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

Period: January 1, 2012 - December 31, 2015

1. Basic information on the institute:

1.1. Legal name and address

Since January 1, 2016:
Institute of Molecular Physiology and Genetics
Slovak Academy of Sciences
Dúbravská cesta 9, SK-840 05 Bratislava
Slovakia

Previous address:
Institute of Molecular Physiology and Genetics
Slovak Academy of Sciences
Vlárska 5, SK-833 34 Bratislava
Slovakia

1.2. URL of the institute web site

http://www.umfg.sav.sk

1.3. Executive body of the institute and its composition

Directoriat	Name	Age	Years in the position
Director	doc. Ing. Oľga Križanová, DrSc.	56	2009 - 2015
	Ing. Zdena Sulová, DrSc.	59	2015 - present
Deputy director	doc. RNDr. Ľubica Lacinová, DrSc.	57	2009 - present
Scientific secretary	RNDr. Viera Boháčová, CSc.	52	2011 - present

1.4. Head of the Scientific Board

doc. RNDr. Ľubica Lacinová, DrSc. 2008 – 2013
doc. Ing. Albert Breier, DrSc. 2013 – 2015
Ing. Alexandra Zahradníková, DrSc. 2015 – present

1.5. Basic information on the research personnel

1.5.1. Number of employees with university degrees (PhD students included) engaged in research projects, their full time equivalent work capacity (FTE) in 2012, 2013, 2014, 2015, and average number of employees in the assessment period

	2012		2013		2014		2015		total		
	number	FTE	number	FTE	number	FTE	number	FTE	number	averaged number per year	averaged FTE
Number of employees with university degrees	36,0	25,591	34,0	24,650	35,0	26,626	29,0	22,526	**134,0**	**33,5**	**24,848**
Number of PhD students	9,0	9,707	10,0	8,667	7,0	8,251	4,0	5,541	**30,0**	**7,5**	**8,042**
Total number	45,0	35,298	44,0	33,317	42,0	34,877	33,0	28,067	**164,0**	**41,0**	**32,890**

1.5.2. Institute units/departments and their FTE employees with university degrees engaged in research and development

Research staff	2012		2013		2014		2015		average	
	No.	FTE	No.	FTE	No.	FTE	No.	FTE	No.	FTE
Institute in whole	36,0	25,591	34,0	24,650	35,0	26,626	29,0	22,526	**33,5**	**24,848**
Department of Cell Physiology and Genetics	14,0	9,535	13,0	9,257	14,0	8,901	14,0	3,464	**13,8**	**7,789**
Department of Cell Physiology and Genetics (from 1 May 2015)	0,0	0,000	0,0	0,000	0,0	0,000	10,0	3,749	**10,0**	**3,749**
Department of Muscle Cell Research	8,0	6,216	7,0	5,550	6,0	5,225	8,0	2,097	**7,3**	**4,772**
Department of Muscle Cell Research (from 1 May 2015)	0,0	0,000	0,0	0,000	0,0	0,000	9,0	4,520	**9,0**	**4,520**
Department of Transport Proteins	14,0	9,840	14,0	9,843	15,0	12,500	16,0	4,143	**14,8**	**9,082**
Department of Transport Proteins (from 1 May 2015)	0,0	0,000	0,0	0,000	0,0	0,000	10,0	4,553	**10,0**	**4,553**

The table reflects the changes of organizational structure in connection with the delimitation of some employees to MMC SAS on 1 May, 2015 (see Chapter 4).

1.6. Basic information on the funding of the institute

Institutional salary budget and others salary budget

Salary budget	2012	2013	2014	2015	average
Institutional Salary budget *[thousands of EUR]*	446,412	457,635	484,197	410,585	**449,707**
Other Salary budget *[thousands of EUR]*	91,838	111,757	98,094	30,013	**82,926**

1.7. Mission Statement of the Institute as presented in the Foundation Charter

Basic Purpose and Field of Activity

1. Scientific activities of Institute of Molecular Physiology and Genetics, Slovak Academy of Sciences focus on the studies in normal and pathological physiology, molecular biology, and biochemistry and biophysics of processes that occur in cells of animals, including humans.
2. Institute of Molecular Physiology and Genetics, Slovak Academy of Sciences provides doctoral studies in accredited scientific fields of biochemistry, animal physiology, and biophysics, in terms of applicable legal regulations.
3. Institute of Molecular Physiology and Genetics, Slovak Academy of Sciences fosters cooperation with worksites devoted to related scientific fields, universities and research centres, both home and abroad.
4. Institute of Molecular Physiology and Genetics, Slovak Academy of Sciences ensures publication of results of scientific and research activities by means of periodical and non-periodical press. It publishes the international journal General Physiology and Biophysics in English language.
5. Institute of Molecular Physiology and Genetics, Slovak Academy of Sciences offers consulting and expert services associated with the primary activity of the Institute.

1.8. Summary of R&D activity pursued by the institute during the assessment period in both national and international contexts, (recommended 5 pages, max. 10 pages)

The research activities of the Institute were focussed on the molecular principles of the basic cellular processes related to ion channels and transport proteins and on their malfunction in cardiac, neurological and oncological diseases. The majority of our original results were published in renowned international scientific journals that are indexed in WOS databases. In addition, the Institute publishes an international scientific journal "General Physiology and Biophysics" which is indexed in CC, WOS, SCOPUS and other databases. The main activities of the Institute could be summarised as:

1. **Molecular physiology of cardiac calcium signalling**
2. **Molecular basis of neuronal excitability**
3. **Multidrug resistance development in leukaemia cells**
4. **Gasotransmitter signalling in regulatory pathways**
5. **Study of the human genome**

1. Molecular physiology of cardiac calcium signalling

At the centre of our interests was the cardiac ryanodine receptor (RYR2), the key protein of calcium signalling and excitation–contraction coupling, which provides calcium for systolic contraction and regulates calcium homeostasis during diastole. To perform its function, RYR2 integrates numerous regulatory signals controlling the intensity of contraction. The mechanisms by which RYR2 fulfils its basic role in health and how they change in cardiac diseases was not fully understood, since only a relatively small fraction of RYR2 channels is recruited during cell activity. RYR2s form clusters in numerous independent calcium-releasing units, which are distributed between myofibrils and triggered in synchrony during systole. The reliable beat-to-beat function of cardiac myocytes is based on optimized molecular and cellular processes not yet mechanistically explained. Additionally, during diastole, when calcium accumulates into sarcoplasmic reticulum, RYR2s function as a safety valve opening spontaneously for a moment to release excess calcium to cytosol. To understand this dual function of RYR2, we adopted complex but focussed approaches.

- To find out how the RYR2 function is modulated by major intracellular players identified previously, we studied the activity of individual RYR2s reconstructed in planar lipid

bilayers. This allowed the recording of open/close transitions and determining RYR2 open probabilities at a wide range of Ca^{2+}, Mg^{2+} and ATP at the cytosolic side and of Ca^{2+} at the luminal side (Tencerova et al., J Gen Physiol 2012). This study revealed a new synergic mechanism of allosteric regulation of RYR2 by multiple ligands that explained RYR2 behaviour in systolic and diastolic phases. This finding attracted editorial comment by Dulhunty et al. (J Gen Physiol 2012). Regulation of RYR2 by calsequestrin (CSQ2), a potential luminal Ca^{2+} sensor of RYR2, was further elucidated in Gaburjakova et al., Cell. Molec. Life Sci. 2013, where, in collaboration with the Ohio State University College of Medicine (USA), we critically summarised the current knowledge about RYR2-CSQ2 interactions with a focus on structure-function relationships.

- We investigated the coupled gating of multiple RYR2s and obtained evidence that tight functional communication between RYR2s substantially affects their gating behaviour. This further strengthens our hypothesis that the main purpose of RYR2 coupling is the synchronisation of channel gates to ensure correlated Ca^{2+} fluxes (Gaburjakova and Gaburjakova, BBA-Biomembranes 2014).
- The benefit of RYR2 clustering into calcium release units was assessed from observations of RYR2 activity in isolated cardiac myocytes by the electrophysiological patch-clamp technique combined and synchronised with confocal fluorescence microscopy. This allowed recording intracellular calcium signals at high temporal and spatial resolution and determining their relation to RYR2 function *in situ* (Janíček et al., PLoS One 2013). Extensive analysis of hundreds of elementary calcium release events allowed for an interpretation by an original mathematical model that revealed the behaviour of RYR2 in dyadic clusters (Janíček et al., J Physiol 2012) and allowed for constructing the first mathematical model of calcium release units (Zahradnikova and Zahradnik, Front Physiol 2012).
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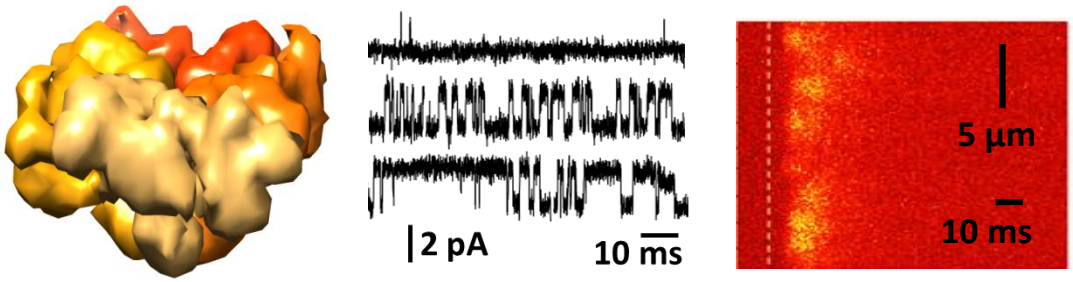


Left: Ryanodine receptor molecule. Size: 28 × 28 × 20 nm. *Centre*: Three levels of activity of a single ryanodine receptor molecule. *Right*: Calcium spikes (yellow patches) generated by a cluster of ryanodine receptors inside a cardiac cell (red area) synchronised by the voltage stimulus (vertical line).

- The question of how the regulatory mechanisms of RYR2 function translate to the formation of arrhythmogenic calcium waves in diseased myocardium was tackled by computer modelling. The data from our previous works were integrated into a mathematical model that allowed for reconstructing principal observations on calcium waves and identifying the critical factors in failing calcium signalling (Petrovič et al., J Gen Physiol 2015).
- The molecular structure of RYR2 and what we can learn from it was approached by x-ray crystallography of RYR2 domain constructs obtained by the expression of the N-terminal region of the human RYR2 region (Borko et al., Acta Cryst. D 2014, and Borko et al., Protein Pept Lett 2013). The resolution at 2.4 Å allowed the determination of the structure of the selected RYR2 region, which is the target of over 30 arrhythmogenic mutations, localisation of the region into cryo-electron microscopy maps to reveal structural changes upon open/close transitions and the determination of the binding locus of the spinophilin/protein phosphatase 1 complex on the RYR surface. This study was performed in collaboration with the Institute of Molecular Biology SAS, Cardiff University (Wales) and University of Vienna (Austria).
- In collaboration with University Paris-Sud (France), we participated in a study on the role of the GTPase dynamin protein OPA1 in mitochondrial biogenesis related to the adaptive response of skeletal muscle to training and stress (Caffin et al., J Physiol 2013). We

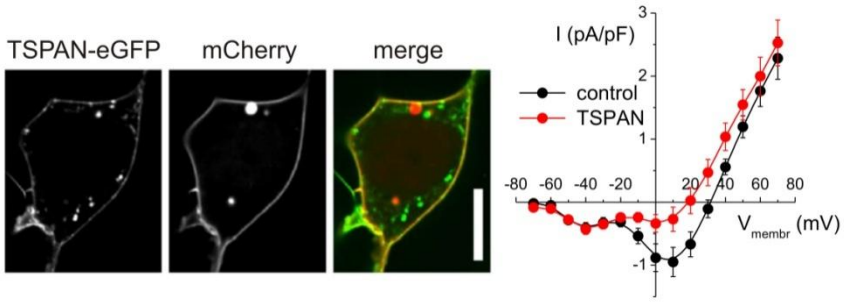
were invited to participate in reviewing the literature on mitochondria morphology, fusion/fission in relation to respiratory chain function (Piquereau et al., Cardiovasc Res 2012). The review, which revealed the importance of mitochondria in cardiac pathologies and as a potential target for pharmacological therapies, attracted editorial comment (Hall and Hausenloy, Cardiovasc Res. 2012).

In the evaluated period, the Institute participated in 19 articles on the cardiovascular topic published in international journals. The major focus of our activity was the molecular and cellular physiology of cardiac muscle cells with excursions to the cellular mechanisms of skeletal muscle cells or model tissue culture cells. Altogether, these studies received 69 citations in the period 2012 to 2014 and 48 citations in 2015 and attracted 2 editorial comments. Six of these publications were included in the set for which the collective from IMPG SAS and Institute of Molecular Biology SAS was awarded the Prize of the Slovak Academy of Sciences, 2014 for research. Authorship of 8 articles was solely by researchers of the Institute and 12 articles were prepared in domestic and foreign collaborations. Authors from the Institute were the first authors in 11 studies and the corresponding authors in 12 studies. We have published 3 review articles and 1 book chapter. The project APVV-0721-10 that examined the relationship between calcium signalling and myocardial remodelling (principal investigator A. Zahradnikova), financed by the Slovak Research and Development Agency, was evaluated as "project solved in excellent quality", and was included in the annual publication of this Agency.

2. Molecular basis of neuronal excitability

Start of neuroscience research in our institute dates back to the early 2000s when new cell culture and patch clamp laboratories were established with the help of grants from Volkswagen Stiftung and the FP6 Marie Curie research training network. International collaboration with participating laboratories and scientists is still active. The focus of the research group was on the structure, function and regulation of neuronal voltage-dependent calcium channels (VDCC).

