocytes in development of myocardial hypertrophy	APVV-15-0302	1.7.2016 - 30.4.2018	250 000.00	119 689.00	Alexandra Zahradníková	С
Establishment of methodology of bovine ovarian tissue cryopreservation for the purposes of the gene banking	APVV-15-0196	1.7.2016 - 30.6.2020	247 055.00	59 950.00	Jana Antalíková	W
Towards highly selective cancer treatment: Endogenous lipoprotein-DARPin complexes as a new generation of targeted drug delivery vehicles	APVV-15-0485	1.7.2016 - 30.6.2020	247 283.00	47 093.00	Boris Bilčík	W
The role of organelle interactions in lipid homeostasis	APVV-15-0654	1.7.2016 - 30.6.2020	233 800.00	172 000.00	Ivan Hapala	С
Learning and neuronal plasticity in songbirds	APVV-15-0077	1.7.2016 - 30.6.2020	178 598.00	138 965.00	Ľubica Niederová- Kubíková	С
Novel synergistic antitumour properties of nuclear retinoid X receptor (RXR) agonists as a consequence of the conditional RXR-RAR heterodimer formation in human breast cancer cells	APVV-15-0372	1.7.2016 - 30.6.2020	249 814.00	40 400.00	Zdena Sulová	W
Defense mechanisms of neoplastic cells against chemical stress	APVV-15-0303	1.7.2016 - 30.6.2020	200 000.00	80 500.00	Zdena Sulová	W
Prenatal and postnatal effects of δ and μ opioid receptor ligands on the hippocampal development and function	APVV-15-0388	1.7.2016 - 30.6.2020	249 991.00	119 720.00	Ľubica Lacinová	С
Smart MoS2 platform for cancer diagnosis and targeted treatment	APVV-15-0641	1.7.2016 - 30.6.2020	249 717.00	43 000.00	Albert Breier	W
Progressive methods for elimination of development and spread of bacterial resistance against relevant antibiotics	APVV-16-0171	1.7.2017 - 30.6.2020	200 000.00	25 000.00	Anna Kopčáková (Javorský)	W

APVV-16-0120	1.7.2017 - 30.6.2021	210 000.00	27 565.00	Silvia Bágeľová Poláková	W
APVV-16-0439	1.7.2017 - 30.6.2021	248 739.00	39 471.00	Zdena Sulová	W
APVV17-0130	1.7.2018 - 30.6.2022	239 000.00	45 273.00	Silvia Bágeľová Poláková	W
APVV-17-0297	1.7.2018 - 30.6.2022	249 100.00	249 000.00	Klaudia Čobanová	С
APVV-17-0371	1.8.2018 - 30.6.2022	233 542.00	105 518.00	Ľubor Košťál	С
APVV-17-0028	1.8.2018 - 31.7.2022	249 998.00	140 179.00	Andrea Lauková	С
APVV-18-0219	1.7.2019 - 30.6.2022	230 000.00	92 800.00	Silvia Bágeľová Poláková	С
APVV-18-0096	1.7.2019 - 30.6.2023	178 951.00	133 930.00	Jana Královičová	С
APVV-18-0131	1.7.2019 - 30.6.2023	241 058.00	95 199.00	Zora Váradyová	W
APVV-18-0389	1.7.2019 - 30.6.2023	224 672.00	224 672.00	Dušan Fabian	С
APVV-19-0111	1.7.2020 - 30.6.2024	248 810.00	64 996.00	Jana Antalíková	W
APVV-19-0435	1.7.2020 - 30.6.2024	230 000.00	128 525.00	Ľubica Lacinová	С
APVV-19-0093	1.7.2020 - 30.6.2024	230 000.00	167 406.00	Zdena Sulová	С
APVV-19-0094	1.7.2020 - 30.6.2024	249 941.00	100 000.00	Zdena Sulová	W
APVV-20-0141	1.7.2021 - 30.6.2024	180 000.00	35 000.00	Silvia Bágeľová Poláková	W
APVV-20-0166	1.7.2021 - 30.6.2025	230 004.00	135 004.00	Roman Holič	С
APVV-20-0344	1.7.2021 - 30.6.2025	210 000.00	147 892.00	Ľubica Niederová- Kubíková	С
APVV-20-0243	1.7.2021 - 30.6.2025	220 000.00	24 000.00	Zdena Sulová	W
APVV-20-0314	1.7.2021 - 30.6.2025	180 000.00	29 088.00	Mário Šereš	W
APVV-20-0202	1.7.2021 - 30.6.2025	220 000.00	100 181.00	Eliyahu Dremencov	С
APVV-20-0494	1.7.2021 - 30.6.2025	230 570.00	18 000.00	Alexandra Poturnayová	W
APVV-20-0204	1.7.2021 - 30.6.2025	249 428.00	80 000.00	Andrea Lauková	W
APVV-20-0129	1.8.2021 - 30.6.2025	170 000.00	118 000.00	Mária Balážová	С
	APVV-16-0439 APVV17-0130 APVV-17-0297 APVV-17-0371 APVV-18-0219 APVV-18-0219 APVV-18-0131 APVV-18-0389 APVV-19-0111 APVV-19-0435 APVV-19-0093 APVV-19-0094 APVV-20-0141 APVV-20-0166 APVV-20-0314 APVV-20-0314 APVV-20-0202 APVV-20-0494 APVV-20-0204	APVV-16-0439 1.7.2017 - 30.6.2021 APVV17-0130 1.7.2018 - 30.6.2022 APVV-17-0297 1.7.2018 - 30.6.2022 APVV-17-0371 1.8.2018 - 30.6.2022 APVV-18-0219 1.7.2019 - 30.6.2022 APVV-18-0219 1.7.2019 - 30.6.2022 APVV-18-031 1.7.2019 - 30.6.2023 APVV-18-0389 1.7.2019 - 30.6.2023 APVV-19-0111 1.7.2020 - 30.6.2024 APVV-19-0435 1.7.2020 - 30.6.2024 APVV-19-0093 1.7.2020 - 30.6.2024 APVV-20-0141 1.7.2020 - 30.6.2024 APVV-20-0141 1.7.2021 - 30.6.2024 APVV-20-0141 1.7.2021 - 30.6.2025 APVV-20-0314 1.7.2021 - 30.6.2025 APVV-20-0314 1.7.2021 - 30.6.2025 APVV-20-0494 1.7.2021 - 30.6.2025	APVV-16-0439 1.7.2017 - 30.6.2021 248 739.00 APVV17-0130 1.7.2018 - 30.6.2022 239 000.00 APVV-17-0297 1.7.2018 - 30.6.2022 249 100.00 APVV-17-0371 1.8.2018 - 30.6.2022 233 542.00 APVV-17-0028 1.8.2018 - 31.7.2022 249 998.00 APVV-18-0219 1.7.2019 - 30.6.2022 230 000.00 APVV-18-0096 1.7.2019 - 30.6.2023 178 951.00 APVV-18-0131 1.7.2019 - 30.6.2023 241 058.00 APVV-18-0389 1.7.2019 - 30.6.2023 224 672.00 APVV-19-0111 1.7.2020 - 30.6.2024 248 810.00 APVV-19-0435 1.7.2020 - 30.6.2024 230 000.00 APVV-19-0093 1.7.2020 - 30.6.2024 230 000.00 APVV-20-0141 1.7.2021 - 30.6.2024 249 941.00 APVV-20-0344 1.7.2021 - 30.6.2025 230 004.00 APVV-20-0344 1.7.2021 - 30.6.2025 220 000.00 APVV-20-0344 1.7.2021 - 30.6.2025 220 000.00 APVV-20-0494 1.7.2021 - 30.6.2025 220 000.00 APVV-20-0494 1.7.2021 - 30.6.2025 230 570.00 APVV-20-0204 1.7.2021 - 30.6.2025	APVV-16-0439 1.7.2017 - 30.6.2021 248 739.00 39 471.00 APVV17-0130 1.7.2018 - 30.6.2022 239 000.00 45 273.00 APVV-17-0297 1.7.2018 - 30.6.2022 249 100.00 249 000.00 APVV-17-0371 1.8.2018 - 30.6.2022 233 542.00 105 518.00 APVV-17-0028 1.8.2018 - 31.7.2022 249 998.00 140 179.00 APVV-18-0219 1.7.2019 - 30.6.2022 230 000.00 92 800.00 APVV-18-0399 1.7.2019 - 30.6.2023 178 951.00 133 930.00 APVV-18-0311 1.7.2019 - 30.6.2023 241 058.00 95 199.00 APVV-18-0389 1.7.2019 - 30.6.2023 224 672.00 224 672.00 APVV-19-0111 1.7.2020 - 30.6.2024 248 810.00 64 996.00 APVV-19-0435 1.7.2020 - 30.6.2024 230 000.00 128 525.00 APVV-19-0093 1.7.2020 - 30.6.2024 230 000.00 167 406.00 APVV-20-0141 1.7.2021 - 30.6.2025 230 004.00 135 004.00 APVV-20-0344 1.7.2021 - 30.6.2025 230 000.00 147 892.00 APVV-20-0344 <	APVV-16-0439 1.7.2017 - 30.6.2021 248 739.00 39 471.00 Zdena Sulová APVV17-0130 1.7.2018 - 30.6.2022 239 000.00 45 273.00 Silvia Bágelová Poláková APVV-17-0297 1.7.2018 - 30.6.2022 249 100.00 249 000.00 Klaudia Čobanová APVV-17-0371 1.8.2018 - 30.6.2022 233 542.00 105 518.00 Lubor Košťál APVV-17-0028 1.8.2018 - 31.7.2022 249 998.00 140 179.00 Andrea Lauková APVV-18-0219 1.7.2019 - 30.6.2022 230 000.00 92 800.00 Silvia Bágelová Poláková APVV-18-0096 1.7.2019 - 30.6.2023 178 951.00 133 930.00 Jana Královičová APVV-18-0389 1.7.2019 - 30.6.2023 224 672.00 224 672.00 Dušan Fabian APVV-19-0111 1.7.2020 - 30.6.2024 248 810.00 64 996.00 Jana Antaliková APVV-19-0093 1.7.2020 - 30.6.2024 230 000.00 128 525.00 Lubica Lacinová APVV-19-0094 1.7.2020 - 30.6.2024 249 941.00 100 000.00 Zdena Sulová APVV-20-0141 1.7.2021 - 30.6.2024 249 941.00 100 000.00 Zdena Sulová APVV-20-0141 1.7.2021 - 30.6.2024 249 941.00 100 000.00 Zdena Sulová APVV-20-0141 1.7.2021 - 30.6.2024 249 941.00 100 000.00 Zdena Sulová APVV-20-0141 1.7.2021 - 30.6.2024 249 941.00 100 000.00 Zdena Sulová APVV-20-0141 1.7.2021 - 30.6.2025 230 004.00 135 004.00 Roman Holič APVV-20-0344 1.7.2021 - 30.6.2025 220 000.00 24 000.00 Zdena Sulová APVV-20-0344 1.7.2021 - 30.6.2025 220 000.00 29 088.00 Mário Šereš APVV-20-0494 1.7.2021 - 30.6.2025 220 000.00 100 181.00 Eliyahu Dremencov APVV-20-0494 1.7.2021 - 30.6.2025 230 570.00 18 000.00 Andrea Lauková

^{*-&}quot;C" coordinator,"W" work package leader,

2.4.4. List of projects of the Scientific Grant Agency of the Slovak Academy of Sciences and the Ministry of Education, VEGA (for funding specify only total sum obtained from all VEGA grants in particular year)

During the evaluated period, a total of 74 VEGA projects were solved at the Centre of Biosciences SAS. List of selected most important VEGA projects:

- Bacteriocins produced by probiotic strains of the phylum Firmicutes and their use to improve health of food-producing animals. VEGA 2/0004/14, Andrea Lauková (principal investigator), 2014-2016.
- The effect of female body condition on preimplantation embryo development and success of biotechnological techniques in reproductive practice. VEGA 2/0001/14, Dušan Fabian (principal investigator), 2014-2017.
- Changes of leukemia cells drug sensitivity induced by changes of membrane drug transporters expression profile. VEGA 2/0028/15, Albert Breier (principal investigator), 2015-2018.
- Yeast phosphatidylinositol transfer proteins: lipid homeostasis and resistance to azole antimycotics. VEGA 2/0111/15, Peter Griač, (principal investigator), 2015-2018.
- Novel pathways of N-type (CaV2.2) calcium channels regulation. VEGA 2/0107/16, L'ubica Lacinová (principal investigator), 2016-2018.
- Tetraspanins and partner molecules presence in the reproductive system of cattle, their participation in gamete interaction. VEGA 2/0037/16, Jana Antalíková, (principal investigator), 2016-2019.
- The role of lipid droplets in the biotechnology of squalene production in yeast. VEGA 2/0064/16, Ivan Hapala, (principal investigator), 2016-2019.
- Bioactive substances, their significance and use to improve animals health. VEGA 2/0006/17, Andrea Lauková (principal investigator), 2017-2020.
- Digestive modulation by phytogenic and mineral feed additives in farm animals. VEGA 2/0069/17, L'ubomíra Grešáková, (principal investigator), 2017-2020.
- Analyses of allele-specific regulation of CD33 expression. VEGA 2/0057/18, Jana Královičová (principal investigator), 2018-2021
- Investigation of the mechanism of action of novel putative antidepressant drugs: pyridoindole derivatives and trace amine-associated receptor-1 (TAAR1) ligands. VEGA 2/0046/18, Eliyahu Dremencov (principal investigator), 2018-2021
- Brain plasticity associated with learned vocal communication in songbirds. VEGA 2/0068/20, L'ubica Niederová Kubíková, (principal investigator), 2020-2023.

VEGA	2016	2017	2018	2019	2020	2021
Number of projects	33	27	26	28	32	34
Funding in the year for institute (EUR)	238 624	211 712	209 697	217 986	240 913	247 745

2.4.5. List of projects supported by EU Structural Funds

In the evaluated period, we submitted projects within the Support of Industrial Research and Development Centre in the area of specialization RIS3 SK 2. These projects were intended not only to improve the infrastructure, but mainly to implement scientific results into a specific application, which was utilized by partners from the manufacturing sector.

The projects focused on the dairy industry:

- 1. Centre for the Development and Application of Advanced Methods and Procedures in the Milk Production and Processing Sector, value 1,620,000 €
- 2. A New Perspective on the Quality and Health Safety of Non-bovine Milk and Milk Products, value 7,405,000 €

After evaluation, these projects were not funded.

2.4.6. List of other projects funded from national resources

Title	Туре	Grant number	Duration	Total funding	Funding for the institute	Responsible person	Status*
Role of Neurosecretory Neurons and Calcium Signalling in Depression and Addictive Behaviour: Assessment by in-vivo Electrophysiology	SAS Scholars hip		8.10.2013 - 7.10.2017	160 000.00	160 000.00	Eliyahu Dremencov	С
Characterization of novel genes involved in meiotic chromosome segregation	SASPRO	SASPRO 1970/01/02	1.4.2015 - 31.3.2018	186 506.00	186 506.00	Silvia Bágeľová Poláková	С
Mitochondria-endoplasmic reticulum functional interplay in Wolfram Syndrome: emerging role for heart and brain protection	SASPRO	SASPRO 0063/01/02	1.3.2015 - 31.12.2018	153 825.00	153 825.00	Michal Cagalinec	С
Lipid metabolisms as a crucial regulator of mitochondrial function	SAS- MOST	SAS-MOST JRP 2016/4	1.3.2017 - 28.2.2020	74 800.00	74 800.00	Mária Balážová	С
Hormonal dysregulations in a diabetic pregnancy	Bilateral	DAAD-1476	1.1.2015 - 31.12.2016	1 936.00	1 476.00	Štefan Čikoš	С
Characterization of novel interaction partners of the N-type (Cav2.2) calcium channel	Bilateral	DAAD	1.1.2016 - 31.12.2017	4 388.00	3 148.00	Ľubica Lacinová	С
Plant extracts and essential oils as feed additives in animal nutrition: effects on meat quality and intestinal physiology	Bilateral	SAS-CNR	1.1.2016 - 31.12.2017		770.00	Iveta Plachá	С
Bacteriocins and their benefits in reduction of spoilage, biofilm- producing bacteria from food products and food industry environment	Bilateral	SK-PT-18-0005	1.1.2019 - 31.12.2022	5 400.00	5 400.00	Andrea Lauková	С
Bacteriocins, a safe way to inhibit resistant bacteria from pigs for healthy farming.	Bilateral	SK-SRB-18-0001	1.2.2019 - 31.12.2021	4 470.00	4 470.00	Andrea Lauková	С
Binding properties and function of selected yeast and human lipid transfer proteins	Bilateral / Mobility	Mob-Open-20-06	1.1.2021 - 31.12.2022	6 000.00	6 000.00	Peter Griač	С
Precursors of cardiolipin biosynthesis: reasons for aberrant accumulation, effects on mitochondrial function and morphology	MAD	SAV-AV ČR 15-02	1.1.2015 - 31.12.2017	2 422.00	2 422.00	Mária Balážová	С
Study of CD molecules on mammalian sperm	MAD	SAV-AV ČR 15-05	1.1.2015 - 31.12.2017	2 370.00	2 370.00	Jana Jankovičová	С
Role of the lipid composition of the yeast plasma membrane on resistance to antifungal drugs and other stress factors	MAD	SAV-AV ČR 16-12	1.1.2016 - 31.12.2017	1 900.00	1 900.00	Martin Valachovič Zuzana Pevalová	C/C
Barth syndrome - Study of mitochondrial morphology in a novel yeast model	MAD	SAV-AV ČR 18-25	1.1.2018 - 31.12.2021	3 117.00	3 117.00	Mária Balážová	С
Study of molecules involved in fertilization process of mammals	MAD	SAV-AV ČR 18-17	1.1.2018 - 31.12.2021	2 238.00	2 238.00	Jana Jankovičová	С
Exploring the molecular determinants and functional role of T-type channel dimerization	MAD	SAV-AV ČR 18-22	1.1.2018 - 31.12.2020	979.00	979.00	Ľubica Lacinová	С
Benefits of Bacteriocins Application In Horse Diet	MAD	PL-SK project 2019-2022	1.1.2019 - 31.12.2022		-	Andrea Lauková	С
Study of membrane proteins associated with extracellular vesicles in the mammalian reproductive tract	MAD	SAV-AV ČR-21- 05	1.1.2021 - 31.12.2022	3 000.00	3 000.00	Katarína Michalková	С
Application of thymol as feed additive in rabbit nutrition	Mobility	Mob-Open-20-02	1.1.2021 - 31.12.2022	6 000.00	6 000.00	Iveta Plachá	С

^{* &}quot;C" coordinator

2.4.7. List of projects funded from private funds

Molecular and physiological properties of honeybee royal jelly proteins.

- Coordinator: Katarína Bíliková, 4/2021 3/2022, cooperation with Japan Royal Jelly Co. Ltd. -Tokyo – Japan (total funding 30 000 €/ funding in the year 2021 - 18 527 €)
- The scientific program is focused mainly on the research on honeybee royal jelly as a health promoting substance and as a functional food. The aim is identification of the compounds of royal jelly responsible for the positive effects on human immunity and for protection against of some civilization diseases in order to apply the knowledge in the development of a new products of the JRJ company.

Monitoring of the physiological potential of royal jelly based on new scientific knowledge.

- Coordinator: Katarína Bíliková, 4/2021 12/2021, cooperation with Laboratoires ARKOPHARMA, Carros, France (total funding 80 000 €/ funding in the year 2021 11 864 €)
- The aim of the Project was identifying and testing substances responsible for the medicinal effects of honeybee products in order to gain new knowledge to elucidate their physiological activity as well as to their contribution to human health with the aim their usage in the industrial context of the pharmaceutical company Arkopharma. The research was focused on testing of the quality and storage conditions of the royal jelly and honey used for production of Arkopharma's products, and checking the content of active substances in the final products.

2.4.8. List of projects funded from other competitive funds

none

2.5. PhD studies and educational activities

2.5.1. List of accredited programmes of doctoral studies, period of validity, source of funding

4.2.10 Animal Physiology

- Faculty of Natural Sciences, Comenius University in Bratislava
- Faculty of Natural Sciences, University of P.J. Šafárik in Košice

4.1.22 Biochemistry

- Faculty of Chemical and Food Technology, Slovak Technical University in Bratislava
- Faculty of Natural Sciences, Comenius University in Bratislava

4.1.12 Biophysics

- Faculty of Mathematics, Physics and Informatics, Comenius University in Bratislava
- Faculty of Natural Sciences, University of P.J. Šafárik in Košice

6.3.3 Veterinary Morphology and Physiology

- University of Veterinary Medicine and Pharmacy in Košice

4.2.7 Microbiology

- University of Veterinary Medicine and Pharmacy in Košice

The accreditations for all programs were awarded without temporal limitations. Source of funding – budget of the Slovak Academy of Sciences.

2.5.2. Summary table on doctoral studies (number of internal/external PhD students at the end of the year; number of foreign PhD students, number of students who successfully completed their theses during the year, number of PhD students who guit the programme during the year)

PhD study		2016		2017			2018		2019			2020				2021		
Number of potential PhD supervisors		49		51			43		45		46			49				
PhD students	number, end of year	defended thesis	students quitted	number, end of year	defended thesis	students quitted	unumber, end of yea	defended thesis	students quitted	number, end of year	defended thesis	students quitted	number, end of year	defended thesis	students quitted	number, end of year	defended thesis	students quitted
Internal total	22	5	2	23	5	0	25	5	1	30	1	1	28	6	1	26	6	1
from which foreign citizens	0	0	0	0	0	0	1	0	0	1	0	0	1	0	0	4	0	0
External	2	0	0	2	0	0	2	0	0	2	0	0	2	0	0	2	0	0
Other supervised by the research employees of the institute	1	0	0	1	1	0	1	0	0	3	0	0	2	0	0	1	1	0

2.5.3. PhD carrier path – Information on the next career steps of the PhD graduates who received their degree from the institute

Ing. Monika Buríková, PhD. (2016) - postdoc at BMC SAS; maternity leave

Mgr. Żofia Janštová, PhD. (2016) – postdoctoral fellow, Biotalentum Kft, Godollo, Hungary

Mgr. Kristína Lukáčová, PhD. (2016) - non-science field

Mgr. Katarína Pichová, PhD. (2016) - postdoc at CBs SAS

MVDr. Eva Straková, PhD. (2016) - unemployed

MVDr. Monika Wencelová, PhD. (2016) - Austrian Federal Ministry of Social Affairs, Health, Care and Consumer Protection, Vienna, Austria (Position - Junior Expert)

Ing. Martina Guzyová, PhD. (2017) - postdoc at FCFT SUT, maternity leave

Mgr. Veronika Kovaříková, PhD. (2017) – postdoc at CBs SAS

MVDr. Vladimíra Oceľová, PhD. (2017) - Scientist, Biomin, Austria

Mgr. Lucia Pavlíková, PhD. (2017) – postdoc at CBs SAS

RNDr. Jana Pisarčíková, PhD. (2017) - School of Optometry & Vision Science, University of New South Wales, Sydney, Australia.