- Mammalian expression systems (HEK293, CHO) were used for the investigation of the role of individual amino acids in the regulation of VDCC and/or channel modulation by interacting proteins and pharmacological substances. We suggested a model explaining the negative voltage threshold for activation of low-voltage-activated (T-type, Ca_V3) calcium channels (Karmazinova et al., Pflugers Arch, 2015). The closed state of these channels is stabilised by a gating brake in the loop connecting domains I and II, which directly interacts with the voltage sensor (S4 segment) in Domain I. The activation of the voltage sensor in Domain I is sufficient for the pore opening of the channel, while the activation of voltage sensors in all four channel domains is required for the pore opening of high-voltage-activated calcium channels. Therefore, lower depolarization is required for the activation of current flow through the Ca_V3 channels.
- The number of genes in the human genome was found to be surprisingly low. Therefore, complex human physiology should require multiple networks of protein-protein interactions. In line with this assumption, we described the modulation of VDCC by new interaction partners. A syntaxin-1A/$Ca_V3.2$ channel signalling complex potently modulated $Ca_V3.2$ channel activity, by reducing channel availability (Weiss et al., J Biol Chem, 2012). Tetraspanin-13 attenuated the efficiency of coupling between voltage sensor activation and the pore opening of the channel and accelerated voltage-dependent activation and inactivation of the $Ca_V2.2$ (Mallman et al., Sci Rep, 2013).



Green-marked tetraspanin protein (TSPAN) is co-localised with a membrane marker mCherry. High-voltage activated calcium current is inhibited when TSPAN is expressed.

- Two VDCCs belonging to the L-type class ($Ca_V1.2$ and $Ca_V1.3$) have a specific role in neuronal excitability. In recent years, it was revealed that while these two isoforms are very closely related structurally and, except for a slightly more negative activation threshold of $Ca_V1.3$ they also have similar functional properties, their role in cellular excitability is both tissue-specific and different. In accordance with the essential role of calcium signalling in neuronal development, the differentiation of PC12 cells into cholinergic-like neurons correlated with the upregulation of L-type calcium channels (LTCC). Nevertheless, chronic inhibition of LTCC did not affect the neurodifferentiation of PC12 cells (Lichvarova et al., Gen Physiol Biophys, 2012). The absence of calcium entry through LTCC was not compensated by the upregulation of other calcium transporting proteins because the downregulation of $Ca_V1.2$ or $Ca_V1.3$by siRNA did not alter the expression of inositol-1,4,5-trisphosphate receptor (IP3R) and ryanodine receptors (RyR) or Na-Ca-exchanger (Lichvarova and Lacinova, Gen Physiol Biophys, 2015).
- We adopted two *in vitro* models of neuronal injury. The first was based on an addition of the transforming growth factor β1 (TGFβ1) to the primary cell culture, and the second was a fibrotic scar model according to Kimura-Koruda et al. (Mol Cell Neurosci 2010) based on a co-culture of meningeal fibroblasts and cerebellar astrocytes. TGFβ1 significantly decreased the expression of IP3R1, IP3R2, RyR1, RyR2 and SERCA2. Altered calcium signalling suppressed the neurite outgrowth and significantly decreased the length of the mitochondria and the frequency of mitochondrial fusion (Jaskova et al., Neuroreport, 2013). In contrast, TGFβ1 altered neither neurite outgrowth nor the expression of calcium transporters in the primary culture of hippocampal neurons. When cells were cultured on an *in vitro* model of fibrotic scar, the suppression of neurite outgrowth was similar for both CGCs and hippocampal neurons while VDCC were not altered in CGCs or in hippocampal neurons in either model. We demonstrated the differential role of voltage dependent potassium and sodium currents in altered neuronal development in these two models of neuronal injury. These results were presented at a conference (Jaskova et al., Proc of Czech and Slovak Physiol Meeting, 2015) and will be published in 2016.
- In 2012, the Slovak Academy of Sciences started a SAS Scholarship Programme intended for excellent foreign scientists under the age of 40. E. Dremencov won one out of three awarded scholarships, joined the laboratory, and strengthened the neuroscience research in the institute. He established single-unit in vivo extracellular recording from different types of brain neurons, such as monoamine- and neuropeptide-secreting neurons (Dremencov et al., J Mol Neurosci 2015). Because of the critical role of these neurons in pathophysiology and the treatment of certain brain disorders (such as depression, anxiety, and post-traumatic stress disorder), in vivo electrophysiological identification and the characterisation of these neurons has an excellent potential to assist the discovery of new central nervous system medications.
- We investigated the neuronal mechanism of the beneficial mood effect of voluntary physical exercise using an animal model of voluntary wheel running in rats (VWR). Our research focussed on the effect of the VWR on the firing activity of 5-HT, NE, and DA neurons. The exposure to VWR led to the tonic activation of 5-HT neurons; it may explain, at least in part, the beneficial mood effect of the voluntary physical exercise. These results were

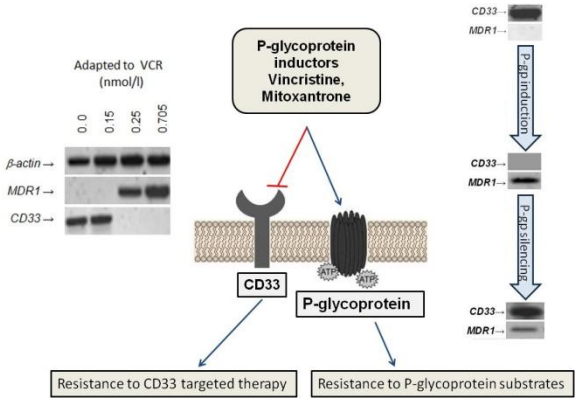
presented at a conference (Dremencov et al., Eur Neuropsychopharm, 2015) and will be published in 2016.

During the evaluated period, 5 articles dealing with structure and function of calcium channels and 9 articles focused on physiology of CNS were published. These articles were cited 24 times during 2012-2014 and 7 times in 2015.

3. Multidrug resistance development in leukaemia cells

We traditionally use the multidrug-resistant (MDR) variant of mouse lymphocytic leukaemia L1210 cell lines, in which P-gp expression was evoked by selection under vincristine (VCR) selective pressure (L1210/VCR) or by transfection with the human gene encoding P-gp (L1210/T). During the period 2012 to 2015, we established further MDR cell variants from human acute myeloid leukemia cells SKM-1 and MOLM-13 (Imrichova et al., Gen Physiol Biophys, 2014, Imrichova et al., Eur J Pharm SCI, 2015, Messingerová et al., Toxicol In Vitro, 2015a): SKM-1/VCR, SKM-1/MTX, SKM-1/LEN and SKM-1/AzaC were obtained from parental cells SKM-1 by selection with VCR, mitoxantrone (MTX), lenalidomide (LEN) and azacytidine (AzaC), respectively; MOLM-13/VCR, MOLM13/MTX and MOLM-13/AzaC were obtained from parental MOLM-13 cells by selection with VCR, MTX and AzaC, respectively. These cell variants represent an interesting model for the study of relationships between different mechanisms of MDR development. Our main findings on these cell variants in the reported period are as follows:

- Overexpression of P-gp induced by AzaC selective pressure in human AML cell lines (SKM-1 and MOLM-13) is associated with either the suppression of constitutive anti-apoptotic NF-κB pathway by lowering *nfkb1* gene expression (gene encoding protein P105/50, a member of the canonical NF-κB pathway) or the upregulation of inducible NF-κB pathway by increased *nfkb2* gene expression (gene encoding protein P100/52, a member of the non-canonical NF-κB pathway, Messingerova et al., Toxicol In Vitro, 2015a). The overexpression of P-gp in these cells is accompanied by a significant increase in the activity of glutathione S-transferase (GST, a MDR marker, detoxification enzyme).
- Markedly lower levels of UDP-glucose (glucose donor for the trans-glycosylation reaction) in the P-gp positive L1210 cells variants than in the parental cell line was observed. Decreased UDP-glucose level results in reduced cellular ceramide glucosylation in P-gp positive L1210 cell variants, which becomes a specific phenotype feature of these cells. Ceramide glucosylation is performed by glucosylceramide synthase (GCS). The overexpression of P-gp associated with the elevation of ceramide glucosylation and CGS expression has been previously observed by other authors and shown to suppress the proapoptotic effect of ceramides. From this point, P-gp positive L1210 cells differ from several other MDR cells. Due to decreased ceramide glucosylation caused in P-gp positive L1210 cells by limitation with UDP-glucose, an elevation of ceramides proapoptotic effects was observed when compared to the parental cells (Turakova et al., Anticancer Res, 2015).
- We demonstrated that P-gp expression in the human AML cell lines (SKM-1 and MOLM-13) is associated with complete elimination of CD33 transcription and protein expression on the surface of cells. Silencing of P-gp expression with an appropriate siRNA led to the elevation of CD33 expression. CD33 represents a possible target for therapy with humanised antibodies linked with an anticancer drug; however, several authors have shown that this therapy seems to be antagonised by the presence of P-gp in cells. Our findings indicated that the decrease in the effectiveness of CD33-targeted immunotherapy associated with P-gp expression might be based on a reciprocal expression pattern of P-gp and CD33 in AML cells (Imrichova et al., Eur J Pharm Sci, 2015).



Reciprocal expression of P-gp and CD33 in human acute myeloid leukaemia cells.

- We have observed the co-expression of P-gp and nestin (a marker of neuronal stem cells) in the resistant variants of SKM-1 and MOLM-13 cells. In solid tumours, nestin is considered as an angiogenesis marker and its co-expression with P-gp in tumour tissues indicates a poor prognosis for the patient. The fact that nestin is co-expressed with P-gp in the resistant variants of leukaemia cells suggests that it has an additional role in neoplastic cells, distinct from the regulation of angiogenesis (Imrichova et al., Gen Physiol Biophys, 2014).
- The sensitivity of P-gp positive L1210/VCR or L1210/T cells to cisplatin was lower compared to that of the parental L1210 cells. The decrease of cisplatin toxicity in P-gp positive L1210 cells was associated with the deregulation of cisplatin-induced apoptosis (namely associated with altered levels of Bcl-2 protein and caspase-3). However, the retention of cisplatin within parental L1210 or P-gp positive L1210/VCR or L1210/T cells was similar (Gibalova et al., Toxicol In Vitro, 2012). This indicated an additional role of P-gp as an antiapoptotic regulatory protein independent of its transport activity. We described this additional function of Pgp in a review paper (Breier et al., Anti-Cancer Agents Med Chem, 2013: New insight into P-Glycoprotein as a drug target) that was invited by editors of the international journal “Anti-Cancer Agents in Medicinal Chemistry”. This paper was the most cited paper of this journal published in 2013: http://benthamscience.com/journals/anti-cancer-agents-in-medicinal-chemistry/most-cited-articles/.
- Overexpression of P-gp in L1210 cells is negatively controlled by *all-trans* retinoic acid via the activation of retinoic acid nuclear receptors (Breier et al., Neoplasma, 2014). Crosstalk between retionoic acid receptors and P-gp mediated multidrug resistance we described in one book chapter (Sulová et al.: Are nuclear receptors for retinoids involved in the control of the expression and activity of P-glycoprotein? Nova Biomedical Books, ISBN 978-1-62100-656-5, 2012)
- We also studied the effectiveness of myelodisplastic syndrome treatment with immuno-modulating drug lenalidomide by monitoring lactate dehydrogenase, metalloproteinase 3 and 9 activities or calnexin and thioredoxin content in blood plasma of 13 patients with $5q^-$ variant of myelodisplastic syndrome (Messingerova et al., Gen Physiol Biophys, 2015b)
- Characterisation of vincristine as an inductor of multidrug resistance we described in one book chapter (Breier et al.: Vincristine as an Inductor of Drug Resistance Marker Expression in Neoplastic Cells, Nova Science Publishers, ISBN 978-1-62808-886-1, 2013)

During the years 2012-2015, we published 10 papers, indexed in WOK, on the topic of P-gp mediated MDR that were cited 72 times (without self-citation). The project APVV-02-90-10 on the topic of P-gp (principal investigator Z. Sulova), financed by the Slovak Research and Development Agency, was evaluated as "project solved in excellent quality", and was included in the annual publication of this Agency. We described the main results of a five-year research study conducted by our team in a monograph (Breier et al. 2013: P-glycoprotein mediated multidrug resistance of cancer tissue: Implication for cancer chemotherapy. ISBN 978-80-89233-55-7, PETRUS, 2012). Our team was identified as a "scientific collective with output exceeding worldwide mean" by the independent agency

ARRA (http://www.arra.sk/english), included in the book "Top Scientific Teams and People at SAS" published by the Slovak Academy of Sciences, and awarded the Gold Plaque on the occasion of the 60th anniversary of the Slovak Academy of Sciences in 2013.

4. Gasotransmitter signalling in regulatory pathways

This topic started in our institute in 2008, when our scientists, in collaboration with teams from the Faculty of Chemical and Food Technology STU and the Institute of Normal and Pathological Physiology SAS, published the paper: "H2S and HS- donor NaHS releases nitric oxide from nitrosothiols, metal nitrosyl complex, brain homogenate and murine L1210 leukaemia cells" (Ondrias et al., Pflugers Arch 2008). This very original finding oriented the involved scientists towards the intensive study of signalling pathways mediated by "gasotransmitters" – gaseous signalling molecules (NO, H2S) in normal and pathological physiology. During the assessed periods, 9 papers in WOS indexed journals were published that were cited 58 times (without self-citation). This topic was investigated by a team with two leading scientific personalities (O. Krizanova and K. Ondrias), which was identified as a "scientific collective with output exceeding worldwide mean" by the independent agency ARRA, included in the book "Top Scientific Teams and People at SAS" published by the Slovak Academy of Sciences, awarded the Gold Plaque on the occasion of the 60th anniversary of the Slovak Academy of Sciences in 2013.