RNDr. Jana Ščerbová, PhD. (2017) – postdoc at CBs SAS

MVDr. Ivana Kubašová, PhD. (2018) – postdoc at CBs SAS

Mgr. Katarína Macková, PhD. (2018) - postdoctoral fellow, Institute for Biomedicine, Bolzano, Italy

Mgr. Lucia Moravčíková (Lapínová), PhD. (2018) – postdoc at CBs SAS, maternity leave

Ing. Lucia Pokorná, PhD. (2018) - postdoc at CBs SAS

Mgr. Veronika Virčíková, PhD. (2018) - non-science field

MVDr. Anna Čuvalová, PhD. (2019) – private sector (microbiology), Slovakia

Mgr. Ivana Mišová, PhD. (2019) - science field - private company, Slovakia; maternity leave

Mgr. Martin Cagala, PhD. (2020) - postdoc at CBs SAS

Mgr. Zsofia Csáky, PhD. (2020) - science field - private company, Hungary; maternity leave

MVDr. Monika Holodová, PhD. (2020) – Assistant Professor, Faculty of Medicine, PJ Šafárik University Košice, Slovakia

Ing. Szilvia Kontár, PhD. (2020) - postdoc at CBs SAS

RNDr. Martina Kšiňanová, PhD. (2020) – postdoc at CBs SAS

Mgr. Dominika Kubalová, PhD. (2020) - product manager at pharmaceutical company, Slovakia

Mgr. Simona Kureková, PhD. (2020) - postdoctoral fellow, Department of Biology, Faculty of Medicine and Dentristy, Palacký University Olomouc, Czech Republic

Mgr. Daniela Ledecká, PhD. (2020) - non-science field

RNDr. Dominika Batťányi (Mravčáková), PhD. (2021) – postdoc at CBs SAS

Ing. Ivana Borovská, PhD. (2021) - postdoc at CBs SAS

MVDr. Lívia Karahutová, PhD. (2021) – postdoc at CBs SAS

Ing. Zuzana Kočibálová, PhD. (2021) – postdoctoral fellow, Department of Molecular Biosciences, the Wenner-Gren Institute, Stockholm University, Stockholm, Sweden

Ing. Tomáš Kyca, PhD. (2021) - postdoc at CBs SAS

Mgr. Justína Mertušová (Polomová), PhD. (2021) - science publishing - CVTI, Slovakia

PhDr. Jozef Pisko, PhD. (2021) – postdoc at CBs SAS

2.5.4. Summary table on educational activities

Teaching	2016	2017	2018	2019	2020	2021
Lectures (hours/year)*	181	154	176	99	157	79
Practicum courses (hours/year)*	290	183	222	382	287	219
Supervised diploma and bachelor thesis (in total)	53	59	64	50	51	51
Members in PhD committees (in total)	14	7	9	9	13	13
Members in DrSc. committees (in total)	2	0	2	0	2	0
Members in university/faculty councils (in total)	4	4	4	5	5	5
Members in habilitation/inauguration committees (in total)	5	5	3	2	4	4

2.5.5. List of published university textbooks

BREIER, Albert - LAKATOŠ, Boris - VAREČKA, Ľudovít - MIHALOV, J. - BARTEKOVÁ, Monika. Princípy molekulárnej medicíny [The principle of Molecular Medicine: University textbook]. Bratislava: Fakulta chemickej a potravinárskej technológie STU, 2017, p. 306, ISBN 978-80-89597-59-8, e-book.

SOPKOVÁ, Drahomíra - VLČKOVÁ, Radoslava - ONDRAŠOVIČOVÁ, Silvia - ANDREJČÁKOVÁ, Zuzana - PETRILLA, Vladimír - FAIX, Štefan - FABIAN, Dušan. Veterinárna fyziológia II: pre poslucháčov ŠP Všeobecné veterinárske lekárstvo a Hygiena potravín. [Veterinary Physiology II: textbook for students of University of Veterinary Medicine and Pharmacy], Eds. Katarína Holovská, Zuzana Maková. Košice: UVLF, 2019, p. 183, ISBN 978-80-8077-647-3.

SOPKOVÁ, Drahomíra - VLČKOVÁ, Radoslava - **FABIAN, Dušan**. Fyziológia endokrinológie a reprodukcie : pre poslucháčov ŠP Vzťah človek - zviera a jeho využitie v canisterapii a hipoterapii. [Physiology of Endocrinology and Reproduction: textbook for students of University of Veterinary Medicine and Pharmacy], Eds. Igor Valocký, Zuzana Maková. Košice : UVLF, 2020. 77 s. ISBN 978-80-8077-676-3

2.5.6. Number of published academic course books

N/A

2.5.7. List of joint research laboratories/facilities with universities (2016-2021)

Joint research laboratory: Institute of Molecular Physiology and Genetics, CBs SAS and Faculty of Chemical and Food Technology, Slovak University of Technology in Bratislava

Joint research laboratory: Institute of Animal Physiology, CBs SAS and University of Pavol Jozef Safarik in Kosice

Joint Research laboratories: Institute of Animal Biochemistry and Genetics, CBs SAS and Faculty of Natural Sciences. Comenius University. Bratislava

Joint research laboratory: Institute of Animal Biochemistry and Genetics, CBs SAS and Faculty of Mathematics, Physics and Informatics, Comenius University in Bratislava

2.5.8. Supplementary information and/or comments on doctoral studies and educational activities – focused on what changes have occurred since the last evaluation in 2016

Traditionally, PhD studies at CBs SAS have an international component. In the assessed period, three graduate students were awarded fellowships to perform a short-term visit at collaborating institutions abroad:

- Jana Pisarčíková (09/28/2016-01/31/2016): SAIA Short-Term Fellowship, 4-month stay in the laboratory of Prof. Angela Calderon, Drug Discovery and Development Department, Auburn University, Harrison School of Pharmacy, United States.
- **Dominika Kubalová (09/15/2018-12/15/2018):** EMBO Short-Term Fellowship, 3-month stay in European Molecular Biology Laboratory (EMBL), Structural and Computational Biology Unit, Heidelberg, Germany, the laboratory of Dr. Anne-Claude Gavin.
- **Alexandra Piteľová (2021):** Scholarships of Dr. Ludmila Sedlárová Rabanová for short-term stay in Department of Cell Biology, Charles University, Prague, Czech Republic.

In addition, graduate students gain international experience by active participation at international conferences. In 2016-2021, our graduate students received travel grants to attend conferences abroad and awards for presentations at conferences abroad or at international conferences organized in Slovakia:

- **Ivana Borovská (2019):** Travel grant to attend the symposium "Horizons in Molecular Biology" in Göttingene, Germany. Title of presentation: "Mutations in RNA Recognition Motifs of PUF60 and U2AF65 Occuring in Cancer and their Impact on 3' Splice Site Selection".
- **Daniil Grinchii (2019):** Travel grant to attend conference of European College of Neuropsychopharmacology (ECNP) in Copenhagen, Denmark. Title of presentation:"Ligands of trace amine-associated receptor 1 modulate in vivo excitability of rat serotonin and dopamine, but not norepinephrine neurons.
- **Lucia Lapínová (2016):** EBSA 2016 award for best presentation in competition "EBSA student competition", 4th European Joint Theoretical / Experimental Meeting on Membranes", September 7-9, 2016, Bratislava, Slovakia. Title of presentation: "Grina modulates G-protein-mediated inhibition of Cav2.2 calcium channels".
- **Zsófia Csáky (2016):** a winner of "the Best Young Scientist Poster Award", 43rd Annual Conference on Yeasts 2016, May 10-13, 2016, Smolenice, Slovakia, Title of presentation: "Mechanisms of squalene toxicity in yeast cells defective in lipid droplet biogenesis".
- **Zsófia Csáky (2017):** a winner of "the Best Short Oral Presentation", Yeast Lipid Conference 2017, May 17-19, 2017, Paris, France. Title of presentation: "Lipotoxicity of squalene to yeast cells defective in lipid droplet biogenesis."
- **Justína Polomová (2017):** "the Best Student Poster", 44th Conference of Czech and Slovak Ethological Society, November 22-25 2017, Jihlava, Czech Republic.
- **Katarína Pichová (2018):** "the Best scientific poster presentation" selected by Department of Experimental Medicine, Medical University of Silesia in Katowice, 5th International Seminar on Behavioral Methods, September 27-29, 2018, Krakow, Poland.
- **Justína Polomová (2019):** "the Best Poster Presentation", 6th European Student Conference on Behaviour and Cognition, September 4-7, 2019, Padua, Italy, Title of presentation: "Are naive zebra finch females able to discriminate between different male songs?"
- **Justína Mertušová (Polomová) (2020):** a winner of "the Best Presentation", 47th Conference of Czech and Slovak Ethological Society, October 30-31, 2020, on line form.
- 15 PhD students spent short (less than one month) or longer period in the collaborating labs abroad:
- Mgr. Dominika Čimborová (2016): short-term stay, Institute of Experimental Medicine, the Czech Academy of Sciences, Prague, Czech Republic.
- Mgr. Zsófia Csáky (2016): 2x short-term stay, Institute of Physiology, the Czech Academy of Sciences, Prague, Czech Republic.
- **MVDr. Ivana Kubašová (2016):** short-term stay, Kielanowski Institute of Animal Physiology and Nutrition, Polish Acadmy of Sciences, Jabłonna, Poland.
- MVDr. Ivana Kubašová (2017): 1-month stay at University of Natural Sciences, Ås, Norway.

- **RNDr. Lucia Moravčíková (Lapínová) (2017):** 2-month stay at Institute of Experimental and Clinical Pharmacology and Toxicology, the laboratory of Prof. Norbert Klugbauer (DA/AD project between Slovakia and Germany).
- Mgr. Zsófia Csáky (2017): 10-month stay at Université de Fribourg, Fribourg, Switzerland, the laboratory of prof. Schneiter.
- MVDr. Monika Holodová (2017): 1-month Short-Term Scientific Mission (STSM) at Department of Animal Nutrition and Feed Management, Faculty of Veterinary Medicine and Animal Science, Poznan University of Life Sciences, Poznan, Poland
- **Mgr. Dominika Kubalová (2017):** short-term stay at Tunghai University in Taiwan, Tunghai, Taiwan (SAS-MOST Joint Research Project).
- Mgr. Zuzana Skalná (2017): 1-month stay at University of Bristol, United Kingdom.
- **Mgr. Paulína Káňovičová (2018):** short-term stay at Tunghai University in Taiwane (bilateral collaboration SAS-MOST Joint Research Project).
- **Mgr. Dominika Mravčáková (2018):** 1-month stay in the laboratory of Prof. Dr. Adam Cieslak, Poznan University of Life Sciences, Poland.
- Mgr. Dominika Mravčáková (2018): 1-month stay in Department of Immunology, Veterinary Research Institute, Brno, Czech Republic.
- MVDr. Eva Bino (2017): short-term stay at INRA, Jouy-en-Josas, France.
- **MVDr. Eva Bino (2018):** 1-month stay at University in Madrid, Faculty of Veterinary Medicine, Madrid, Spain.
- MVDr. Eva Bino (2018): short-term stay at Masaryk University, Brno, Czech Republic.
- **RNDr. Dominika Mravčáková (2019):** short-term stay in Department of Veterinary Medicine and Animal Production, University of Naples "Federico II", Naples, Italy.
- RNDr. Dominika Mravčáková (2019): short-term stay in Laboratory of Veterinary Epidemiology and Economics, Faculty of Veterinary Medicine, Warsaw University of Life Sciences, Warsaw, Poland.
- **RNDr. Dominika Mravčáková (2019):** short-term stay in Department of Animal Nutrition, Faculty of Veterinary Medicine and Animal Science, Poznan University of Life Sciences, Poznan, Poland.
- Mgr. Katarína Kucková (2019): short-term stay in Department of Animal Nutrition, Faculty of Veterinary Medicine and Animal Science, Poznan University of Life Sciences, Poznan, Poland.
- **Mgr. Kristína Bačová (2019):** 3-month stay (Ernst-Mach scholarship, Austria-Slovakia), Institute of Animal Nutrition and Functional Plant Compounds, Vienna University, Vienna, Austria.
- **Mgr. Paulína Káňovičová (2019):** short-term stay in Department of Chemistry, Tunghai University, Taichung, Taiwan.
- PhDr. Jozef Pisko (2020): 5-month stay, the Faculty of Medicine, Martin Luther University, Halle, Germany.
- **RNDr. Dominika Mravčáková (2020):** 3-month stay at University of Las Palmas de Gran Canaria, Faculty of Veterinary Medicine, Department of Animal Pathology, Animal Production, and Food Science and Technology, Las Palmas de Gran Canaria, Spain.
- **Ing. Daniel Petrič (2020):** 2-month stay in Department of Animal Nutrition, Faculty of Veterinary Medicine and Animal Science, Poznan University of Life Sciences, Poznan, Poland.
- **Ing. Daniel Petrič (2021):** 1-month stay in Department of Animal Nutrition, Faculty of Veterinary Medicine and Animal Science, Poznan University of Life Sciences, Poznan, Poland.
- Mgr. Alexandra Piteľová (2021): 1-month stay in the Laboratory of GenoMik, Faculty of Life Sciences, Charles University, Prague, Czech Republic.
- **PhDr. Jozef Pisko (2021):** 5-month stay, Faculty of Medicine, Martin Luther University, Halle, Germany.

Additional honours including 18 awards for presentations at national conferences in Slovakia, 1x award "Student of the Year 2015/2016" (Kristína Lukáčová), 1x award of SAS Presidium to a PhD student who is a co-author of the publication published in a high-impacted journal Plos Genetics (Ivana Mišová, 2017). 1x Certificate of merit in competition: Prize of Dr. L'udmila Sedlárová Rabanová, Faculty of Natural Sciences, Comenius University, Bratislava (Lucia Pokorná, 2018),1x award of the Dean of Faculty of Natural Sciences, Comenius University (Justína Polomová, 2019), 1x Prize of Zdenek Veselovsky to a first-author of publication published in Proceedings of the Royal Society B in 2019 (Justína Mertušová, (Polomová) 2019),1x Prize of the Slovak Academy of Agricultural Sciences for best publications with significant theorethical contribution (Lívia Karahutová, 2020), and a winner of PhD student competition of the Slovak Academy of Sciences in 2021 (Ivana Borovská, 2021).

2.6. Societal impact

2.6.1. The most important case studies of the research with direct societal impact, max. 4 for institute with up to 50 average FTE researchers per year, 8 for institutes with 50 – 100 average FTE researchers per year and so on. Structure: Summary of the impact; Underpinning research; References to the research; Details of the impact; Sources to corroborate the impact. One page per one case study

Health risk assessment of the pesticide fipronil

<u>Summary of the impact:</u> The results of this study were used by organizations conducting a human health risk assessment. American authorities requested our research team for detailed data.

Underpinning research & References to the research: In this study, the possible toxicity of phenylpyrazole fipronil, the related commercial product FIPRON spot-on and FIPRON spot-on secondary ingredients on the developmental capacities and quality of mouse preimplantation embryos was evaluated. During in vitro tests, isolated two-cell stage embryos were cultured in media supplemented with the listed chemicals until blastocyst formation. Stereomicroscopic evaluation of in vitro-produced embryos showed that fipronil at 1 µM and higher concentrations negatively affected embryonic development. Fluorescence staining revealed that the obtained blastocysts displayed lower numbers of blastomeres at 10 µM concentrations and an elevated incidence of cell death at 1 µM concentrations. The presence of FIPRON spot-on at a concentration equivalent to 10 µM fipronil caused massive degeneration of all embryos. Secondary ingredients (butylhydroxyanisolum, butylhydroxytoluenum) at corresponding concentrations negatively impacted the development and quality of preimplantation embryos as well. During in vivo tests (daily oral administration of fipronil during the preimplantation period) in embryos collected from treated female mice, a significantly elevated incidence of cell death was observed even at the acute reference dose. Fipronil impaired the development and quality of mouse preimplantation embryos in both in vitro and in vivo tests. Embryotoxicity of the commercial product FIPRON spot-on was potentiated by the presence of secondary ingredients (10.1016/j.tox.2018.08.008).

<u>Details of the impact & Sources to corroborate the impact:</u> Two organizations conducting a human health risk assessment used these results in their evaluation process. The United States Environmental Protection Agency Office of Pesticide Programs (https://www.epa.gov/pesticides) and California Department of Pesticide Regulation (https://www.epa.gov/pesticides) and California Department of Pesticide Regulation (https://www.epa.gov/pesticides) and California Department of Pesticide Regulation (https://www.cdpr.ca.gov/dprabout.htm) asked our research team for detailed data from the experiments to include in the risk assessment (United States Environmental Protection Agency, Fipronil: Draft Risk Assessment for Registration Review, 2020, https://www.regulations.gov/document/EPA-HQ-OPP-2011-0448-0076).

Beneficial microbiota in dairy products for functional food

<u>Summary of the impact:</u> A national milk producer requested our research team to provide details about the strains included in the producer's dairy functional products.

<u>Underpinning research & References to the research:</u> Lump cheese from Slovak ewe's milk is produced from unpasteurized ewe's milk without any added culture. Because of the traditional processing and shaping by hand into a lump, this cheese was given the traditional specialty guaranteed (TSG) label. To date, there exist only a limited number of detailed studies regarding individual microbiota and their benefits in ewe milk lump cheese and raw goat milk. Therefore, it was requested from both producers and consumers to study the beneficial effects of bacteriocin (antimicrobial peptide)-producing strains of lactic acid bacteria and their utilization in dairy functional products. In our laboratory, some strains have been isolated and characterized for this purpose: Enterococcus durans ED26E/7, E. mundtii EM2/2, Lactiplantibacillus plantarum LP17L/1 and Lactococcus lactis MK1/3. The strains were sequenced and deposited in GenBank under accession numbers and deposited in the Czech Culture Collection with CCM number (following the Budapest Treaty on the Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure)

as involved in dairy drink as functional food. Based on their possible stimulation of phagocytic activity, optimizing GIT microbiota, they contribute to the health of consumers. They were assessed as safe regarding EFSA rulesusing animal models such as Balb/c mice, or broiler rabbits. The strains also produced the highest value of the lactase enzyme β-galactosidase, which is used for lactose-intolerant product preparation. Partially purified bacteriocin substances produced by the mentioned strains showed the highest inhibition activity/bioactivity against the principal dairy contaminant bacteria *Staphylococcus aureus* and listeriae (25 600-102 400 AU/mL). (10.3390/foods11070959, 10.3390/ijerph17249504, 10.3390/foods10123091, 10.11111/jpn.13570).

<u>Details of the impact & Sources to corroborate the impact:</u> Given the potential beneficial properties of strains of lactic acid bacteria isolated in our laboratory, a national milk producer requested our research team to provide detailed data and characterization of the strains that will be included in dairy functional products produced in Slovakia.

Safety and efficacy assessment of selenium feed supplements for all animal species and consumers

<u>Summary of the impact:</u> This research was used for the evaluation report of the European Union regarding selenium content.

<u>Underpinning research & References to the research:</u> Four studies deal with selenium (Se) deposition in edible tissues and/or products of ruminants, broiler chickens and laying hens (10.1016/j.smallrumres.2012.10.009, 10.2754/avb200372030339, 10.2754/avb201382010043, 10.1007/s12011-011-9125-7). The studies compared the effect of feed supplementation with selenium (total 0.3 mg Se/kg) from inorganic and organic sources (sodium selenite and selenized yeast) on the mineral and antioxidant status of livestock. Our findings indicated the better bioavailability of organic Se from Se-yeast due to its higher absorption and retention compared with sodium selenite as an inorganic source of Se. The significantly higher Se concentration in the edible tissues and products of farm animals supplemented with Se-yeast may provide a substantially larger transfer of the metabolically desirable form of selenium (selenomethionine) via the food chain into the human population. However, the inorganic source of Se was as effective as the organic source in supplying this essential trace element for improving the antioxidant status of animals.

<u>Details of the impact & Sources to corroborate the impact:</u> Using trace elements as feed additives in animal nutrition must be safe and efficacious for all animal species/categories and safe for the consumer, provided that their total maximum authorized content in complete feed is respected. Following a request from the European Commission, the Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) was asked to deliver a scientific opinion on the safety and efficacy of mineral feed additive for all animal species. The FEEDAP Panel adopted opinions on the use of Se feed additives in the frame of re-evaluation based on the results of peer-reviewed scientific papers and other scientific reports. The results of our four abovementioned studies were used by the FEDAP Panel for the regular evaluation of the safety and efficacy of Se compounds as feed additives for all animal species and the risk assessment of consumer safety (EFSA 2016, doi.org/10.2903). Based on published literature data, including our results, the executive summary of the evaluation report of the European Union concluded that the use of sodium selenite as a source of Se in animal nutrition (up to the maximum authorized Se level in feed) is safe for the consumer and does not raise concerns for the environment.

Latrophilin as a differential marker of myeloid malignancies

We verified the reciprocal relationship between ABCB1 (for P-glycoprotein) and ADGRL1 (for latrophilin 1) gene expression, which we found in the AML cell lines SKM-1 and MOLM-13 in samples from 17 patients with newly diagnosed myelodysplastic syndrome without previous chemotherapy. This identified the ADGRL1 gene as a differential marker for myeloid malignancies of blood with underdeveloped MDR mediated by P-gp. (10.3390/cancers13143629).

2.6.2. List of the most important studies and/or other activities commissioned for the decision-making authorities, the government and NGOs, international and foreign institutes (title, name of institution, contract value, purpose (max 20 words))

Expert's reports for the government and NGOs:

Name of expertise: Training on use of animals in scientific experiments

Recipient of expertise: State Veterinary and Food Administration of the Slovak Republic Compiled by Prof. DVM. Štefan Faix, DrSc.

Brief description: Lectures for employees SAS and Universities in Slovakia on the use of animals in scientific procedures

2.6.3. List of contracts and research projects with industrial and other commercial partners, incl. revenues (study title, name of institution, contract value, country of partner, purpose (max 20 words))

Study title: industrial utilization of the selected probiotic strains

Name of the institution: International Probiotic Company s.r.o. InProCo in Košice

Contract value: not specified Country of partner: Slovakia

<u>Purpose:</u> Based on this licence contract (from 2016 up to now), provider/licensor approves acceptor/purchasor for industrial utilization of the selected probiotic strains as biological material to be involved in the probiotic products for broiler rabbits, of which is acceptor/purchasor producer, and which will be sold on consumer market using registered mark of acceptor/purchasor PRORABBIT (EF2019-CCM7420) and PROBIODOG (L. fermentum AD1-CCM7421).

Study title: research results utilized in industrial dairy practice

Name of the institution: Leonteus s r.o. Kozí vŕšok location Ventúrska 3, Bratislava

<u>Contract value:</u> not specified <u>Country of partner:</u> Slovakia

<u>Purpose:</u> Future contract agreement (from 2018 up to now) to utilize results from the project APVV-17-2008 in industrial dairy practice between Institute of Animal Physiology SAS in Košice and customer Leonteus s r.o. Kozí vŕšok location Ventúrska 3, Bratislava, workplace in Kozí vŕšok, Ivachnová 304, 034 83 Liptovská Teplá in representation of Ing. Martin Gračka.