5. Study of the human genome

The team, led by L. Kádasi, was involved in international scientific network that published the paper: "Reconstructing Roma History from Genome-Wide Data" (PLoS One, 2013). This paper brought evidence for Eastern Europe being a major source of European ancestry, and north-west India being a major source of the South Asian ancestry in the Romani people (Roma).

The team, led by L. Kádasi, continued to conduct research oriented on monogenic diseases (alkaptonuria, phenylketonuria, non-syndromic hearing loss, myotonic dystrophy, primary congenital glaucoma etc.). They identified 39 novel neurofibromatosis 1 gene mutations in Slovak patients. Moreover, they provided an analysis of leucine-rich repeat kinase 2 and Parkinson protein 2 gene mutations in Slovak Parkinson disease patients. In the assessed period, they published 17 papers in WOS-indexed journals on this topic that were cited 67 times.

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 (ratios in percentage)

Peer reviewed papers in impacted journals, monographs, chapters in monographs

basic research/applied research - 95 %/ 5 %

international/regional - 95 %/ 5 %

2.1.2 List of selected publications documenting the most important results of basic research. The total number of publications listed for the assessment period should not exceed the average number of employees with university degrees engaged in research projects. The principal research outputs (max. 5, including Digital Object Identifier - DOI) should be underlined

Times cited: citations 2012 - 2015

1. BARANČÍK, Miroslav - **BOHÁČOVÁ, Viera - GIBALOVÁ, Lenka** - SEDLÁK, Ján - **SULOVÁ, Zdena - BREIER, Albert**. Potentiation of Anticancer Drugs: Effects of Pentoxifylline on Neoplastic Cells. In International Journal of Molecular Science, 2012, vol. 13, no. 1, p. 369-382. **(2.598 - IF2011)**. ISSN 1422-0067. **4 - times cited**

2. BORKO, Ľubomír - BAUEROVÁ-HLINKOVÁ, Vladena - HOSTINOVÁ, Eva - GAŠPERÍK, Juraj - BECK, K - LAI, F.A. - **ZAHRADNÍKOVÁ, Alexandra** - ŠEVČÍK, Jozef. Structural insights into the human RyR2 N-terminal region involved in cardiac arrhythmias. In Acta Crystallographica D, 2014, vol. D70, p. 2897-2912. **(7.232 - IF2013)**. ISSN 0907-4449. **2 - times cited**

3. **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. **(2.610 - IF2012)**. ISSN 1871-5206. **53 - times cited**

4. **GABURJÁKOVÁ, Jana - GABURJÁKOVÁ, Marta**. Coupled gating modifies the regulation of cardiac ryanodine receptors by luminal Ca2+. In Biochimica et Biophysica Acta : Biomembranes, 2014, vol. 1838, iss. 3, p. 867-873. **(3.431 - IF2013)**. ISSN 0005-2736. **3 - times cited**

5. **GABURJÁKOVÁ, Marta** - BAL, Naresh C. - **GABURJÁKOVÁ, Jana** - PERIASAMY, M. Functional interaction between calsequestrin and ryanodine receptor in the heart. In Cellular and Molecular Life Sciences, 2013, vol. 70, no. 16, p. 2935-2945. **(5.615 - IF2012)**. ISSN 1420-682X. **5 - times cited**

6. **GIBALOVÁ, Lenka - ŠEREŠ, Mário - RUSNÁK, Andrej** - DITTE, Peter - LABUDOVÁ, Martina - **UHRÍK, Branislav** - PASTOREK, Jaromír - SEDLÁK, Ján **- BREIER, Albert - SULOVÁ, Zdena**. P-glycoprotein depresses cisplatin sensitivity in L1210 cells by inhibiting cisplatin-induced caspase-3 activation. In Toxicology in vitro : the official journal of the European Society for Toxicology in Vitro, 2012, vol. 26, no. 3, p. 435 - 444. **(2.775 - IF2011)**. ISSN 0887-2333, DOI: 10.1016/j.tiv.2012.01.014. **14 - times cited**

7. **IMRICHOVÁ, Denisa - MESSINGEROVÁ, Lucia - ŠEREŠ, Mário - KAVCOVÁ, Helena - PAVLÍKOVÁ, Lucia - COCUĽOVÁ, Martina - BREIER, Albert - SULOVÁ, Zdena**. Selection of resistant acute myeloid leukemia SKM-1 and MOLM-13 cells by vincristine-, mitoxantrone- and lenalidomide-induced upregulation of P-glycoprotein activity and downregulation of CD33 cell surface exposure. In European Journal of Pharmaceutical Sciences, 2015, vol. 77, p. 29-39. **(3.350 - IF2014)**. ISSN 0928-0987. **0 - times cited**

8. **JANÍČEK, Radoslav - HOŤKA, Matej - ZAHRADNÍKOVÁ, Alexandra, ml. - ZAHRADNÍKOVÁ, Alexandra - ZAHRADNÍK, Ivan**. Quantitative Analysis of Calcium Spikes in Noisy Fluorescent Background. In PLoS ONE, 2013, vol. 8, iss. 5, e64394. **(3.730 - IF2012)**. ISSN 1932-6203. **5 - times cited**

9. **JANÍČEK, Radoslav - ZAHRADNÍKOVÁ, Alexandra, ml. - POLÁKOVÁ, Eva - PAVELKOVÁ, Jana - ZAHRADNÍK, Ivan - ZAHRADNÍKOVÁ, Alexandra**. Calcium spike variability in cardiac myocytes results from activation of small cohorts of RYR2 channels. In Journal of Physiology : A publication of the Physiological Society, 2012, vol. 590, p. 5091-5106. **(4.718 - IF2011)**. ISSN 0022-3751, DOI: 10.1113/jphysiol.2012.234823. **1 - times cited**

10. **JAŠKOVÁ, Katarína - PAVLOVIČOVÁ, Michaela** - CAGALINEC, Michal - **LACINOVÁ, Ľubica -** JURKOVIČOVÁ, Dana. TGF beta 1 downregulates neurite outgrowth, expression of Ca2+ transporters, and mitochondrial dynmics of in-vitro cerebellar granule cells. In Neuroreport, 2014, vol. 25, iss. 5, p. 340-346. **(1.644 - IF2013)**. ISSN 0959-4965. **0 - times cited**

11. **KARMAŽÍNOVÁ, Mária - JAŠKOVÁ, Katarína** - GRIAČ, Peter - PEREZ-REYES, Edward **- LACINOVÁ, Ľubica**. Contrasting the roles of the I-II loop gating brake in $Ca_V3.1$ and $Ca_V3.3$ calcium channels. In Pflugers Archiv-European Journal of Physiology, 2015, vol. 467, iss. 12, p. 2519–2527**. (4.101 - IF2014)**. ISSN 0031-6768, DOI: 10.1007/s00424-015-1728-y. **0 - times cited**

12. **KOMÍNKOVÁ, Viera - ONDRIAŠ, Karol - TOMÁŠKOVÁ, Zuzana.** Inhibitory effect of glybenclamide on mitochondrial chloride channels from rat heart. In Biochemical and biophysical research communications, 2013, vol. 434, no. 4, p. 836-840. **(2.406 - IF2012)**. ISSN 0006-291X. **1 - times cited**

13. **LENČEŠOVÁ, Ľubomíra - HUDECOVÁ, Soňa** - CSÁDEROVÁ, Lucia - **MARKOVÁ, Jana - ŠOLTÝSOVÁ, Andrea** - PASTOREK, Michal - SEDLÁK, Ján - WOOD, M.E. - WHITEMAN, Mathew - **ONDRIAŠ, Karol - KRIŽANOVÁ, Oľga**. Sulphide signalling potentiates apoptosis through the up-regulation of IP3 receptors types 1 and 2. In Acta Physiologica : Official Journal of the Federation of European Physiological Societies, 2013, vol. 208, no. 4, p. 350-361. **(4.382 - IF2012)**. ISSN 1748-1708. **8 - times cited**

14. **MARKOVÁ, Jana - HUDECOVÁ, Soňa - ŠOLTÝSOVÁ, Andrea - ŠÍROVÁ, Marta** - CSÁDEROVÁ, Lucia - **LENČEŠOVÁ, Ľubomíra - ONDRIAŠ, Karol - KRIŽANOVÁ, Oľga.** Sodium/calcium exchanger is upregulated by sulfide signaling, forms complex with the Beta1 and Beta3 but not Beta2 adrenergic receptors, and induces apoptosis. In Pflugers Archiv-European Journal of Physiology, 2014, vol. 466, no. 7, p. 1329-1342. **(3.073 - IF2013)**. ISSN 0031-6768. **2 - times cited**

15. MALLMANN, Robert T. - WILMES, Thomas - **LICHVÁROVÁ, Lucia** - BUHRER, Anja - LOHMULLER, Barbara - CASTONGUAY, Jan - **LACINOVÁ, Ľubica** - KLUGBAUER, Norbert. Tetraspanin- 13 modulates voltage-gated Cav2.2 Ca2+ channels. In Scientific Reports, 2013, vol. 3, article Number: 1777. **(2.927 - IF2012)**. ISSN 2045-2322. **2 - times cited**

16. **MESSINGEROVÁ, Lucia - IMRICHOVÁ, Denisa - KAVCOVÁ, Helena** - TURÁKOVÁ, Katarína - **BREIER, Albert - SULOVÁ, Zdena**. Acute myeloid leukemia cells MOLM-13 and SKM-1 established for resistance by azacytidine are crossresistant to P-glycoprotein substrates. In Toxicology in vitro : the official journal of the European Society for Toxicology in Vitro, 2015, vol. 29, p. 1405-1415. **(2.903 - IF2014)**. ISSN 0887-2333. **0 - times cited**

17. **MIŠÁK, Anton - GRMAN, Marián - MÁLEKOVÁ, Ľubica - NOVOTOVÁ, Marta - MARKOVÁ, Jana - KRIŽANOVÁ, Oľga - ONDRIAŠ, Karol - TOMÁŠKOVÁ, Zuzana**. Mitochondrial chloride channels: electrophysiological characterization and pH induction of channel pore dilation. In European Biophysics Journal with Biophysics Letters, 2013, vol. 42, no. 9, p. 709 -720. **(2.274 - IF2012)**. ISSN 0175-7571. **0 - times cited**

18. **NICHTOVÁ, Zuzana - NOVOTOVÁ, Marta** - KRÁLOVÁ, Eva - STANKOVIČOVÁ, Tatiana. Morphological and functional characteristics of models of experimental myocardial injury induced by isoproterenol. In General Physiology and Biophysics, 2012, vol. 31, p. 141-151. **(1.192 - IF2011)**. ISSN 0231-5882. **13 - times cited**

19. PACAK, Karel - **ŠÍROVÁ, Marta** - GIUBELLINO, A - **LENČEŠOVÁ, Ľubomíra** - CSÁDEROVÁ, Lucia - LAUKOVÁ, Marcela - **HUDECOVÁ, Soňa - KRIŽANOVÁ, Oľga**. NF-κB inhibition significantly upregulates the norepinephrine transporter system, causes apoptosis in pheochromocytoma cell lines and prevents metastasis in an animal model. In International Journal of Cancer, 2012, vol. 31, no. 10, p. 2445-2455. **(5.444 - IF2011)**. ISSN 0020-7136. **5 - times cited**

20. PETROVIČ, Pavol - **VALENT, Ivan - COCHEROVÁ, Elena** - **PAVELKOVÁ, Jana - ZAHRADNÍKOVÁ, Alexandra.** Ryanodine receptor gating controls generation of diastolic calcium waves in cardiac myocytes. In Journal of General Physiology, 2015, vol. 145, no. 6, p. 489-511. **(4.788 - IF2014)**. ISSN 0022-1295. **1 - times cited**

21. PIQUEREAU, Jérôme - CAFFIN, Fanny - **NOVOTOVÁ, Marta** - PROLA, Alexandre - GARNIER, A. - MATEO, Philippe - FORTIN, Dominique - HUYNH, Le Ha - NICOLAS, Valérie - ALAVI, Marcel V. - BRENNER, Catherine - VENTURA-CLAPIER, Renée - VEKSLER, Vladimir - JOUBERT, F. Down-regulation of OPA1 alters mouse mitochondrial morphology, PTP function, and cardiac adaptation to pressure overload. In Cardiovascular Research, 2012, vol. 94, p. 408-417. **(6.064 - IF2011)**. ISSN 0008-6363. **41 - times cited**

22. POLÁK, Emil - FICEK, Andrej - **RADVÁNSZKY, Ján - ŠOLTÝSOVÁ, Andrea** - URGE, O. - CMELOVÁ, Eleonora - KANTARSKÁ, Dana - **KÁDAŠI, Ľudevít.** Phenylalanine hydroxylase deficiency in the Slovak population: Genotype-phenotype correlations and genotype-based predictions of BH4-responsiveness. In Gene, 2013, vol. 526, no. 2, p. 347-355. **(2.196 - IF2012)**. ISSN 0378-1119, . DOI: 10.1016/j.gene.2013.05.057. **1 - times cited**

23. **TENCEROVÁ, Barbora - ZAHRADNÍKOVÁ, Alexandra - GABURJÁKOVÁ, Jana - GABURJÁKOVÁ, Marta**. Luminal Ca2+ controls activation of the cardiac ryanodine receptor by ATP. In Journal of General Physiology, 2012, vol.140., p. 93-108. **(3.841 - IF2011)**. ISSN 0022-1295., DOI: 10.1085/jgp.201110708. **6 - times cited**

24. **TOMÁŠOVÁ, Lenka - PAVLOVIČOVÁ, Michaela - MÁLEKOVÁ, Ľubica - MIŠÁK, Anton** - KRISTEK, František - **GRMAN, Marián** - ČAČÁNYIOVÁ, Soňa - TOMÁŠEK, Milan - **TOMÁŠKOVÁ, Zuzana** - PERRY, Alexis - WOOD, Mark E. - **LACINOVÁ, Ľubica - ONDRIAŠ, Karol** - WHITEMAN, Mathew. Effects of AP39, a novel triphenylphosphonium derivatised anethole dithiolethione hydrogen sulfide donor, on rat haemodynamic parameters and chloride and calcium Ca(v)3 and RyR2 channels. In Nitric Oxide : Biology and Chemistry, 2015, vol. 46, p. 131-144. **(3.521 - IF2014)**. ISSN 1089-8603. **3 - times cited**

25. WEISS, Norbert - HAMEED, Shahid - FERNÁNDEZ-FERNÁNDEZ, José M. - FABLET, Katell - **KARMAŽÍNOVÁ, Mária** - POILLOT, Cathy - PROFT, Juliane - CHEN, Lina - BIDAUD, Isabelle - MONTEIL, Arnaud - HUC-BRANDT, Sylvaine **- LACINOVÁ, Ľubica** - LORY, Philippe - ZAMPONI, Gerald W. - DE WAARD, Michel. A Cav3.2/syntaxin-1A signaling complex controls T-type channel activity and low-treshold exocytosis. In Journal of Biological Chemistry, 2012, vol. 287, no. 4, p., 2810-2818**. (4.773 - IF2011)**. ISSN 0021-9258. **21 - times cited**

2.1.3 List of monographs/books published abroad

none

2.1.4. List of monographs/books published in Slovakia

BREIER, Albert - **GIBALOVÁ, Lenka** - **ŠEREŠ, Mário** - BARANČÍK, Miroslav - **SULOVÁ, Zdena**. P-glycoprotein mediated multigrug resistance of cancer tissue: Implication for cancer chemotherapy. Reviewers Brtko J., Sedlak J. Bratislava : Petrus, 2012. 100 p. ISBN 978-80-89233-55-7.

KRIŽANOVÁ, Oľga: Transportné systémy pre vápnik - od štruktúry po funkciu [Calcium transport systems – from structure to function]- Martin : Jesseniova lekárska fakulta UK, 2012. - 61 p. ISBN 978-80-89544-24-0.

KÁDAŠI, Ľudevít - RADVÁNSZKY, Ján. Časté monogénne dedičné ochorenia na Slovensku. [Frequent monogenic disorders in Slovakia] Vyd. 1. Bratislava : VEDA, vydavateľstvo Slovenskej akadémie vied, 2014. 655 p. ISBN 978-80-224-1363-3**.**

2.1.5. List of other scientific outputs specifically important for the institute, max. 10 items

SULOVÁ, Zdena - BRTKO, Július - MACEJOVÁ, Dana - **BREIER, Albert**. Are nuclear receptors for retinoids involved in the control of the expression and activity of P-glycoprotein? In Retinoic Acid: Structure, Mechanisms, and Roles in Disease. - New York, USA : Nova Biomedical Books, 2012, p. 29 - 51. ISBN 978-1-62100-656-5.

BREIER, Albert - **IMRICHOVÁ, Denisa** - PAULÍKOVÁ, Helena - BARANČÍK, Miroslav **- SULOVÁ, Zdena**. Vincristine as an Inductor of Drug Resistance Marker Expression in Neoplastic Cells. In COELLO, Juan M. - SABRES, Yolanda D. (eds.) Vincristine : Clinical Uses, Pharmacokinetics and Impacts on Health. - New York : Nova Science Publishers, Inc., 2013, p. 1-31. ISBN 978-1-62808-886-1.

PIQUEREAU, Jérôme - **NOVOTOVÁ, Marta** - GARNIER, A. - JOUBERT, F. - VEKSLER, Vladimir - VENTURA-CLAPIER, Renée. Cardiac Metabolic Adaptation During Postnatal Development. Editor: Ostadal B., Dhalla N.S. In Cardiac Adaptation. Springer Verlag New York USA, 2013, p. 79-98. ISBN 978-1-4614-5203-4_5.

DREMENCOV, Eliyahu. PATHOPHYSIOLOGY OF MOOD DISORDERS: NORADRENERGIC MECHANISMS. In Neurobiology of Mood Disorders : editors: Guiard Bruno P., Dremencov Eliyahu. - Sharjah : Bentham Science Publisher, 2014, p. 107-126. ISBN 978-1-60805-578-4.

LACINOVÁ, Ľubica - **LICHVÁROVÁ, Lucia**. Pharmacology of Voltage-Gated Calcium Channels in Clinic. In Pathologies of Calcium Channels. - Berlin : Springer-Verlag, 2014, p. 297-314. ISBN 978-3-642-40281-4.

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

none

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

none

2.1.8. Table of research outputs (as in annual reports).

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.

Scientific publications	2012			2013			2014			2015			total			
	number	No. / FTE	No. / salary budget	number	No. / FTE	No. / salary budget	number	No. / FTE	No. / salary budget	number	No. / FTE	No. / salary budget	number	averaged number per year	av. No. / FTE	av. No. / salary budget
Scientific monographs and monographic studies in journals and proceedings published abroad *(AAA, ABA)*	0,0	0,000	0,000	0,0	0,000	0,000	0,0	0,000	0,000	0,0	0,000	0,000	**0,0**	**0,0**	**0,000**	**0,000**
Scientific monographs and monographic studies in journals and proceedings published in Slovakia *(AAB, ABB)*	2,0	0,057	0,004	0,0	0,000	0,000	1,0	0,029	0,002	0,0	0,000	0,000	**3,0**	**0,8**	**0,023**	**0,002**
Chapters in scientific monographs published abroad *(ABC)*	1,0	0,028	0,002	2,0	0,060	0,004	2,0	0,057	0,004	0,0	0,000	0,000	**5,0**	**1,3**	**0,038**	**0,003**
Chapters in scientific monographs published in Slovakia *(ABD)*	1,0	0,028	0,002	0,0	0,000	0,000	0,0	0,000	0,000	0,0	0,000	0,000	**1,0**	**0,3**	**0,008**	**0,001**
Scientific papers published in journals registered in Current Contents Connect *(ADCA, ADCB, ADDA, ADDB)*	20,0	0,567	0,045	15,0	0,450	0,033	12,0	0,344	0,025	22,0	0,784	0,054	**69,0**	**17,3**	**0,524**	**0,038**
Scientific papers published in journals registered in Web of Science Core Collection and SCOPUS *(ADMA, ADMB, ADNA, ADNB)*	4,0	0,113	0,009	8,0	0,240	0,017	4,0	0,115	0,008	2,0	0,071	0,005	**18,0**	**4,5**	**0,137**	**0,010**
Scientific papers published in other foreign journals (not listed above) *(ADEA, ADEB)*	0,0	0,000	0,000	0,0	0,000	0,000	0,0	0,000	0,000	0,0	0,000	0,000	**0,0**	**0,0**	**0,000**	**0,000**
Scientific papers published in other domestic journals (not listed above) *(ADFA, ADFB)*	0,0	0,000	0,000	1,0	0,030	0,002	2,0	0,057	0,004	1,0	0,036	0,002	**4,0**	**1,0**	**0,030**	**0,002**
Scientific papers published in foreign peer-reviewed proceedings *(AEC, AECA)*	1,0	0,028	0,002	3,0	0,090	0,007	0,0	0,000	0,000	0,0	0,000	0,000	**4,0**	**1,0**	**0,030**	**0,002**
Scientific papers published in domestic peer-reviewed proceedings *(AED, AEDA)*	2,0	0,057	0,004	10,0	0,300	0,022	15,0	0,430	0,031	3,0	0,107	0,007	**30,0**	**7,5**	**0,228**	**0,017**
Published papers (full text) from foreign and international scientific conferences *(AFA, AFC, AFBA, AFDA)*	0,0	0,000	0,000	1,0	0,030	0,002	0,0	0,000	0,000	0,0	0,000	0,000	**1,0**	**0,3**	**0,008**	**0,001**
Published papers (full text) from domestic scientific conferences *(AFB, AFD, AFBB, AFDB)*	4,0	0,113	0,009	0,0	0,000	0,000	0,0	0,000	0,000	0,0	0,000	0,000	**4,0**	**1,0**	**0,030**	**0,002**

- **Supplementary information and/or comments on the scientific outputs of the institute.**

Four publications in the assessed period require comment.

The results published in the article (1, see below) were obtained during the postdoctoral stay of A. Zahradnikova, jr. at Université Paris-Sud, Faculté de Pharmacie, Châtenay-Malabry, France, and correctly bear that affiliation. The publication is listed in the ARL database because it states "Dr Zahradniková is currently on leave from the Institute of Molecular Physiology and Genetics, the Slovak Academy of Sciences, Bratislava, Slovakia." and was declared in the Annual Report of IMPG SAS as "Type B".

1. GHIGO, A. – PERINO, A. – MEHEL, H. – **ZAHRADNÍKOVÁ, Alexandra, ml.** – MORELLO, F. – LEROY, J. – NIKOLAEV, V. O. – DAMILANO, F. – CIMINO, J. – DE LUCA, E. – RICHTER, W. – WESTENBROEK, R. – CATTERALL, W. A. – ZHANG, J. – YAN, C. – CONTI, M. – GOMEZ, A. M. – VANDECASTEELE, G. – HIRSCH, E. – FISCHMEISTER, R. Phosphoinositide 3-kinase gamma protects against catecholamine-induced ventricular arrhythmia through protein kinase A-mediated regulation of distinct phosphodiesterases. In Circulation: journal of The American Heart Association, 2012, vol. 126, no. 17, pp. 2073-2083. (14.739 – IF2011). (2012 – Current Contents). ISSN 0009-7322. Type: ADCA

The articles (2 – 4, listed below) authored by Oľga Križanová, Karol Ondriaš, Andrea Šoltýsová, Jana Feruszová, Soňa Hudecová, Ľudevít Kádasi, Marián Grman, published in 2015 do not contain affiliation to IMPG SAS in the printed versions. However, all three articles are based on the results obtained at and using funding from the projects of IMPG SAS during the evaluation period when these authors were at full capacity employed at IMPG SAS. These authors, who underwent, on 1 May 2015, delimitation to the Center for Molecular Medicine SAS (presently Institute for Clinical and Translational Research BMC SAS), intentionally did not include their affiliation to IMPG SAS in these publications and refused to do so post-publication. The IMPG SAS brought the conflict of interests to the Ethical Committee of SAS with the request to assess the rightness of affiliation. The Ethical Committee of SAS qualified the action of the mentioned authors as a serious breach of ethical conduct and proposed that the Presidium of SAS summons the authors to submit corrections of the affiliation to the respective journals and that these publications should be considered as affiliated to the Institute of Molecular Physiology and Genetics SAS. The Presidium of SAS accepted the proposal on the 37th session on 2 June 2016. Therefore, the following three publications were included in the ARL as a result of IMPG SAS.

2. CORTESE-KROTT, Miriam M. – KUHNLE, Gunter G.C. – DYSON, Alex – FERNANDEZ, Bernadette O. – **GRMAN, Marián** – DUMOND, Jenna F. – BARROW, Mark p. – MCLEOD, George – NAKAGAWA, Hidehiko – **ONDRIAŠ, Karol** – NAGY, Péter – KING, Bruce S. – SAAVEDRA, Joseph E. – KEEFER, Larry K. – SINGER, Mervyn – KELM, Malte – BUTLER, Anthony – FEELISCH, Martin. Key bioactive reaction products of the NO/H2S interaction are S/N-hybrid species, polysulfides and nitroxyl. In Proceedings of the National Academy of Sciences of the United States of America, 2015, vol. 112, iss. 34, p. E4651-E4660. (9.674 – IF2014). (2015 – Current Contents). ISSN 0027-8424. Type: ADCA

3. STRAČINA, Tibor – SLANINOVÁ, Iva – POLANSKÁ, Hana – AXMANOVÁ, Martina – OLEJNÍČKOVÁ, Veronika – KONEČNÝ, P. – MASARIK, Michal – **KRIŽANOVÁ, Oľga** – NOVÁKOVÁ, Marie. Long-Term Haloperidol Treatment Prolongs QT Interval and Increases Expression of Sigma 1 and IP3 Receptors in Guinea Pig Hearts. In Tohoku Journal of Experimental Medicine, 2015, vol. 236, no. 3, p. 199-207. (1.351 – IF2014). (2015 – Current Contents). ISSN 0040-8727. Type: ADCA

4. **ŠOLTYSOVÁ, Andrea** – BREZA, J. – TAKÁČOVÁ, Martina – **FERUSZOVÁ, Jana** – **HUDECOVÁ, Soňa** – NOVOTNÁ, B. – ROZBORILOVÁ, E. – PASTOREKOVÁ, Silvia – **KÁDAŠI, Ľudevít** – **KRIŽANOVÁ, Oľga**. Deregulation of energetic metabolism in the clear cell renal cell carcinoma: A multiple pathway analysis based on microarray profiling. In International Journal of Oncology, 2015, vol. 47, no. 1, p. 287-295. (3.025 – IF2014). (2015 – Current Contents). ISSN 1019-6439. Type: ADCA

2.2. Responses to the research outputs (citations, etc.)

2.2.1. Table with citations per annum.

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) have to be listed separately.