Study title: hybridomas producing monoclonal antibodies

<u>Name of the institution:</u> EXBIO Praha, a.s., its registered office at Nad Safinou II 341, 252 50 Vestec, Czech Republic

Contract value: not specified

Country of partner: Czech Republic

<u>Purpose:</u> Since 2019 up to now, the Institute of Animal Biochemistry and Genetics CBs SAS provides hybridomas producing monoclonal antibodies (CD9 - IVA50, CD18-IVA35, CD41/61-IVA30, CD45R-IVA103, CD62L-IVA94, Bovine IgG light chain IVA- 285-1, MHC class I-IVA26).

<u>Study title:</u> Monitoring of markers of multidrug resistance in patients with acute myeloid leukemia and myelodysplastic syndrome.

Name of institution: National Oncology Institute

Contract value: Nom-profit contract

Country of partner: Slovakia

Purpose:

Primary goal: Identification of biomarkers of resistance in patients with myelodysplastic syndrome and acute myeloid leukemia

Secondary goals: To find out the pharmacotherapeutic and diagnostic procedures in the management of the researched population. Analysis of the responses of cancer patients to treatment with different pharmacotherapeutics

- 2.6.4.1 List of intangible fixed assets (internally registered IP (confidential know-how), patent applications, patents granted, trademarks registered) denoting background IPR
- 2.6.4.2 List of licences sold abroad and in Slovakia, incl. revenues (background IPR identification, name of institution, contract value, country of partner, purpose (max 20 words))
- 2.6.5. Summary of relevant activities, max. 300 words (describe the pipeline of valorization in terms of Number of disclosure, Number of registered IP internally, number of CCR/LIC contracts and their respective summary values, the support you are receiving in specific points internally at the institute, at SAS, externally also the limitations and drawbacks.

2.7. Popularisation of Science (outreach activities)

2.7.1. List of the most important popularisation activities, max. 20 items

- Researchers and PhD. students from the Centre of Biosciences SAS regularly participated in the European Researchers' Nights, a public science festival held every September. It presents variety of interesting research topics to the general public and young people. These activities for the popularisation of science include numerous oral, audiovisual, and poster presentations of scientific results and laboratory practice, accompanied by discussions and interviews with researchers, exhibitions, and various competitions.
- Open Door Days at the institutes of the Centre of Biosciences SAS for students and the general
 public are organized yearly as the part of the Week of Science and Technology in the Slovak
 Republic (organized by the Ministry of Education, Science, Research and Sport of the Slovak
 Republic).
- 3. Researchers and PhD. students from the Centre of Biosciences SAS regularly contribute articles to the content of the scientific portal Veda na dosah, www.vedanadosah.sk.
 - Mgr. Marta Gaburjáková, PhD. "Aby srdce fungovalo tak, ako má" (To make the heart work as it should), 2019
 - Mgr. Jana Gaburjáková, PhD.: "Ako reaguje srdce, keď je človek v strese" (How the heart responds when a person is stressed). 2019
 - RNDr. L'ubor Košťál CSc., RNDr. Boris Bilčík, PhD. "Spôsob chovu sliepok je odrazom spoločnosti. Ako sú na tom Slováci?" (The way hens are bred reflects society. How are Slovaks doing?), 2020
 - Mgr. Silvia Bágeľová Poláková, PhD. "Slovenskí vedci spravili významný objav pre onkologický výskum" (Slovak scientists make an important discovery for cancer research), 2021
- 4. Young researcher Mgr. Katarína Macková, PhD. participated in "Roadshow mladých vedcov SAV po školách Slovenska" (Roadshow of young scientists SAS in Slovakian schools) (https://www.sav.sk/index.php?doc=services-news&source_no=20&news_no=8495), 2019
- 5. PhD. student, Mgr. Paulína Káňovičová and young researcher Mgr. Katarína Macková, PhD. from the Centre of Biosciences SAS participated in Science Slam Event, https://vedanadosah.cvtisr.sk/tag/science-slam/, 2020
- 6. Researchers from the Centre of Biosciences SAS regularly contribute articles to the content of the scientific journal for science and technology Quark, www.quark.sk
 - RNDr. Boris Bilčík, PhD., Mgr. Mariana Máčajová, PhD.: "S prepeličkami proti rakovine" (With quails against cancer), 2017
 - Mgr. Martina Garaiová, PhD., Mgr. Roman Holič, PhD.: "Mikroskopicka tovaren" (Microscopic factory), 2020
- 7. Senior researchers from the Centre of Biosciences SAS are often guests in the slovak national telecommunication media RTVS, www.rtvs.sk
 - prof. RNDr. L'ubica Lacinová, DrSc., "Nočná pyramída" (Night pyramid), 2016

- RNDr. L'ubor Košťál, CSc.: "Správanie sa zvierat v zajatí a vo voľnej prírode" (Behavior of animals in captivity and in the wild), 2017
- MVDr. Vladimíra Oceľová, PhD.: European Researcher's Night interview, 2017
- prof. Ing. Albert Breier, DrSc. "Nočná pyramída" (Night pyramid), 2021
- 8. Researchers from the Centre of Biosciences SAS regularly give popularisation lectures for public
 - MVDr. Dušan Fabian, DrSc.: "Vajíčko na vandrovke" (An egg on a hike), Summer School Viva la Science, Slovak university of agriculture in Nitra, annual lecture: 2018-2021
 - prof. MVDr. Vladimír Kmeť, DrSc: "Aj baktérie sa spolu rozprávajú" (Bacteria also talk to each other), Museum of the First Slovak Grammar School in cooperation with Quirinus c.a., Revúca, 2018
 - prof. MVDr. Vladimír Kmeť, DrSc: "Vesmírna mikrobiológia" (Space microbiology), Libresso Books & Coffee, Science café, Prešov, 2020
 - prof. RNDr. L'ubica Lacinová, DrSc.: "Elektrické javy v bunkách" (Electrical phenomena in cells) at Caffee Leháro, Trnava, 2018
- Senior researchers RNDr. Boris Bilčík, PhD. and RNDr. L'ubor Košťál, CSc. are authors of the book chapter "Projekt Prepelica." v Slovenské vesmírne odysey: (spomienky a prognózy pri príležitosti 20. Výročia letu na stanicu Mir)" (The Quail Project. In Slovak space odysseys: (reminiscences and forecasts on the occasion of the 20th anniversary of the Slovak flight to Mir station)), Veda, ISBN 978-80-224-1803-4, 2020
- 10. Senior researcher Mgr. L'ubica Niederová, PhD. gave interview which has been published in magazine Týždeň, "Čo robí behaviorálny neurobiológ?" (What does behavioral neurobiologist do?), https://www.tyzden.sk/veda/38726/co-robi-behavioralny-neurobiolog/, 2017
- 11. Research outcomes of experimental work of Mgr. Silvia Bágeľová Poláková, PhD. and collaborators were communicated via different broadsheet and mainstream media, https://www.trend.sk/spravy/popisali-protein-co-pomaha-opravit-poskodenu-dna-stat-im-to-nechcel-dat-peniaze, https://tech.sme.sk/c/20409451/zistila-ako-si-bunky-opravuju-dna-ocenili-mladu-slovensku-vedkynu.html, 2016
- 12. News and actual activities of researchers and PhD. students from the Centre of Biosciences SAS are regularly posted on SAS webpage and social networks, www.cbv.sav.sk, https://www.facebook.com/centrumbioviedsav

2.7.2. Table of outreach activities according to institute annual reports

Outreach activities	2016	2017	2018	2019	2020	2021	total
Articles in press media/internet popularising results of science, in particular those achieved by the Organization	6	6	1	11	11	12	47
Appearances in telecommunication media popularising results of science, in particular those achieved by the Organization	2	4	1	2	1	1	11
Public popularisation lectures	27	22	27	25	24	14	139

2.8. Background and management. Infrastructure and human resources, incl. support and incentives for young researchers

2.8.1. Summary table of personnel

2.8.1.1. Professional qualification structure (as of 31 December 2021)

		Degre	Res	sition			
	DrSc./DSc	CSc./PhD.	professor	docent/ assoc. prof.	Ι.	II.a.	II.b.
Male	7	17	4	1	6	12	6
Female	3	57	1	0	4	27	29

I. – director of research with a degree of doctor of science/DrSc.

II.a - Senior researcher

II.b - PhD holder/Postdoc

2.8.1.2. Age and gender structure of researchers (as of 31 December 2021)

Age structure of researchers	<	31	31	31-35		36-40		41-45		46-50		51-55		-60	61-65		> 65	
	Α	В	Α	В	Α	В	Α	В	Α	В	Α	В	Α	В	Α	В	Α	В
Male	4.0	1.4	0.0	0.0	3.0	3.0	2.0	1.1	3.0	3.0	2.0	2.2	3.0	1.3	5.0	4.7	4.0	2.5
Female	17.0	6.5	8.0	8.0	8.0	7.2	8.0	7.8	9.0	9.0	3.0	3.3	10.0	9.3	8.0	7.5	1.0	0.5

A – number

B-FTE

2.8.2. Postdoctoral fellowships (list of positions with holder name, starting date, duration. Add brief information about each fellow's career path before and after receiving PhD degree, etc.)

2.8.2.1. MoRePro and SASPRO fellowships

MoRePro

N/A

SASPRO

RNDr. Michal Cagalinec, PhD., SASPRO No:0063/01/02, 03/01/2015 –12/31/2018, 3 years+10 months.

Title: Mitochondria-endoplasmic reticulum functional interplay in Wolfram Syndrome: emerging role for heart and brain protection. During PhD study in the International Laser Centre (Bratislava, Slovakia), Michal Cagalinec specialized in modern methods of fluorescence microscopy and spectroscopy applied to heart and brain research. Notably, he estimated calcium transients, contractility and volume of the cardiac myocytes from spontaneously hypertensive rats treated with antihypertensive drugs. After obtaining PhD. degree in Biophysics in 2006, he aimed mitochondrial fusion/fission dynamics and morphology in neurons related to neurodegenerative diseases using confocal microscopy techniques at the University of Tartu (Tartu, Estonia) for almost 10 years. His active international collaboration is documented by his numerous foreign stays in Switzerland, Czech Republic, and Slovenia, which were funded from received international grants.

Mgr. Silvia Bágeľová Poláková, PhD., SASPRO No:0070/01/02, 04/01/2015 – 03/31/2018, 3 vears

Title: Characterization of novel genes involved in meiotic chromosome segregation. Silvia Bágeľová Poláková was enrolled as a PhD. student at both the Faculty of Natural Sciences, (Comenius

University, Bratislava, Slovakia) and at the Department of Molecular Genetics (Lund University, Lund, Sweden). Her research projects were focused on phylogenomics of nucleo-mitochondrial relationships (petiteness, evolution of mtDNA and "mitochondrial meiosis"?) and genome dynamics in non-conventional yeasts, respectively. After obtaining a PhD in Biochemistry in 2009, she worked as a post-doctoral fellow at the Department of Chromosome Biology of Max F. Perutz Laboratories (University of Vienna, Vienna, Austria) in the laboratory of Dr. Juraj Gregáň. Her project aimed at the identification of new genes required for proper segregation of chromosomes during meiosis: a genome-wide approach. She has received the following competitive fellowships: APVV grants (Slovak grant agency), SASPRO Fellowship, the People Programme (Marie Curie Actions) of the EU FP7 under REA grant agreement No. 0070/01/02, EMBO long-term fellowship, SAIA fellowship, ESF Exchange Grant within the framework of the ESF Activity entitled 'Functional Dynamics in Complex Chemical and Biological Systems', FEBS Collaborative Experimental Scholarship for Central Eastern Europe, Lawski Grant and Socrates/Erasmus Scholarship.

2.8.2.2. Stefan Schwarz fellowships (2016-2021)

RNDr. Katarína Ondáčová (Jašková), PhD., 05/01/2016, 4 years, maternity leave: 07/19/2016–08/2022.

During doctoral studies, Katarína Ondáčová developed an in vitro model of fibrotic scare, which mimicked conditions developing in the brain after traumatic injury. She characterized differences in consequences of such conditions for cerebellar granule cells and hippocampal cells. After graduation in Animal Physiology in 2015, she changed her focus to analysis of novel pathways of regulation of the neuronal $Ca_V2.2$ channel. This is also the topic of her project for Stefan Schwarz fellowship. During 6 months long internship (08/2012–12/2012) in the laboratory of prof. A. Kaasik at University of Tartu (Tartu, Estonia), she investigated mitochondrial dynamics in her fibrotic scare model. During 3 months long internship (03/2015 – 05/2015) in laboratory of prof. I. Forsythe at Leicester University (U.K.), she used electron microscopy for investigation of synaptic vesicle dynamics. In addition to Schwarz fellowship she has won 3 poster prizes, 2 travel grants for mid-term internships and 2 travel grants to visit international conferences.

Mgr. Kristína Lukáčová, PhD., 06/01/2019–05/31/2021, 3 years

Kristína Lukáčová studied mechanisms of neuronal and axonal regeneration in brain areas controlling vocal learning and production in songbirds. She found that dopamine D3 receptors play an important role during the striatal regeneration after injury and their activation accelerates the brain recovery. She started using the MRI technique to scan the brain regeneration process and pointed out the function of cerebellum in the vocal learning. In 2016, she obtained the PhD. degree both at the Comenius University in Bratislava, Slovakia, and at the University of Antwerp, Belgium. She obtained a fellowship and spent almost half a year at this university. Among other prizes, she was awarded in the Competition of young neuroscientists, obtained a travel grant for the International symposium about experimental and clinical neurobiology in 2017, and won the Competition of young scientists up to 35 years old at the Slovak Academy of Sciences in 2019. Her project for the Stefan Schwarz fellowship built upon her strong experience with MRI. She studied lesions of lateral and medial deep cerebellar nuclei and determined their connectivity, including the unknown connections with several vocal brain nuclei. She also found that the lesions affect the song in adult birds which further proved the involvement of cerebellum in this learned behavior.

Mgr. Martina Garaiová, PhD., 05/01/2017–04/30/2019, 2 years, long term-stay abroad 09/23/2017–08/07/2018.

During PhD study, Martina Garaiová focused on studying mechanisms of sterol homeostasis and accumulation of squalene in yeast *Saccharomyces cerevisiae*. After obtaining PhD degree in biochemistry in 2013, she continued in the project of squalene production and she studied the mechanism of squalene lipotoxicity. In addition, she was involved in the project aimed at the study of production of valuable fatty acids (ricinoleic acid, punicic acid) in fission yeast *Schizosaccharomyces pombe*. During her Schwarz fellowship at the Centre of Biosciences, she completed 2 long-term stays in international laboratories in China and Japan, where she was working on lipid droplet biogenesis and biotechnology of lipid production.

2.8.2.3. Postdoctoral positions from other resources (specify)

MMedSc Eliyahu Dremencov, DrSc., SAS Scholarship, 10/08/2013-10/07/2017, 4 years, Title: Role of neurosecretory neurons and calcium signalling in depression and addictive behaviour: Assessment by in vitro electrophysiology. Dr. Dremencov completed PhD study in 2004 by defending dissertation: "Dynamical mechanism of action of antidepressant drugs". After that he continued a scientific career by Postdoctoral Fellowship at University of Ottawa (Canada) and later at University of Groningen (Netherlands). He received international honors and awards in the field of Neuropharmacology (Fellowship Award of European College of Neuropharmacology, Prize for Excellence - Faculty of Medicine at University of Ottawa, Post-Doctoral Fellowship for the Outstanding PhD Graduates of Bar-Ilan University), and travel awards (University of Grenoble in France, and Travel Fellowship to attend the International Meeting of Federation of Biological Psychiatry in Berlin). His current research activities are focused on the central nervous system (CNS) mechanisms of response to different stressors, the role of these response mechanisms in pathophysiology of the stress-related brain disorders (depression, post-traumatic stress disorder or PTSD, etc.), and early preclinical assessment of the novel perspective treatment strategies for these disorders. Dr. Dremencov developed expertise in various research techniques including in vivo electrophysiology, and behavior neuroscience. He is also an Expert Consultant for the EU FP7 and Horizon 2020 Programs. Eliyahu Dremencov, after finishing SAS Scholarship, was accepted to the CBs SAS and supported by internal resources of CBs SAS.

RNDr. Jana Babeľová, PhD., PhDr. Jozef Pisko, PhD., Ing. Petra Sečová, PhD. and Ing. Ivana Borovská, PhD. after completing their PhD study were supported by resources from national project of APVV (Slovak grant agency) and three researches coming from abroad: Mgr. Jana Královičová, PhD. (United Kingdom), Mgr. Matúš Tomko, PhD. (Germany), and Dr. Norbert Weiss, PhD. (Germany) were supported by internal resources of CBs SAS.

2.8.3. Important research infrastructure introduced during the evaluation period with the information about the sources of funding (max. 2 pages)

In December 2015, two major infrastructure projects of the EU Structural Funds, of which SAS Institute of Molecular Physiology and Genetics was a partner, ended.

1. Construction of the University Science Park of the Slovak Academy of Sciences for Biomedicine (ITMS 26240220087), which included the construction of the Pavilion of Medical Institutes on Dubravská cesta 9 in Bratislava. As part of this project, the Institute of Molecular Physiology and Genetics moved from its original seat at Vlárská 5 Bratislava to its new headquarters on a campus at Dubravska cesta. Move of inventory began in December 2015 and ended in February 2016; however, the resumption of all operations at the new site took much longer. It was necessary to fulfill all legislative conditions, including accreditations, to perform chemical and biological experiments with toxic substances and biohazard materials. This process could only start when full inventory was installed at the new place, and this permit was a necessary precondition for applying for permits to work with genetically modified organisms. These lengthy administrative procedures took more than half of 2016, and it became possible to start full unlimited operation of the Institute with the cell lines in the autumn of 2016. Starting research incorporating animal models took even longer, as the accreditation of a new animal facility, part of the Pavilion of Medical Sciences, was a lengthy procedure and the process of the transfer of permits for our experiments to a new location could start only after this accreditation. The optimization of research activities in the new location and adjustment for the needs of respective research teams continued until the end of 2017. All these activities must be considered an introduction of the new infrastructure to full use. Today, the Institute of Molecular Physiology and Genetics, as an organizational unit of the Centre of Bioscience, exists organically merged in the new building, and we note a significant improvement in accommodation, despite some shortcomings in the new building that made the initial period after relocation difficult. The added value of the project is the physical presence of the research teams of the Institute of Molecular Physiology and Genetics in the Pavilion of Medical Institutes of the Slovak Academy of Sciences, which enables sharing of a wide infrastructure for bioscience. It can be stated that practically no technology is missing in this place, without which research could not continue.

2. Completion of infrastructure for modern research of the diseases of civilization (ITMS: 26230120009). The project involved the procurement of research instrumentation infrastructure. This instrument infrastructure was delivered at the end of 2015, when the Institute was still located in the old building. With relatively complex negotiations it was possible to ensure that the devices were delivered, installed and put into operation at the new headquarters of the institute. As part of the project, the Institute of Molecular Physiology and Genetics provided the following: stimulated emission depletion infrastructure, completion of infrastructure for cancer cell biology (including InCell technology), and completion of infrastructure for electrophysiological measurements of ion channels suitable for characterization of molecular processes taking place in nerves and muscles. These devices in the new premises were put into full normal operation in the first half of 2016 and were a major step forward in the infrastructure of the institute, which thus currently has sufficient infrastructure for its research. The connection with other partners of this project allows us to expand the range of methods including other technologies such as MALDI-TOF, FPLC, GS/MS, and HPLC NMR.

Following the implementation of both projects, the previously declared intention of the decision-makers to provide the necessary research support, especially in the area of resources for personnel infrastructure and for maintenance, calibration and servicing of the acquired infrastructure, has disappeared. Therefore, we keep this infrastructure running with significant problems.

Relocation of the Institute of Animal Biochemistry and Genetics to the Slovak Academy of Sciences campus in Bratislava

In 2017, the Institute of Animal Biochemistry and Genetics, the organizational unit of the Centre of Biosciences, moved to space in the reconstructed building on the campus of the Slovak Academy of Sciences in Bratislava from unsuitable premises in Ivanka pri Dunaji. This was the result of more than 10 years of effort and managerial work. The reconstructed building provided new biochemical laboratories with new laboratory furniture, hoods, offices, meeting room and animal facilities for domestic chickens, Japanese quail and songbirds (mainly zebra finches). As in the case of the Institute of Molecular Physiology and Genetics, the administrative work and adjustments to meet the requirements for obtaining permits for laboratory work of public health authorities, and permission from the State Veterinary Administration to operate animal facilities Administration took several months.

Although the relocation process restricted scientific work for several months, it brought new quality to our work conditions, easier communication with the second organizational unit of the Centre of Biosciences located on campus, new motivations and opportunities to collaborate with the other institutes of the Slovak Academy of Sciences and with the relatively close campus of the Faculty of Natural Sciences of Comenius University. Unfortunately, the enjoyment of these new standards and opportunities for scientific work was soon disrupted by the COVID pandemic.

2.9. Supplementary information and/or comments on all items 2.1 – 2.8 (max. 2 pages in total for the whole section)

The period under review was a challenging one for the management and staff of the CBs SAS, as several factors did not allow scientists to concentrate fully on their research work:

- formation of the CBs SAS through the gradual merger of three previously independent SAS organizations
- 2. physical relocation of two of the three organizational units of the CBs SAS to new buildings
- 3. the unsuccessful transformation of the organizations of the SAS from State Contributory Organizations to Public Research Institutions in 2018, which, although it failed for external reasons, took a lot of staff time at all levels of management to prepare
- 4. Covid-19 pandemics and the associated state of emergency in the Slovak Republic, which affected the way of organization and possibilities of experimental research in the CBs SAS
- 5. successful transformation of SAS organizations into public research institutions completed by 31 December 2021

Nevertheless, our researchers published 351 articles in international journals indexed in the WoS (Core Collection) database and another 33 articles in journals indexed in the Scopus database during this period. The number of publications per FTE of researchers in the accreditation period oscillated between 0.75 and 1.00 in each year (Figure 7). During this period, articles originating from the CBs SAS or its three predecessors were cited 9096 times in WoS or Scopus indexed journals. The number of citations per FTE of researchers oscillated between 17 and 25 (Figure 7).

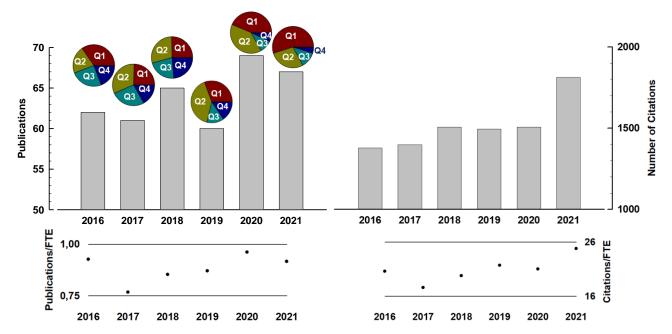


Fig. 7 Overview of the publication activity of the CBs SAS for the period subject to evaluation. Publications in journals indexed in the WoS (Core Collection) and Scopus databases are documented. Quartile rankings are from the JCR.