Citations, reviews	2011		2012		2013		2014		total		
	number	No. / FTE	number	No. / FTE	number	No. / FTE	number	No. / FTE	number	averaged number per year	av. No. / FTE
Citations in Web of Science Core Collection (1.1, 2.1)	456,0	12,919	417,0	12,516	461,0	13,218	514,0	18,313	**1848,0**	**462,0**	**14,047**
Citations in SCOPUS (1.2, 2.2) if not listed above	63,0	1,785	170,0	5,103	118,0	3,383	69,0	2,458	**420,0**	**105,0**	**3,192**
Citations in other citation indexes and databases (not listed above) (3.2,4.2,9,10)	3,0	0,085	1,0	0,030	0,0	0,000	1,0	0,036	**5,0**	**1,3**	**0,038**
Other citations (not listed above) (3, 4, 3.1, 4.1)	2,0	0,057	9,0	0,270	4,0	0,115	6,0	0,214	**21,0**	**5,3**	**0,160**
Reviews (5,6)	0,0	0,000	0,0	0,000	0,0	0,000	0,0	0,000	**0,0**	**0,0**	**0,000**

2.2.2. List of 10 most-cited publications, with number of citations, in the assessment period (2011 – 2014).

Times cited: total citations incl. 2015 / citations 2011-2014

1. **LACINOVÁ, Ľubica**. Voltage-dependent calcium channels. In General Physiology and Biophysics, 2005, vol. 24, suppl., p. 1-78. (0.694 - IF2004). ISSN 0231-5882, **94/48 - times cited**

2. MARX, S. O. - **GABURJÁKOVÁ, Jana** - **GABURJÁKOVÁ, Marta** - HENRIKSON, C. **- ONDRIAŠ, Karol** - MARKS, A. R. Coupled gating between cardiac calcium release channels (ryanodine receptors). In Circulation Research, 2001, vol. 88, iss. 11, p. 1151-1158. (9.193 - IF2000). ISSN 0009-7330, **229/44 - times cited**

3. **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. (2.610 - IF2012). ISSN 1871-5206, **53/28 - times cited**

4. BARANČÍK, Miroslav - **BOHÁČOVÁ, Viera** - **KVACKAJOVA, J**. **- HUDECOVÁ, Soňa** - **KRIŽANOVÁ, Oľga** - **BREIER, Albert**. 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, iss. 1, p. 29-36. (1.212 - IF2000). ISSN 0928-0987, **56/25 - times cited**

5. **ONDRIAŠ, Karol** - STAŠKO, Andrej - ČAČÁNYIOVÁ, Soňa - **SULOVÁ, Zdena** - **KRIŽANOVÁ, Oľga** - KRISTEK, František - MÁLEKOVÁ, Ľubica - KNEZL, Vladimír - **BREIER, Albert**. H2S and HS- donor NaHS releases nitric oxide from nitrosothiols, metal nitrosyl complex, brain homogenate and murine L1210 leukaemia cells. In Pflugers Archiv-European Journal of Physiology, 2008, vol. 457, no. 2, p. 271-279. (3.842 - IF2007). ISSN 0031-6768, 36**/25 - times cited**

6. **BREIER, Albert** - BARANČÍK, Miroslav - **SULOVÁ, Zdena** - **UHRÍK, Branislav**. P-glycoprotein - Implications of metabolism of neoplastic cells and cancer therapy. In Current Cancer Drug Targets, 2005, vol. 5, iss. 6, p. 457-468. ISSN 1568-0096, **59/24 - times cited**

7. BARANČÍK, Miroslav - **BOHÁČOVÁ, Viera** - SEDLÁK, Ján - **SULOVÁ, Zdena** - **BREIER, Albert**. LY294,002, a specific inhibitor of PI3K/Akt kinase pathway, antagonizes P-glycoprotein-mediated multidrug resistance. In European Journal of Pharmaceutical Sciences, 2006, vol. 29, no. 5, p. 426-434. (2.368 - IF2005). ISSN 0928-0987, **52/24 - times cited**

8. **ZAHRADNÍK, Ivan** - **MINAROVIČ, Igor** - **ZAHRADNÍKOVÁ, Alexandra**. Inhibition of the cardiac L-type calcium channel current by antidepressant drugs. In Journal of Pharmacology and Experimental Therapeutics, 2008, vol. 324, iss. 3, p. 977-984. (4.003 - IF2007). ISSN 0022-3565, **41/21 - times cited**

9. **POLÁKOVÁ, Eva** - **ZAHRADNÍKOVÁ, Alexandra, ml. - PAVELKOVÁ, Jana - ZAHRADNÍK, Ivan - ZAHRADNÍKOVÁ, Alexandra**. Local calcium release activation by DHPR calcium channel openings in rat cardiac myocytes. In Journal of Physiology, 2008, vol. 586, iss. 16, p. 3839-3854. (4.580 - IF2007). ISSN 0022-3751, **27/16 - times cited**

10. **ZAŤKOVÁ, Andrea**. An update on molecular genetics of Alkaptonuria (AKU). In Journal of Inherited Metabolic Disease, 2011, vol. 34, no. 6, p. 1127-1136. (3.808 - IF2010). ISSN 0141-8955, **20/16 - times cited**

The list of the most cited publications includes only publications in which there was a substantial intellectual contribution of employees of IMPG SAS. The highly cited publications, in which the contribution of IMPG SAS was less substantial, were omitted in

this list but some of the recent ones (published in 2012-2015) are listed in chapter 2.1.2 (#21 and 25).

2.2.3. List of most-cited authors from the Institute (at most 10 % of the research employees with university degree engaged in research projects) and their number of citations in the assessment period (2011– 2014).

[1] doc. RNDr. Ľubica Lacinová, DrSc. (397 citations)

[2] prof. RNDr. Ľudevít Kádaši, DrSc. (291 citations)

[3] Mgr. Marta Gaburjáková, PhD. (257 citations)

[4] doc. Ing. Albert Breier, DrSc. (251 citations)

- **Supplementary information and/or comments on responses to the scientific output of the institute.**

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

- **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.

1. **Mitochondria-endoplasmic reticulum functional interplay in Wolfram Syndrome: emerging role for heart and brain protection. 7RP Marie Curie Action: Co-funding of Regional, National and International Programmes.** No. 0063/01/02. Coordinator: RNDr. Michal Cagalinec, PhD. 03/2015-12/2018.
2. **FP7 Health: Clinical Development of Nitisone for Alkaptonuria.** DevelopAKUre No. 304985. Coordinator: Royal Liverpool University Hospital Trust (RLUH) Responsible at IMPG SAS: Mgr. Andrea Zaťková, PhD. 11/2012-04/2018.
3. **Reactive Oxygen Species. (COST),** no. BM1203. Coordinator: University Medical Center Mainz, Med. Klinik- Mol. Kardiol., Germany. Responsible at IMPG SAS : doc. Ing. Oľga Križanová, DrSc., 05/2014-12/2016.
4. **Gasotransmitters: from basic science to science to therapeutic applications (ENOG: European Network on Gasotransmitters)** BMBS COST Action BM1005, Coordinator: Prof. Andreas Papapetropoulos, University of Patras, Lab for Molecular Pharmacology, 26504 Patras, Greece, Responsible at IMPG SAS: RNDr. Karol Ondriaš, DrSc. 05/2011-05/2015.
5. **Hypoxia and oxygen sensing, signalling and adaptation. (COST)**, no. TD0901, Coordinator: Prof. Roland H. Wenger, Zurich Center for Integrative Human Physiology ZIHP, Institute of Physiology, University of Zurich, Responsible at IMPG SAS : doc. Ing. Oľga Križanová, DrSc., 07/2009-11/2013.

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

The First European Conference on the Biology of Hydrogen Sulfide, June 15-18, 2012, Smolenice, Slovakia

2.3.3. List of edited proceedings from international scientific conferences.

First European Conference on the Biology of Hydrogene Sulfide: Smolenice Castle, Bratislava, June 15-18, 2012. Bratislava: Institute of Molecular Physiology and Genetics SAS, 2012. 154 p. ISBN 978-80970164-4-9.

2.3.4. List of journals edited/published by the institute:

2.3.4.1. WOS (IF of journals in each year of the assessment period)

General Physiology and Biophysics

IF2011 = 1.192

IF2012 = 0.852

IF2013 = 0.875

IF2014 = 1.173

2.3.4.2. SCOPUS

2.3.4.3. other databases

2.3.4.4. not included in databases

- **National position of the institute**

2.3.5. List of selected projects of national importance

Role of Neurosecretory Neurons and Calcium Signalling in Depression and Addictive Behaviour: Assessment by in-vivo Electrophysiology. SAS Scholarship program, MMedSc. Eliyahu Dremencov, PhD., 10/2013-10/2017.

Center of excellence for glycomics (GLYCOMICS). EU Structural Funds ITMS 26240120031, Coordinator: RNDr. Ján Mucha, CSc., Institute of Chemistry SAS, Responsible at IMPG SAS :Ing. Zdena Sulová, DrSc., 11/2010-10/2014.

Diagnostics of socially important disorders in Slovakia, based on modern biotechnologies (DNA – DG). EU Structural Funds ITMS 26240220058, Coordinator: prof. doc. RNDr. Ľudevít Kádaši, DrSc., 11/2010-10/2013.

Center of excellence for translational research in molecular medicine (TRANSMED 2). EU Structural Funds n.26240120030, Coordinator: MVDr. Juraj Kopáček, DrSc., Institute of Virology SAS, Responsible at IMPG SAS: doc. Ing. Oľga Križanová, DrSc., 06/2010-05/2012.

Building of competency centre for research and development in the field of molecular medicine. EU Structural Funds IMTS 26240220071, Coordinator: prof. RNDr. Ján Turňa, CSc., Comenius University in Bratislava, Responsible at IMPG SAS: Ing. Zdena Sulová, DrSc., 10/2011-10/2015.

University science park for biomedicine Bratislava. EU Structural Funds ITMS 26240220087, Coordinator: prof. RNDr. Jaromír Pastorek, DrSc., Institute of Virology SAS, Responsible at IMPG SAS: doc. Ing. Oľga Križanová, DrSc., 03/2013-12/2015.

Completing the infrastructure for modern research of lifestyle diseases. EU Structural Funds ITMS 26230120006, Coordinator: RNDr. Miroslav Barančík, DrSc., Institute for Heart research SAS, Responsible at IMPG SAS: Ing. Zdena Sulová, DrSc., 10/2015-12/2015.

2.3.6. Projects of the Slovak Research and Development Agency (APVV)

Calcium channels in neuronal excitability. APVV-0212-10, doc. RNDr. Ľubica Lacinová, DrSc., 05/2011-10/2014.

Alternation in cell metabolism associated with drug transporter P- glycoprotein overexpression in leukemia cells. APVV-0290-10, Ing. Zdena Sulová, DrSc., 05/2011-10/2014.

Myocardial remodelling – the role of calcium signalling. APVV-0721-10, Ing. Alexandra Zahradníková, DrSc., 05/2011-10/2014.

IP3 receptors, their modulation andf function in cancer cells. APVV-0045-11, doc. Ing. Oľga Križanová, DrSc., 07/2012-12/2015.

Study of molecular mechanism of H2S biological effects. APVV-0074-11, RNDr. Karol Ondriaš, DrSc. 07/2012-12/2015.

Antitumour effect of biologically active ligands of nuclear retinoid X receptor heterodimers in tissue carcinoma cell lines. APVV-0160-11, Coordinator: Ing. Július Brtko, DrSc., Institute of Experimental Endocrinology SAS, Responsible at IMPG SAS: Ing. Zdena Sulová, DrSc., 07/2012-12/2015.

Possible dual function of P-glycoprotein in leukemia cells: efflux pump and regulatory protein. APVV-14-0334, Ing. Zdena Sulová, DrSc., 07/2015-7/2018.

Functional analysis of newly identified DNA variants in genes responsible for cystic fibrosis and fenylketonuria. APVV-0240-12, prof. doc. RNDr. Ľudevít Kádaši, DrSc., 10/2013-12/2016.

Mechanisms of ryanodine receptor dysregulation. LPP-0441-09, Ing. Alexandra Zahradníková, DrSc., 09/2009-08/2012.

Energetic cross-talks and cytoarchitecture of cardiac myocytes. Role of the mitochondrial protein OPA1. SK-FR-0021-11, RNDr. Marta Novotová, CSc. 01/2012-12/2013.

Preparation of nanostructured interfaces, their integration with bioelements and subsequent use. APVV-0282-11, Coordinator: Ing. Ján Tkáč, DrSc., Institute of Chemistry SAS, Responsible at IMPG SAS: Ing. Zdena Sulová, DrSc., 07/2012-12/2015.

Molecular mechanisms of the crosstalk between stress hormones and hypoxia in tumor cells: effect on expression and function of cancer-related protein CA IX. APVV-0893-11, Coordinator: RNDr. Lucia Csáderová, PhD., Institute of Virology SAS, Responsible at IMPG SAS: doc. Ing. Oľga Križanová, DrSc., 07/2012-12/2015.

Biochips and biosensors for glycorecognition, their development, preparation and application in cancer research. APVV-14-0753, Coordinator: Ing. Jaroslav Katrlík, PhD., Institute of Chemistry SAS, Responsible at IMPG SAS: Ing. Zdena Sulová, DrSc., 07/2015-06/2019.

2.3.7. Projects of the Scientific Grant Agency of the Slovak Academy of Sciences and the Ministry of Education (VEGA)

Overexpression of P-glycoprotein induced cell changes in leukemia cells. VEGA 2/0100/12, doc. Ing. Albert Breier, DrSc., 01/2012-12/2014

Plasticity of the membrane systems of cardiac myocytes. VEGA 2/0116/12, RNDr. Marta Novotová, CSc., 01/2012-12/2014

Competition between Ca2+ and other cation for luminally located binding site on the cardiac ryanodine receptor and its effect on the receptor regulation. VEGA 2/0102/12, Mgr. Jana Gaburjáková, PhD., 01/2012-12/2014

Study of redox and radical regulation of mitochondrial chloride channels from rat heart under oxidative stress. VEGA 2/0094/12, Mgr. Zuzana Tomášková, PhD., 01/2012-12/2014

Principle of gating of voltage-dependent calcium channels. VEGA 2/0044/13, doc. RNDr. Ľubica Lacinová, DrSc., 01/2013-12/2015

Induction of apoptosis through modulation of the IP3 receptors in tumor cells. VEGA 2/0074/13, doc. Ing. Oľga Križanová, DrSc., 01/2013-12/2015

Multidrug resistance of leukemia cells on different drugs. VEGA 2/0182/13, Ing. Zdena Sulová, DrSc., 01/2013-12/2016

Effect of products of interaction of H2S and NO on membrane channels. VEGA 2/0050/13, RNDr. Karol Ondriaš, DrSc., 01/2013-12/2016

Structure-function relationships of the ryanodine receptor. VEGA 2/0148/14, Ing. Alexandra Zahradníková, DrSc., 01/2014-12/2016

2.3.8. Projects of SAS Centres of Excellence

Center of excellence for the treatment of metabolic aspects of development, diagnostics and treatment of cancer diseases. Coordinator: doc. Ing. Oľga Križanová, DrSc., 07/2011-12/2014.

2.3.9. National projects supported by EU Structural Funds

Center of excellence for glycomics (GLYCOMICS). EU Structural Funds ITMS 26240120031, Coordinator: RNDr. Ján Mucha, CSc., Institute of Chemistry SAS, Responsible at IMPG SAS :Ing. Zdena Sulová, DrSc., 11/2010-10/2014.

Diagnostics of socially important disorders in Slovakia, based on modern biotechnologies (DNA – DG). EU Structural Funds ITMS 26240220058, Coordinator: prof. doc. RNDr. Ľudevít Kádaši, DrSc., 11/2010-10/2013.

Center of excellence for translational research in molecular medicine (TRANSMED 2). EU Structural Funds n.26240120030, Coordinator: MVDr. Juraj Kopáček, DrSc., Institute of Virology SAS, Responsible at IMPG SAS: doc. Ing. Oľga Križanová, DrSc., 06/2010-05/2012.

Building of competency centre for research and development in the field of molecular medicine. EU Structural Funds IMTS 26240220071, Coordinator: prof. RNDr. Ján Turňa, CSc., Comenius University in Bratislava, Responsible at IMPG SAS: Ing. Zdena Sulová, DrSc., 10/2011-10/2015.

University science park for biomedicine Bratislava. EU Structural Funds ITMS 26240220087, Coordinator: prof. RNDr. Jaromír Pastorek, DrSc., Institute of Virology SAS, Responsible at IMPG SAS: doc. Ing. Oľga Križanová, DrSc., 03/2013-12/2015.

Completing the infrastructure for modern research of lifestyle diseases. EU Structural Funds ITMS 26230120006, Coordinator: RNDr. Miroslav Barančík, DrSc., Institute for Heart research SAS, Responsible at IMPG SAS: Ing. Zdena Sulová, DrSc., 10/2015-12/2015.

2.3.10. List of journals (published only in the Slovak language) edited/published by the institute:

none

2.3.10.1. WOS (IF of journals in each year of the assessment period)

2.3.10.2. SCOPUS

2.3.10.3. Other databases

2.3.10.4. Not included in databases

- ## Position of individual researchers in an international context

2.3.11. List of invited/keynote presentations at international conferences, as documented by programme or invitation letter

TOMÁŠKOVÁ, Zuzana. Regulation of mitochondrial chloride channels. In Regional Biophysics Conference 2012 : Book of Abstracts. - Kladovo-Belgrade, Serbia, September 03 - 07,2012, p. 30. ISBN 978-86-904161-2-7.

KRIŽANOVÁ, Oľga. NF-kappa B inhibition in pheochromocytoma cell lines causes apoptosis: A novel therapeutic option? 18th World Congress on Advances in

Oncology and 16th International Symposium on Molecular Medicine, 10 -12 October, 2013, Creta Maris, Hersonissos, Crete, Greece. In International Journal of Molecular Medicine, Vol. 32, supplement 1, 2013. S20.

KRIŽANOVÁ, Oľga. Sulphoraphane-induced apoptosis involves the type 1 IP3 receptors. COST- Reactive Oxygen Species, 4 - 7. 11. 2014, Padova, Italy.

ZAHRADNÍKOVÁ, Alexandra. Sparks and waves in cardiac myocytes - insights from an allosteric model of ryanodine receptor gating. XIII International Meeting of the European Calcium Society, ECS 2014, Aix-en-Provence, France, September 13-17, 2014, abstracts book, p. 30-31.

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

Mgr. Marián Grman, PhD,
- Member of Organising Committee: First European Conference on the Biology of Hydrogen Sulfide, Smolenice, Slovakia, 2012

doc. Ing. Oľga Križanová, DrSc.
- Chair of Organising Committee: First European Conference on the Biology of Hydrogen Sulfide, Smolenice, Slovakia, 2012

doc. RNDr. Ľubica Lacinová, DrSc.
- Chair of Organising and Programme Committees: CavNet follow-up meeting: „Ca^{2+} channels in health and disease“, Prague, Czech republic, 2013

Mgr. Anton Mišák, PhD,
- Member of Organising Committee: First European Conference on the Biology of Hydrogen Sulfide, Smolenice, Slovakia, 2012

RNDr. Karol Ondriaš, DrSc.
- Chair of Programme Committee: First European Conference on the Biology of Hydrogen Sulfide, Smolenice, Slovakia, 2012
- Member of Programme Committee: 2nd European Conference on the Biology of Hydrogen Sulfide, Exeter, UK, 2013
- Member of Programme Committee: 3rd International Conference on H_2S Biology and Medicine, Kyoto, Japan, 2014
- Member of Programme Committee: 3rd International Conference on the Biology of Hydrogen Sulfide, Athens, Greece, 2015

Mgr. Zuzana Tomášková, PhD,
- Member of Organising Committee: First European Conference on the Biology of Hydrogen Sulfide, Smolenice, Slovakia, 2012

- **Position of individual researchers in a national context**

2.3.13. List of invited/keynote presentations at national conferences, as documented by programme or invitation letter

BREIER, Albert. New insights into P-glycoprotein as a drug target. In XXIII. Biochemical meeting: Abstracts book, p.103, Masaryk University, Brno, Czech Republic, Aug 26-28, 2012, ISBN 978-80-86313-34-4.

ZAHRADNÍK, Ivan. Väzba excitácie s kontrakciou z hľadiska vápnikovej signalizácie [Excitation-contraction coupling from the aspect of calcium signaling]. In: M. Nováková (Ed.): ČTYŘICET LET KOMISE EXPERIMENTÁLNÍ KARDIOLOGIE: Odkud jsme vyšli a kam směřujeme. 40. pracovní konference Komise experimentální kardiologie při České a Slovenské fyziologické společnosti ČLS JEP, [FORTY YEARS OF THE COMMISSION FOR EXPERIMENTAL CARDIOLOGY: Where we started and to where do we aspire. 40th working conference of the

Commission for Experimental Cardiology at the Czech and Slovak Physiological Societies, ČLS JEP] Vranovská Ves, Oct 17-19, 2012. Department of Fyziology, Faculty of Medicine, Masaryk University, Brno, Czech republic, p. 36

ZAHRADNÍKOVÁ, Alexandra. Regulácia aktivity ryanodínového receptora [Regulation of ryanodine receptor activity]. In: M. Nováková (Ed.): ČTYŘICET LET KOMISE EXPERIMENTÁLNÍ KARDIOLOGIE: Odkud jsme vyšli a kam směřujeme. 40. pracovní conference Komise experimentální kardiologie při České a Slovenské fyziologické společnosti ČLS JEP, [FORTY YEARS OF THE COMMISSION FOR EXPERIMENTAL CARDIOLOGY: Where we started and to where do we aspire. 40th working conference of the Commission for Experimental Cardiology at the Czech and Slovak Physiological Societies, ČLS JEP] Vranovská Ves, Oct 17-19, 2012. Department of Fyziology, Faculty of Medicine, Masaryk University, Brno, Czech Republic, p. 37

KRIŽANOVÁ, Oľga. NF-kappa B inhibition in pheochromocytoma cell lines. In 7th International Symposium on Experimental and Clinical Neurobiology : Programme and Abstract Book, June 23-27. - Košice, Slovakia, 2013, p. 46. ISBN 978-80-263-0388-6**.**

ZAŤKOVÁ, Andrea. DNA diagnostika alkaptonúrie (AKU) a celosvetová databáza mutácií v HGD géne na Slovensku. 18. kolokvium o dedičných metabolických poruchách na tému: Alkaptonúria. 12.12.2013, Bratislava.

LACINOVÁ, Ľubica. Úloha vápnikových kanálov L typu vo vápnikovej signalizácii hipokampálnych neurónov [Role of L-type calcium channels in hippocampal calcium signalling]. In XXIV. Biochemical meeting of Slovak and Czech Society for Biochemistry and Molecular Biology: Abstract book, p. 48, Bratislava, Slovakia, Sept 18 – 21, 2014, ISBN 978-80-970164-6-3.

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

RNDr. Viera Boháčová, CSc.
- Member of Organising Committee XXVIII.Xenobiochemical Symposium, Kremnica, 2015

doc. Ing. Albert Breier, DrSc.
- Member of Organising and Programme Committees, Drobnica memorial, Bojná, 2013
- Member of Organising and Programme Committees, XXIV. Biochemical Symposium, Slovakia, 2014
- Member of Organising Committee XXVIII.Xenobiochemical Symposium, Kremnica, 2015
- Member of Organising Committee, Drobnica memorial, Smrekovica Podsuchá, 2015

Mgr. Marta Gaburjáková, PhD.
- Member of Programme Committee, V. Biophysical Symposium, Bratislava, 2012

Prof. doc. RNDr. Ľudevít Kádaši, DrSc.
- Chairperson of Programme Committee, XXIII.Izakovič memorial, Bratislava, 2012
- Chairperson of Programme Committee, XXIV. Izakovič memorial, Donovaly, 2013
- Chairperson of Programme Committee, XXV.Izakovič memorial, Trenčianske Teplice, 2014
- Member of Programme Committee, XXIV. Biochemical Symposium, Bratislava, 2014

Ing. Helena Kavcová
- Member of Organising Committee XXVIII.Xenobiochemical Symposium, Kremnica, 2015

Silvia Marková
- Member of Organising Committee XXVIII.Xenobiochemical Symposium, Kremnica, 2015

RNDr. Michaela Pavlovičová, PhD.
- Member of Organising Committee, Drobnica memorial, Bojná, 2013

PhDr. Zuzana Klimešová

- Member of Organising Committee, Drobnica memorial, Bojná, 2013
- Member of Organising Committee XXVIII.Xenobiochemical Symposium, Kremnica, 2015
- Member of Organising Committee, Drobnica memorial, Smrekovica Podsuchá, 2015

RNDr. Karol Ondriaš, DrSc.

- Member of Programme Committee, VI. Biophysical Symposium, Martin, 2014

Ing. Andrej Rusnák, PhD.

- Member of Organising Committee, Drobnica memorial, Bojná, 2013
- Member of Organising Committee XXVIII.Xenobiochemical Symposium, Kremnica, 2015
- Member of Organising Committee, Drobnica memorial, Smrekovica Podsuchá, 2015

Ing. Zdena Sulová, DrSc.

- Member of Organising and Programme Committees, Drobnica memorial, Bojná, 2013
- Member of Organising Committee XXVIII.Xenobiochemical Symposium, Kremnica, 2015
- Member of Organising Committee, Drobnica memorial, Smrekovica Podsuchá, 2015

Mgr. Mário Šereš, PhD,

- Member of Organising Committee XXVIII.Xenobiochemical Symposium, Kremnica, 2015

RNDr. Ivan Zahradník, CSc.

- Member of Programme Committee, V. Biophysical Symposium, Bratislava, 2012
- Member of Programme Committee, VI. Biophysical Symposium, Martin, 2014

Ing. Alexandra Zahradníková, DrSc.