Among publications from 2016-2021, articles published in journals in the first and second quartiles of the JCR ranking predominate, with the proportion of articles in the first quartile increasing significantly over the last three years (Figure 7). However, the number of articles in top journals with an impact factor greater than 10 is relatively low. This may be due to the fact that some of our research teams focus on agricultural and veterinary sciences, disciplines in which journals have an objectively lower impact factor. On the other hand, the complicated situation in the support of science from state and public sources in Slovakia puts Slovak research teams at a disadvantage not only in comparison with developed Western countries, but also in relation to some post-communist countries, including the Czech Republic. So, although we are far from being falsely satisfied, the scientific outputs achieved in the period under review are close to the limit of what is achievable in the circumstances described.

The research teams of CBs SAS are largely focused on basic research. This is partly due to the history of the SAS institutes that formed the CBs SAS. On the other hand, there is a lack of industrial

partners in Slovakia willing to collaborate on research tasks with academia. As international project schemes, including those supported by the European Union, prefer research focused on commercial applications or societal impact, such partners are essential for successful project proposals. Although we have made considerable efforts in the last assessment period to attract international funding for our research, we have not been successful. In the past, when the emphasis on basic research in international project schemes was higher, we have been successful in international projects under the EU Framework Programs, Howard Hughes, Fogarty, NATO VW projects and others.

We are making great efforts to ensure a smooth generational change in CBs SAS and to bring talented, motivated young and middle-aged researchers to our institution. We use programs such as SASPRO, the SAS Fellowship or the Schwarz Fund for this purpose. In addition, despite the low salary budget of the CBs SAS, it is our policy to allocate part of this budget to new recruits with international experience. This is despite the fact that this reduces the salary budget for other staff. However, we consider this to be the only way to maintain the quality of research in the CBs SAS and to internationalize our institution.

In order to ensure the quality of doctoral studies at CBs SAS as an external educational institution, our organization maintains effective cooperation with Slovak universities. This allows us to educate multidisciplinary-oriented experts capable of finding employment in research institutions at home and abroad. We are pleased with the recently signed agreement on doctoral studies with Charles University in Prague, which will enable organizations of the Slovak Academy of Sciences to cooperate with this important university in the field of doctoral studies. We hope that similar agreements will be signed with other universities in the Czech Republic and neighbouring countries.

3. <u>Implementation of the recommendations from the previous</u> evaluation period

Because in the last evaluation the individual institutes of the Centre of Bioscience were still independent and were evaluated separately, each institute received its own recommendations, implemented separately at each institute. Therefore, organizational units describe the implementation of the recommendations from the previous evaluation period separately.

Institute of Animal Biochemistry and Genetics CBs SAS

Comments and recommendations for further improvement of the institute

- 1. The relocation of the Institute should be accompanied by a refreshed scientific vision involving other SAS institutes.
- 2. The number of DrSc still needs to be inreased. Every effort should be made to have thesis submitted.
- 3. The quality of publications needs to be increased. This is more important than quantity in the reviewers' opinion
- 4. Efforts should be made to collaborate with international leaders in the field through visiting fellowships, invitations to leading scientists, etc.
- 5. An international advisory board should be established.
- Ad1. During the assessment period, two historically significant milestones in the existence of the Institute of Animal Biochemistry and Genetics were reached. The first, relocation from the unsuitable premises in Ivanka pri Dunaji to the reconstructed building on the campus of the Slovak Academy of Sciences in Bratislava, as the result of more than 10 years of efforts of Institute management, took place in 2017. Relocation has increased the success rate of student recruitment at the BSc, MSc and PhD levels, since the original location of our institution outside the city was a disadvantage leading students to prefer other institutions. It also simplified collaboration with the institutions on campus and with colleagues from the nearby campus of the Faculty of Science of Comenius University. The second significant milestone of 2017 was the merger with the Institute of Molecular Physiology and Genetics into the Centre of Biosciences, joined in 2018 by the Institute of Animal Physiology.
- Ad2. During the evaluation period one of our colleagues, Peter Griac, submitted and defended his DrSc degree.
- Ad3. The management of the organizational part, together with its Scientific Committee of the organizational part, continued in their policy of favouring quality over quantity of publications. This is evidenced by the increased average impact factor of publications of our organizational part over the evaluation period as compared to the previous evaluation period from 2.879 to 3.792.
- Ad4. Our efforts to collaborate with international leaders in the field are evidenced by our participation in the work of several international consortia, in particular through several COST actions. For details, see 2.4
- Ad5. This was recommended independently to all 3 organizational parts of our Centre. An international advisory board for the Centre was established.

Institute of Animal Physiology CBs SAS

Comments and recommendations for further improvement of the institute

- 1. It remains necessary to focus the publication strategy on high-quality peerreviewed journals, and be ambitious in publication of highest quality science.
- 2. More high-level international collaborations with relevant groups need to be developed to give the Institute a better international profile.
- 3. Local collaborations with researchers in other SAS Institutes should be developed where joint interests are present.
- 4. Ideally, the Institute should be on a single site.
- 5. The Institute should implement a clear strategy for the future. In what field could it really make an important contribution? If more money is available, what will be done? What happens if the financial resources drop?
- 6. An international advisory board should be established.
- Ad1. The publication strategy of the Institute has been continually developed with an increasing tendency towards journal quality. The journal allocation in the Q1 and Q2 categories in the appropriate scientific sections has increased and exhibits a sustained increase. Additionally, the level of quality of our results have been supported due to publishing in journals with IFs higher than 5.
- Ad2. We continue in already existing international relationships and cooperation. Opportunities to find/open new collaborations were extremely limited because of the COVID-19 pandemic. However, despite this fact, in the period of "more open" anti-pandemic rules, we tried to create conditions for new collaborations. Our PhD students participated in short-term study stays in Germany and Poland. At the same time, colleagues from Poland participated in experiments at our institute for a 3-month period per study stay. Co-operation with the institution in Italy can also be seen in joint publications. We also continue our cooperation with the Veterinary Faculty of University in Lisbon (Portugal), which started many years ago via an international project and in a bilateral project, and this relationship has been developed continually, resulting in joint results and publications. Similar activity and joint projects are also maintained with the Kielanowski Institute in Poland.
- Ad3. We continue our cooperation on joint projects with the Parasitological Institute of the SAS in Košice. A promising development is cooperation in the framework of the Centre of Biosciences of the SAS.
- Ad4. Conditions in SAS did not allow us to situate institute workplaces in one location as recommended.
- Ad5. Tasks regarding the scientific vision at IAP and strategy for various developing alternatives to support science and research in the Slovak Republic are solved in the framework of CBs.
- Ad6. The establishment of the International Advisory Board is a common recommendation for all three organizational parts of the CBs. It has been solved within the framework of the Centre.

Institute of Molecular Physiology and Genetics CBs SAS

Comments and recommendations for further improvement of the institute:

- 1. The formation of the Centre of Biosciences should be accompanied by a review of the scientific vision, focusing on the highest quality science.
- 2. The expertise of the institute in instrumentation for molecular and cellular physiology should be the basis for technical and intellectual collaborations with others.
- 3. The size of the smallest teams should be increased or the research programmes should be modified to accommodate the staffing level.
- 4. Publication should be encouraged based on quality rather than quantity of output in and opportunities should be made to present the Institute's work at conferences.
- 5. An international advisory board should be established.
- Ad1. The Center of Biosciences was established gradually in 2016-2018 by integrating three institutes of the Slovak Academy of Sciences. There was a wider discussion between the scientific councils of the original institutes and the whole academic community to clearly specify the coherent research directions of the new center. Finally, a research direction model was developed as described in the introduction to Chapter 1.8. A system of the annual evaluation of the scientific production of all researchers was created, implemented by the Attestation Commission of the CBs SAS. After discussing the results achieved, this commission evaluates each investigator and adds recommendations for the following period. Researchers receive comments and recommendations regarding the results of their research as a result of ongoing evaluation. The evaluation of researchers focuses more on the quality of publications and their citation response. Scientists are encouraged to publish more comprehensive articles that provide broader answers to scientific questions and not compete for the number of articles published, regardless of their quality. As far as possible, the most attractive conditions for young researchers, who are motivated to improve their qualifications and design their projects, are created for a problem-free generational exchange.
- Ad2. The infrastructure and methodological equipment of the Institute of Molecular Physiology and Genetics of the CBs SAS as well as other CBs institutes are accessible to employees of other SAS organizations, universities, and other research and development institutions. As part of their research orientation, the staff of the Institute and the entire Center provide expertise and consulting services to anyone who requests it. However, this approach was unfortunately partially limited during the COVID-19 pandemic (2020-2021) by harsh epidemiological measures. In addition to the use of infrastructure in research cooperation, access is also open to the business community in the form of a service provided either free of charge or on the basis of cost calculations in the case of costly methods and equipment operation.
- Ad3. In previous years, the structure and staffing of the Institute of Molecular Physiology and Genetics, CBs SAS, have stabilized, and there are two fully functional departments in this organizational unit one focused on electrophysiology and biophysics and the other on biochemistry and cellular physiology. During the evaluated period, the research programs of these departments were updated as part of the process that takes place within the entire CBs SAS.
- Ad4. The Institute of Molecular Physiology and Genetics CBs SAS has long focused more on quality than on the quantity of scientific publications. We also consider it essential to strive for the scientific work we report, or at least significant parts of it, to be created directly at our workplace as part of the projects addressed at the institute.
- Ad5. The international advisory board of the Centre of Biosciences was created (see Page 1).

4. Research strategy and future development of the institute for the nextfive years (Recommended 3 pages, max. 5 pages)

Research strategy of the institute in the national and international contexts, objectives, and methods (including the information on when the strategy was adopted)

Outline of the general strategy

In line with the general trend of integrating fragmented research in Slovakia, we have recently created the Centre of Biosciences by merging two Slovak Academy of Sciences institutions – the Institute of Animal Biochemistry and Genetics and the Institute of Molecular Physiology and Genetics – since January 1, 2017. The Institute of Animal Physiology merged with the Centre on January 1, 2018.

The creation of the Centre is based on two basic principles:

- 1. building on traditional directions of research and decision-making processes in the management of scientific projects and the basic administration of the original institutes (now organizational parts)
- 2. supporting links between research teams of the organizational parts and creating a common identity for the Centre of Biosciences, based on the identities of individual organizational parts

In addition to sharing the Centre's joint infrastructure (despite the problem of geographical location, with two organizational parts located in Bratislava and one in Košice), joint projects linking research teams between the organizational parts have started to emerge (APVV-19-0094, APVV-20-0202, VEGA 2/0070/19).

Since January 1, 2022, the Centre of Biosciences transformed from a contributory organization to a public research institution with corresponding changes in administration. In the next period, the management of the Centre will focus on two main tasks:

- to implement changes resulting from the change in legal form in accordance with the new Act on Public Research Organizations (Act N° 243/2017) and the amendment to the Act on the Slovak Academy of Sciences (Act N° 133/2002) to take advantage of the new more independent status of the institution
- 2. to positively manage the workplace to create a wide network of horizontal links between scientific teams to fully exploit the potential generated by the creation of the Centre of Biosciences



Our vision for the Centre of Biosciences is a joint organization of three equal organizational units: One plant with three fully developed leaves.



The vision for the future development of our Centre can be summarized in the following points:

- Scientific research is focused on two basic levels: cell biology with strong use of molecular perspectives and integrative animal physiology based on molecular and cellular research.
- Research topics are relevant in the context of global biological research. The results of this
 research are published predominantly in generally accepted international journals or
 internationally peer-reviewed book publications of major publishers.
- The Centre is an attractive place for talented and highly motivated students, postdoctoral fellows and early- or medium-stage researchers with international experience.
- The Centre is a renowned partner of international and domestic research institutions and universities.
- The staff are strongly encouraged to engage in European and global research networks under various project schemes.

SWOT analysis

STRENGTHS

- clearly defined research areas
- quality of infrastructure
- continuous qualification development of employees - 4 new DrSc. degrees awarded during the evaluation period
- stable personal matrix ensuring trouble-free participation in doctoral studies
- participation in university education
- young researchers with postdoctoral or research experience abroad
- high-quality publications with adequate citation response
- cooperation between teams

WEAKNESSES

- relatively low number of publications, which is the main criterion in the annual evaluation of the workplace and also has an impact on the allocated budget
- low number of projects financed from abroad
- insufficient financial resources for motivating existing and recruiting new researchers
- limited ability to recruit and retain the most talented young scientists

OPPORTUNITIES

- recruitment of quality young scientists with international experience
- obtaining funds for research outside the state budget, especially with the use of opportunities arising from the existence of a public research institution
- cooperation with the commercial sphere (biomedical organizations, pharmaceutical and biotechnology companies)

THREATS

- lack of clear science policy objectives in Slovakia
- unstable research funding conditions in Slovakia
- fluctuations in continuous generational exchange
- "brain drain"
- problematic infrastructure sustainability

Research strategies and future plans of individual research teams

Cell Biology

Regulation of RNA splicing

We have recently described a small group of cryptic, transposon-derived exons that are characterized by shared transposon-derived structural features and predicted to be altered by the exonization-inducing mutation (10.1002/mgg3.277, doi: 10.1080/15476286.2020.1805909). Using these model exons, the main aim of our group is to define the in vivo folding pathway of pre-mRNAs during transcription and to understand how they reach their native conformation and how these dynamic rearrangements are used to regulate splicing.

Molecular basis of electrical signaling in excitable cells

We will continue to focus our research on changes in neuronal excitability underlying common pathologies. Established cooperation with the group of Michal Dubovicky enables us to directly relate observed electrophysiological changes to behavioral effects. A new member of our group trained in developing models of hippocampal neurons and neuronal networks will greatly enhance our interpretation of experimental results. Furthermore, we extend our experimental approaches from the analysis of neuronal excitability at the level of individual neurons and neuronal networks to the analysis of biochemical alterations in neuronal metabolism and the regulation of calcium homeostasis. Our recent projects are dedicated to studying the consequences of maternal depression on the offspring brain. This study includes an investigation of the effects of antidepressant therapy with mirtazapine. Additionally, we are starting to characterize excitability changes related to amyotrophic lateral sclerosis in an animal model.

For more effective use of neuronal excitability assessment for the prediction of the effectiveness of novel CNS drugs, we are aiming to develop a novel experimental approach allowing us to examine the activity of the individual brain neurons in freely moving, behaving laboratory animals.

While we will continue to characterize the cardiac ryanodine channel (RYR2) and mitochondrial chloride channels isolated from the heart as attractive molecular targets for a novel pharmacological treatment of cardiac arrhythmias, we will intensify collaboration with the neuro-research units by investigating neuronal intracellular Ca2+ and mitochondrial CI- channels and assessing the role of their dysfunction in various neuronal pathologies.

Furthermore, we aim to develop and validate a new diagnostic method that will combine an excellent binding affinity and selectivity of DNA aptamers to their targets to guarantee early detection of specific pathological conditions. In addition, expertise in the quartz crystal microbalance method will be employed to greatly advance the investigation of molecular interactions implicated in ion channel regulation by novel pharmaceutics.

Phospholipid metabolism

We will continue with the investigation of lipid metabolism. We plan to finish studies of the molecular mechanisms of yeast lipid transfer proteins (LTP) implicated in resistance to antimycotic drugs. We will explore LTPs as targets in combating fungal diseases. We also plan to study the LTP of the malaria-causing pathogen *Plasmodium falciparum* to understand how this pathogen acquires lipids from its hosts with the goal of searching for novel antimalarial targets.

Regarding mitochondrial lipid metabolism, our future study will focus on the effect of PG accumulation in the inherited mitochondrial disorder Barth Syndrome, which will be studied in yeast and human cell lines. Furthermore, we propose the role of PG as a regulatory molecule, in yeast as a regulator of mitochondrial lipid synthesis, and in the lung cells as a crucial regulatory lipid in the suppression of inflammation.

Neutral lipid metabolism and production of value-added lipids

The utilization of external sterols was suggested as one of the antifungal resistance mechanisms in some pathogenic fungi. The distribution of internalized sterols between membranes and lipid droplets is important in this process; however, the mechanisms that regulate this balance are not understood. We aim to describe machinery and key players in this process. In addition, we would like to extend our lipotoxicity studies to other ergosterol precursors (in addition to squalene) that readily accumulate in fungal cells when exposed to various antifungals.

The group working on the production of value-added lipids aims to further manipulate modified microorganisms to increase the accumulation of PuA to maximal levels. To achieve this aim, we will characterize the role of other genes from pomegranate in this process. Furthermore, we will broaden the spectrum of produced value-added lipids in yeasts to squalene and calendic acid, and we will include oleaginous microorganisms in our future research.

Multidrug resistance of leukemia cells

In the field of drug resistance in blood malignancies, we will focus on several issues. In addition to the search for new agents that are active in cells with induced (multiple) drug resistance, we will study the causes of resistance to hypomethylating agents used in the treatment of patients with AML or MDS unsuitable for induction therapy or bone marrow transplantation. To understand this issue, we have prepared a review article $\underline{10.1016/j.drup.2022.100805}$. We will also focus on substances that inhibit either histone deacylase or proteasome-mediated protein hydrolysis. Furthermore, we will focus on the altered response of cells after the induction of the ABCB1 transporter to various stress conditions, such as ERS (induced by tunicamycin or thapsigargin), irradiation with UV or γ beams or stress caused by substances with prooxidizing effects.

We will look for links between the development of resistance and the cellular content of miRNAs. To better understand the function of miRNAs in the development of drug resistance, we have published a review article 10.3390/cancers14041090. The initial part of this research is the determination of the cell content of various miRNAs in different variants of leukemic cells using a miRNA microarray chip (Agilent USA), which took place at the beginning of this year, with the data currently being bioinformatically processed.

In investigating the role of latrophilin expression in myeloid leukemia blasts, we will focus mainly on the description of changes caused by the administration of either its endogenous ligand FLRT3-protein or its xenoligand α -latrotoxin. We will also focus on the analysis of molecular forms of downstream Tim3 and galectin-9 proteins induced by latrophilin.

Research oriented in this way has the potential to bring new insights needed to understand the ways in which leukemic cells resist treatment within currently used treatment protocols.

Integrative Animal Physiology

Reproductive and Developmental Biology

Identification of new proteins and molecular mechanisms required for faithful chromosome segregation

We will focus on the characterization of molecular pathways underpinning the relationship between DNA repair and gene repression in fission yeast. On the basis of the strong similarities of basic mechanisms of chromosome segregation and DNA repair between *S. pombe* and humans, it is very likely that the identified regulators are shared by both species.

The role of tetraspanins in gamete development, maturation and fertilization

We will focus on the identification of potential partners of CD9, CD81, CD151, CD63, and other tetraspanins (such as integrins and components of lipid rafts) in cells of the male and female reproductive tracts, including gametes, using cattle as a model organism. To elucidate the role of the tetraspanin web members in gamete development, maturation, and fertilization, we will use a comprehensive approach involving histological analysis, biochemical assays, and molecular biology techniques.

Early embryo-maternal interactions

We will study early embryo-maternal interactions in physiological as well as unfavorable conditions of maternal health or under the influence of harmful environmental conditions, focusing on molecular mechanisms by which known endogenous and exogenous factors cause preimplantation development failure. Signaling pathways activated by specific ligands originating from the environment and from maternal organisms will be analyzed. Taking into account the complexity of the maternal environment, the relevant cell receptors will be investigated with emphasis on possible interactions between receptors activated by the same or by concurrent ligands. In addition, the effectivity of two basic reparatory mechanisms in preimplantation embryos, the elimination of apoptotic cells by phagocytosis, and the repair of damaged DNA by activation of reparatory proteins will be studied. The results will provide new information on the physiological abilities of early (undifferentiated and first-level-differentiated) embryonic cells to address externally induced disorders.

Neurobiology and Behavior

We are aiming for preclinical evaluation of the revolutionary novel **treatment strategies for CNS disorders**, namely, targeted nanotechnology-based intrabrain delivery of neurotrophic factor-coding mRNA and "smart" deep brain stimulation. This will involve stimulation of one brain area with a "smartly" designed train of electrical pulses generated in accordance with the simultaneously recorded neuronal activity in another brain area. These evaluations will be performed with a multidisciplinary approach, e.g., using a combination of molecular, behavioral, electrophysiological, and neuroimaging methods, as well as advanced methods of data mining.

Future plans in the field of **vocal learning** will build on our strong background in dopaminergic neurotransmission and neurogenesis, both important for structural and functional neuroplasticity. We will study the role of dopamine signaling as an internal reward system and neurogenesis in learned behavior (birdsong). We will employ the modern method of optogenetic manipulation, enabling us to modify dopaminergic neurotransmission at a specific time during the song as well as to manipulate the activity of newborn neurons during singing.

The **poultry behavior and welfare** group will focus on the study of cognition/emotion interactions, the identification of behavioral, endocrine, and neurobiological indicators of positive welfare, and the development of precision livestock farming tools using technologies such as infrared thermography, accelerometry, and machine learning (in collaboration with the Faculty of Mathematics, Physics and Informatics, Comenius University Bratislava) for the recording of animal-based measures of welfare.

Digestive tract physiology

Our research will focus on nutrition, digestive physiology, and microbiota to improve animal health. For this purpose various sources of trace elements, phytoadditives (medicinal plants, essential oils), beneficial bacterial strains and/or their combination will be investigated, from their effects on the molecular regulation mechanisms to the optimization of digestive physiology. Through the antioxidant properties of bioactive substances contained in phytoadditives (phytobiotics), we plan to strengthen the antioxidant protection of the body and increase the stability and quality of animal products. The study of metabolic and functional processes in the animal gut, focusing in particular on the transport mechanisms and bioavailability of trace elements and phytobiotics, can bring a better understanding of the mechanisms of action of the bioactive components present in feed toward desired overall animal health. Moreover, increasing micronutrient absorption and availability could reduce methane production and heavy metal pollution from animal husbandry. Our research will also focus on the antibiofilm strategy as one form of combating antibiotic bacterial resistance. The basic goal will be to gain new knowledge about biofilm formation relevant to virulence and antibiotic resistance with a focus on carbapenemases, beta-lactamases with an extended spectrum of action, and methicillin resistance, which are among the most important mechanisms of resistance. In addition, we will study the effect of plant secondary metabolites, bacterial surfactants, and short peptides on biofilm formation and quorum-sensing resistant bacteria. We will look for new possible applications of beneficial bacteriocin-producing bacteria in food protection, animal health, and prevention, as well as in companion animals. We will perform model application experiments in which we will study the interactions of the microorganism and the host organism. As part of new scientific directions, we will study the skin microbiota of healthy animals. The results of this research will contribute to a better understanding of their role during the disease and define the possibilities of suppressing the skin pathogenic microbiota by bacteriocin-producing bacteria or by the bacteriocins themselves.

Chorioallantoic membrane - in vivo model for the diagnosis and therapy of microbial infections

The treatment of various microbial and yeast infections is currently a major challenge in human and veterinary medicine because of frequent antibiotic resistance. We will focus on CAM as an in vivo model for photodynamic diagnosis and treatment of yeast and bacterial infections, examining angiogenic changes, the expression of selected genes, and histological and immunohistochemical changes after application of the treatment.