- Member of Programme Committee, VI. Biophysical Symposium, Martin, 2014

- **Supplementary information and/or comments documenting the international and national status of the Institute**

List of invited presentations at international and national scientific institutions:

ZAHRADNÍK, Ivan. Recent progress in understanding of ryanodine receptor function, INSERM U769, Cardiologie Cellulaire et Moleculaire,,Faculté de Pharmacie, University Paris Sud, Chatney-Malabry, FR, Sept 18, 2012

ZAHRADNÍKOVÁ, Alexandra. Structure and function of ryanodine receptors. INSERM U769, Cardiologie Cellulaire et Moleculaire, Faculté de Pharmacie, Châtenay-Malabry Cedex. Paris, FR, May 21, 2013

LACINOVÁ, Ľubica. Regulácia T-typu vápnikových kanálov napätím a farmakologickými látkami. [Regulation of T-type calcium channels by voltage and pharmacological agents], Faculty of Medicine, Masaryk University, Brno, Czech Republic, Sept 19, 2013

LACINOVÁ, Ľubica. Geneticky modifikované plodiny. [Gene modified crops], Faculty of Social Studies, Masaryk University, Brno, Czech Republic, Sept 17, 2013

LACINOVÁ Ľubica Low-voltage-activated calcium channels: why do they open so easily? Institute of Phamacy, Center of Chemistry and Biomedicine, University of Innsbruck, Austria, January 30, 2015.

2.4. Tables of project structure, research grants and other funding resources

- **International projects and funding**

2.4.1. Major projects within the European Research Area and other important project – Framework Programmes of the EU, ERA-NET, European Science Foundation, NATO, COST, INTAS, etc. (here and in items below please specify: 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 "I"),

	Project title	Typ / Project number	Duration in months	Funding for the Institute (EUR)	Role of the Institute / Responsible person
2012	Hypoxia and oxygen sensing, signalling and adaptation	COST/TD0901	07/2009-11/2013	7667 (2012-2013)	Co-investigator/Oľga Križanová "I"
	Gasotransmitters: from basic science to science to therapeutic applications (ENOG: European Network on Gasotransmitters)	COST/BM1005	5/2011-5/2015	11667 (2012-2015)	Co-investigator/Karol Ondriaš "I"
	Clinical Development of Nitisone for Alkaptonuria (DevelopAKUre)	FP7 Health/304985	11/2012-04/2018	34092,5 (2012-2015)	Co-investigator/Andrea Zaťková "W"
2013					
2014	Reactive Oxygen Species	COST/BM1203	05/2014-05/2016	6000 (2014-2015)	Co-investigator/Oľga Križanová "I"
2015	Mitochondria-endoplasmic reticulum functional interplay in Wolfram Syndrome: emerging role for heart and brain protection	FP7 Marie Curie Action/ 0063/01/02	03/2015-12/2018	15939 (2015)	Coordinator/Michal Cagalinec "C"

2.4.2. Other international projects, incl. total funding and funding for the institute

Possible correlations between expression/activity of various proteins/enzymes markers and incidence of myelodysplastic syndrome (MDS) and its development to acute myeloid leukemia (AML) in samples from patients treated and untreated with Lenalidomide, as well as Lenalidomide's effects on expression/activity of some markers using the leukemic cell lines (CELGENE). Coordinator: doc. Ing. Albert Breier, DrSc., Contract with company Celgene. 10/2009-12/2014, total funding: 94000 €; funding for IMPG SAS (2012-2015): 76458.3 €

2.4.3. Other important, international projects and collaborations without direct funding (max. 10 projects)

- **National projects and their funding**

2.4.4. Projects supported by the Slovak Research and Development Agency (APVV)

Role of the Institute e.g. coordinator “C”, investigator “I”.

	Project title	Typ / Project number	Duration in months	Funding for the Institute (EUR)	Role of the Institute / Responsible person
2012	Mechanisms of ryanodine receptor dysregulation	LPP-0440-09	09/2009-08/2012	17077 (2012)	Coordinator/Alexandra Zahradníková "C"
	Calcium channels in neuronal excitability	APVV-0212-10	05/2011-10/2014	153910 (2012-2014)	Coordinator/Ľubica Lacinová "C"
	Alternation in cell metabolism associated with drug transporter P-glycoprotein overexpression in leukemia cells	APVV-0290-10	05/2011-10/2014	144633 (2012-2014)	Coordinator/Zdena Sulová "C"
	Myocardial remodelling – the role of calcium signalling	APVV-0721-10	05/2011-10/2014	205013 (2012-2014)	Coordinator/Alexandra Zahradníková "C"
	IP3 receptors, their modulation andf function in cancer cells	APVV-0045-11	07/2012-12/2015	95745,5 (2012-2015)	Coordinator/Oľga Križanová "C"
	Study of molecular mechanism of H2S biological effects	APVV-0074-11	07/2012-12/2015	81262 (2012-2015	Coordinator/Karol Ondriaš "C"
	Study of channel properties of novel crown ethers containing polymers in lipid	APVV/SK-FR-0014-11	01/2012-12/2013	2257 (2012-2013)	Coordinator/Karol Ondriaš "C"
	Energetic cross-talks and cytoarchitecture of cardiac myocytes. Role of the mitochondrial protein OPA1	APVV/SK-FR-0021-11	01/2012-12/2013	3669 (2012-2013)	Coordinator/Marta Novotová "C"
	Antitumour effect of biologically active ligands of nuclear retinoid X receptor heterodimers in tissue carcinoma cell lines	APVV-0160-11	07/2012-12/2015	32581 (2012-2015)	Co-investigator/Zdena Sulová "W"
	Preparation of nanostructured interfaces, their integration with bioelements and subsequent use	APVV-0282-11	07/2012-12/2015	19500 (2012-2015)	Co-investigator/Zdena Sulová "W"
	Molecular mechanisms of the crosstalk between stress hormones and hypoxia in tumor cells: effect on expression and function of cancer-related protein CA IX	APVV-0893-11	07/2012-12/2015	18926,8 (2012–2015)	Co-investigator/Oľga Križanová "W"
2013	Functional analysis of newly identified DNA variants in genes responsible for cystic fibrosis and fenylketonuria	APVV-0240-12	10/2013-12/2016	20127 (2013-2015)	Coordinator/Ľudevít Kádaši "C"
2014					
2015	Possible dual function of P-glycoprotein in leukemia cells: efflux pump and regulatory protein	APVV-14-0334	07/2015-07/2018	17800 (2015)	Coordinator/Zdena Sulová "C"
	Biochips and biosensors for glycorecognition, their development, preparation and application in cancer research	APVV-14-0753	07/2015-06/2019	2000 (2015)	Co-investigator/Zdena Sulová "W"

2.4.5. Projects supported by the Scientific Grant Agency of the Slovak Academy of Sciences and the Ministry of Education (VEGA) for each year, and their funding

VEGA	2012	2013	2014	2015
Number	16	14	13	15
Funding in the year (EUR)	104094	93442	92241	86866.5

[1]

- **Summary of funding from external resources**

2.4.6. List of projects supported by EU Structural Funds

2.4.7. Summary of external resources of the EU Structural Funds (ERDF/ESF)

Role of the Institute in the project, e.g. coordinator "C", work package leader "W", investigator "I".

Year	Project title	Project number	Duration in months	Funding for the Institute (EUR)	Role of the Institute
2012	Diagnostics of socially important disorders in Slovakia, based on modern biotechnologies (DNA – DG)	ITMS 26240220058	11/2010-10/2013	397083,6 (2012-2014)	Coordinator/Ľudevít Kádaši "C"
	Center of excellence for translational research in molecular medicine (TRANSMED 2)	ITMS 26240120030	06/2010-10/2012	2308,6 (2012)	Co-investigator/ Oľga Križanová "W"
	Center of excellence for glycomics (GLYCOMICS)	ITMS 26240120031	11/2010-10/2014	138211,7 (2012-2014)	Co-investigator/ Zdena Sulová "W"
	Building of competency centre for research and development in the field of molecular medicine	ITMS 26240220071	10/2011-10/2015	70900 (2012-2015)	Co-investigator/ Zdena Sulová "I"
2013	University science park for biomedicine Bratislava	ITMS 26240220087	03/2013-12/2015		Co-investigator/ Oľga Križanová "W"
2014					
2015	Completing the infrastructure for modern research of lifestyle diseases.	ITMS 26230120006	10/2015-12/2015	2142700 (2015)	Co-investigator/ Zdena Sulová "W"

All Structural Funds projects were of the ERDF type.

[1] Excluding projects for the popularisation of science

External resources	2012	2013	2014	2015	total	average
External resources (milions of EUR)	0,532	0,643	0,304	2,239	**3,718**	**0,929**
External resources transfered to coooperating research institute (milions of EUR)	0,038	0,051	0,050	0,009	**0,148**	**0,037**

- **Supplementary information and/or comments on research projects and funding sources**

2.5. PhD studies and educational activities

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

IMPG SAS is accredited in following programs:

- 4.2.10 Animal Physiology
  – Faculty of Natural Sciences, Comenius University in Bratislava

- 4.1.22 Biochemistry
  – Faculty of Chemical and Food Technology, Slovak Technical University in Bratislava

- 4.1.12 Biophysics
  – Faculty of Natural Sciences, University of P.J. Šafárik in Košice

The accreditations for all programs were awarded without temporal limitations.

2.5.2. Summary table on doctoral studies (number of internal/external PhD students; number of foreign PhD students, number of students who successfully completed their theses, number of PhD students who quit the programme*)*

PhD study	31.12.2012			31.12.2013			31.12.2014			31.12.2015		
Number of potential PhD supervisors	14			13			16			13		
PhD students	number	defended thesis	students quitted	number	defended thesis	students quitted	number	defended thesis	students quitted	number	defended thesis	students quitted
Internal	9,0	2,0	0,0	10,0	1,0	0,0	7,0	4,0	1,0	4,0	4,0	0,0
External	1,0	1,0	0,0	1,0	0,0	0,0	1,0	0,0	0,0	2,0	0,0	0,0
Other supervised by the research employees of the institute	3,0	0,0	0,0	4,0	0,0	0,0	4,0	1,0	0,0	2,0	2,0	0,0

2.5.3. Summary table on educational activities

Teaching	2012	2013	2014	2015
Lectures (hours/year)[2]	175	210	178	19
Practicum courses (hours/year)[2]	98	112	164	150
Supervised bachelor theses (in total)	5	5	5	9
Supervised diploma theses (in total)	14	15	14	14
Supervised PhD theses (in total)	17	18	17	16
Members in PhD committees (in total)	14	16	18	17
Members in DrSc. committees (in total)	4	4	4	5
Members in university/faculty councils (in total)	5	4	4	5
Members in habilitation/inauguration committees (in total)	0	3	1	0

2

2.5.4. List of published university textbooks

DOBROTA, Dušan - BRECHTLOVÁ, M. - DRGOVÁ, A. - GUZY, J. - HALČÁK, L. - JEŽOVÁ, Daniela - KAPLÁN, Peter - **KRIŽANOVÁ, Oľga** - KRON, I. - LEHOTSKÝ, Ján - LÍŠKA, B. - MAREKOVÁ, Mária - PECHÁŇ, Ivan - PODHRADSKÝ, J. - RAČAY, P. Lekárska biochémia [Medical Biochemistry] : university textbook. 1. slov. vyd. Martin : Osveta, 2012. 723 p. ISBN 978-80869-293-9.

UHRÍKOVÁ, Daniela - WACZULÍKOVÁ, Iveta – ZIEGELHÖFFER, Attila – HIANIK, Tibor - **GABURJÁKOVÁ, Jana - GABURJÁKOVÁ, Marta** - **ZAHRADNÍKOVÁ, Alexandra –** URBANÍKOVÁ, Ľubica – BELIČKA, Michal - **TOMÁŠOVÁ, Lenka**. Biofyzika - Vybrané kapitoly [Biophysics - selected chapters : University textbooks. - Bratislava : Univerzita Komenského v Bratislave, 2015, p. 250. ISBN 978-80-223-3800-4.

2.5.5. Number of published academic course books

Two academic course books were published:

KRIŽANOVÁ, Oľga. Nervový systém a základy neuronálnych signalizácii [Nervous system and the basics of neuronal signalizing] [elektronický zdroj]. 1. vyd. Martin: Jesséniova lekárska fakulta Univerzity Komenského, 2012. 1 CD-ROM. ISBN 978-80-89544-25-7.

KRIŽANOVÁ, Oľga. Vybrané biochemické a molekulárne-biologické metódy v lekárskom výskume a medicínskej diagnostike. [Selected methods of biochemistry and molecular biology for medical research and medical diagnostic] [elektronický zdroj]. 1.vyd. Martin : Vydavateľ Jesséniova lekárska fakulta Univerzity Komenského, 2012. 1 CD-ROM. ISBN 978-80-89544-23-3.

[2] Do not include time spent with bachelor, diploma or PhD students during their supervising

2.5.6. List of joint research laboratories/facilities with universities

[1] Joint research laboratories: Laboratory of Genetics IMPG SAS and Department of Molecular Biology Faculty of Natural Sciences, Comenius University in Bratislava (until May 1, 2015)

[2] Joint research laboratories: Department of Transport Proteins IMPG SAS and Faculty of Chemical and Food Technology, Slovak University of Technology in Bratislava

- **Supplementary information and/or comments on doctoral studies and educational activities**

Traditionally, PhD studies at IMPG SAS have an international component. In the assessed period, three graduate students were awarded fellowships to perform a total of 5 long-term visits at collaborating institutions abroad:

- **Katarína Ondáčová (Jašková) (2012):** Scholarship "European Social Fund Doctoral Studies and Internationalisation Programme DoRa", 4.5-month stay at the Faculty of Medicine, University Tartu, Estonia, in the laboratory of Dr A. Kaasik.
- **Lucia Messingerová (2012/2013):** SAIA scholarship, 6-month stay at Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins Hospital, Baltimore, MD, USA, in the laboratory of Dr S. D. Gore.
- **Lucia Lichvárová (2014):** National Scholarship Program, 2-month stay at the Faculty of Medicine, University Tartu, Estonia, in the laboratory of Dr A. Kaasik.
- **Lucia Lichvárová (2014):** Scholarship "European Social Fund Doctoral Studies and Internationalisation Programme DoRa", 3-month stay at the Faculty of Medicine, University Tartu, Estonia, in the laboratory of Dr A. Kaasik.
- **Katarína Ondáčová (Jašková) (2015):** National Scholarship Program, 2-month stay at Faculty of Medicine, University Leicester, United Kingdom in the laboratories of prof. Ian Forsythe and Dr Vincenzo Marra.

Additionally, graduate students gain international experience by active participation at international conferences. In 2012-2015, our graduate students received 6 travel grants to conferences/workshops and 2 awards for presentations at conferences abroad.

Additional honours included 11 awards for presentations at conferences (national and international) in Slovakia; 1 motivational stipend awarded by the Dean of FNS, Comenius University; 2 awards in the competition of PhD students in Physiology and General Biology, and 3 awards for excellent scientific results in the National Competition of Slovak Society for Biochemistry and Molecular Biology (member of FEBS and IUBMB) for young scientists (PhD. students and postdocs).

The quality of our PhD education is further illustrated by the current positions of students that finished their PhD study in the assessed period:

In the academia:

- **Anton Caro (2012):** Postdoctoral Fellow, CBMN, Université de Bordeaux/CNRS, Pessac, France (2012-present)
- **Barbora Tencerova (2012):** Postdoctoral Fellow, Department of Biomedicine, University of Bergen, Bergen, Norway (2012-present)
- **Radoslav Janicek (2013):** Postdoctoral Fellow, Department of Pharmacology & Physiology, Rutgers, UMDNJ – New Jersey Medical School, Newark, NJ, USA (2013-2015); Postdoctoral Fellow, Department of Physiology, University Bern (Switzerland) (2015-present)

- **Lucia Lichvárová (2015):** Postdoctoral Fellow, Centre for Disease Models and Biomedical Imaging, University of Tartu, Estonia (2015); Assistant, Department of Anatomy, Faculty of Science, University of Fribourg, Switzerland (2016-present)

Outside of academia:

- **Andrea Faltinova (2015):** Slovak representative for EDQM (European Directorate for The Quality of Medicines & Health Care); Slovak representative for PEMSAC (The Platform of European Market Surveillance Authorities for Cosmetics)

2.6. Social impact

2.6.1. List of the most important results of applied research projects. Max. 10 items

Although fundamental research constitutes 95 % of research at IMPG SAS, the Institute traditionally performs activities with potential societal impact.

1. POLAK, EMIL – FICEK, ANDREJ – **RADVANSZKY, JAN**; – **SOLTYSOVA, ANDREA** – URGE, OTTO – CMELOVA, ELEONORA – KANTARSKA, DANA – **KADASI, LUDEVIT**. Phenylalanine hydroxylase deficiency in the Slovak population: Genotype-phenotype correlations and genotype-based predictions of BH4-responsiveness. Gene, 2013, vol. 526, iss. 2, p 347-355 (2.196 – IF2012) ISSN: 0378-1119.
2. **MESSINGEROVA, LUCIA** – JONASOVA, ANNA – BARANCIK, MIROSLAV – **POLEKOVA, LENKA** – **SERES, MARIO – GIBALOVA – LENKA – BREIER, ALBERT – SULOVA ZDENA** Lenalidomide treatment induced the normalization of marker protein levels in blood plasma of patients with 5q-myelodysplastic syndrome. General Physiology and Biophysics, 2015, vol. 34, iss. 4, p 399-406, (1.173 IF2014) ISSN: 0231-5882.
3. SAKTHIVEL SRINIVASAN – **ZATKOVA – ANDREA** – NEMETHOVA – MARTINA – SUROVY, MILAN – **KADASI, LUDEVIT** – SARAVANAN, MADURAI P. Mutation Screening of the HGD Gene Identifies a Novel Alkaptonuria Mutation with Significant Founder Effect and High Prevalence, Annals of Human Genetics, 2014, vol. 78, iss. 3, p 155-164, (1.926, IF2013), ISSN: 0003-4800
4. **SULOVÁ, ZDENA – MESSINGEROVÁ LUCIA – ŠEREŠ, MÁRIO** – BARANČIK, MIROSLAV – **BREIER, ALBERT** Final Report for project investigation: “Correlations between expression/activity of marker proteins/enzymes in patients with myelodysplastic syndrome treated or non-treated by Lenalidomide”. Internal document. Provided to Celgene corp. (USA) in July 2013.

2.6.2. List of the most important studies commissioned for the decision-making authorities, the government and NGOs, international and foreign institutes

2.6.3. List of contracts and research projects with industrial and other commercial partners, incl. revenues

Project CELGENE: Possible correlations between expression/activity of various proteins/enzymes markers and incidence of myelodysplastic syndrome (MDS) and its development to acute myeloid leukemia (AML) in samples from patients treated and untreated with Lenalidomide, as well as Lenalidomide's effects on expression/activity of some markers using the leukemic cell lines.

Coordinator: doc. Ing. Albert Breier, DrSc., contract with company Celgene (USA), 10/2009-12/2014

2.6.4. List of licences sold abroad and in Slovakia, incl. revenues

2.6.5. List of most important social discourses under the leadership or with significant participation of the institute (max. 10 items)

2.6.6. Summary of relevant activities, max. 300 words

The main activity of the Institute towards the society represents research oriented on applications to medicine. During the assessed period, application-oriented research was conducted predominantly using the financial support of the following three projects:

1. **Diagnostics of socially significant diseases in Slovakia, based on modern biotechnologies**, Project of structural funds EU ITMS 26240220058.
   In Slovak phenylketonuria (PKU) patients, based on correlation between the mutation of *PAH* (phenylalanine hydrolase) gene and patients phenotype and with the aid of published results of clinical studies and database information, the effectiveness of tetrahydrobiopterine therapy in Slovak PKU patients was predicted (Polák et al., Gene, 2013).
2. **Correlations between expression/activity of marker proteins/enzymes in patients with myelodysplastic syndrome treated or non-treated by Lenalidomide**. Contracted research financed by Celgene Corporation (USA).
   Effectiveness of lenalidomide therapy in a subgroup of patients with myelodysplatic syndrome characterized by deletion localized in q arm of fifth chromosome was assessed (Messingerova et al., Gen Physiol Biophys, 2015). On request of the National Institute of Oncology in Bratislava, blood samples of more than 150 leukaemia patients were analysed for the presence of the expression of drug transporters involved in multidrug resistance.
3. **Clinical Development of Nitisinone for Alkaptonuria**. Project of 7. FP EU Health no. 304985
   Complex mutation analysis of gene encoding the enzyme homogentisate oxidase, mutation of which is responsible for alkaptonuria, was performed in patients from Slovakia and from abroad (Sakthivel et al., Ann Hum Genet, 2014). A public online database of mutations in the HGD gene occurring in patients with alkaptonuria was created: http://hgddatabase.cvtisr.sk.

Laboratory of Genetics, a joint laboratory of the Institute of Molecular Physiology and Genetics SAS (until 1 May 2015) and Faculty of Natural Sciences, Comenius University in Bratislava was responsible for projects 1 and 3, and Department of Transport Proteins of Institute of Molecular Physiology and Genetics SAS was responsible for project 2.

2.7. Popularisation of Science (outreach activities)

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

Meno	Spoluautori	Typ[1]	Názov	Miesto zverejnenia	Dátum alebo počet za rok
doc. RNDr. Ľudevít Kádaši, DrSc.		TV	"Science Spectrum" Human molecular genetics	RTVS, STV2	18.12.2012
doc.RNDr. Ľubica Lacinová, DrSc.		PB	Biotechnology and contemporary art	MENSA	29.11.2012
doc.RNDr. Ľubica Lacinová, DrSc.		RO	Rubikon	RTVS, Radio Devín	30.11.2012
doc.RNDr. Ľubica Lacinová, DrSc.		TV	Transgenic animals and plants	TV Markíza	16.11.2012
Ing. Alexandra Zahradníková, DrSc.	editor Tomas Prokopcak	IN	Biophysicist Zahradníková: Slovaks have achieved significant results	Sme.sk	12.1.2012
doc. RNDr. Ľubica Lacinová, DrSc.		PB	Artist or scientist? Art in the era of biotechnologies	EMAG (European Mensas Annual Gathering)	31.7.2013

doc. RNDr. Ľubica Lacinová, DrSc.		PB	Is Scientific Advice to Policy Makers Value-free?	UNESCO Conference on Emerging Ethical Issues in Science and Technology	30.5.2013
Ing. Alexandra Zahradníková, DrSc.		PB	Researchers' night	Slovak National Museum	27.9.2013
Ing. Alexandra Zahradníková, DrSc.	moderator Katarina Kacerova,	RO	guest of "Magnet"	RTVS, Radio Regina	5.1.2013
Mgr. Andrea Zaťková, PhD.		TL	Alkaptonuria –black bone disease in Slovakia	Lekárnické listy, 12/2013, str. 30-31	16.12.2013
doc. Ing. Albert Breier, DrSc.		TV	The main reports: "The controversial chemical"	TV Markíza	27.11.2014
doc. Ing. Albert Breier, DrSc.		TV	The main reports: "Chicken or the egg, and osteoporosis"	TV JOJ	29.3.2014
Ing. Matej Hoťka		RO	guest of "Nočná pyramída"	RTVS Radio Slovensko	12.12.2014
prof. RNDr. Ľudevít Kádaši, DrSc.		TV	New hope for diabetics	TA3	17.2.2014
prof. RNDr. Ľudevít Kádaši, DrSc.		TL	Spinal muscle dystrophies	Carissimi	2014
Ing. Alexandra Zahradníková, DrSc.	•M. Hoťka, G. Gajdošíková, Z. Nichtová, M. Novotová, L. Novota, A. Zahradníková, jr., I. Zahradník	PB	Information booth "Live cardiac cells" at Researchers' night	Stará tržnica, Bratislava	26.9.2014
Ing. Alexandra Zahradníková, DrSc.	Frederique Hazéová	IN	interview "Nobel prize for chemistry: How the microscope became a nanoscope "	Science.sk	8.10.2014
doc. RNDr. Ľubica Lacinová, DrSc.	Ivica Ruttkayová	RO	"Rubikon": Sustainable development	RTVS, Radio Devín	29.11.2015
Ing. Alexandra Zahradníková, DrSc.	Pavol Petrovič, Ivan Valent, Elena Cocherová, Jana Pavelková	IN	Calcium waves generated by the cardiac RyR channel, Youtube video	https://youtu.be/4PmnQryo6No	17.6.2015

PB – popularisation lectures, TL –press media, TV, RO – telecommunication media, IN - internet,

2.7.2. Table of outreach activities according to institute annual reports

Outreach activities	2012	2013	2014	2015	total
Articles in press media/internet popularising results of science, in particular those achieved by the Institute	5	11	12	5	33
Appearances in telecommunication media popularising results of science, in particular those achieved by the Institute	6	4	9	2	21
Public popularisation lectures	4	5	9	0	18

- **Supplementary information and/or comments on popularisation activities, max. 300 words**

2.8. Background and management. Human resources and implementation of recommendations from previous assessment

2.8.1. Summary table of personnel

Personnel	2012	2013	2014	2015
All personnel	65,0	63,0	59,0	45,0
Research employees from Tab. Research staff	36,0	34,0	35,0	29,0
FTE from Tab. Research staff	25,591	24,650	26,626	22,526
Average age of research employees with university degree	41,1	42,6	43,0	42,7

2.8.1.1. Professional qualification structure (as of 31.12. 2015) FEMALE

FEMALE	AGE								
Number of	< 30	31 - 34	35 - 39	40 - 44	45 - 49	50 - 54	55 - 59	60 - 64	> 65
DrSc. / prof.							3	1	
II.a / Assoc. prof.			1	3		1		1	
Other researchers PhD./CSc.	3	2	1	2		1			
doc. / Assoc. prof.									

2.8.1.2. Professional qualification structure (as of 31.12. 2015) MALE

MALE	AGE								
Number of	< 30	31 - 34	35 - 39	40 - 44	45 - 49	50 - 54	55 - 59	60 - 64	> 65
DrSc. / prof.							1		
II.a / Assoc. prof.		1	1	1					1
Other researchers PhD./CSc.	2		1						
doc. / Assoc. prof.									

2.8.2. Postdoctoral and mobility scheme

2.8.2.1. Postdoctoral positions supported by national and international resources

Mgr. Zuzana Nichtová, PhD., RNDr. Katarína Ondáčová, PhD. and Ing. Matej Hoťka, PhD. were supported by resources of IMPG SAS after completing their PhD. study.

2.8.2.2. Postdoctoral positions supported by external funding

2.8.2.3. SAS stipends and SASPRO stipends

MMedSc. Eliyahu Dremencov, PhD. - SAS Scholarship program, 10/2013-10/2017

RNDr. Michal Cagalinec, PhD. – SASPRO, 03/2015- 12/2018

2.8.2.4. Internal funding - the Slovak Academy of Sciences Supporting Fund of Stefan Schwarz

In 2012 - 2015, three postdoctoral positions supported from the Fund of Stefan Schwarz continued from the previous assessment period
Mgr. Zuzana Tomášková, PhD. (since January 1, 2010)
RNDr. Mária Karmažínová, PhD. (since May 1, 2011)
Mgr. Mário Šereš, PhD. (since January 1, 2012)

2.8.3. Important research infrastructure *(max. 2 pages)*

For many years, the Institute achieves results that, according to the results of the previous accreditation, rank the institute among the best institutes of the Slovak Academy of Sciences. Researchers of IMPG SAS have ample experience in electrophysiology, cell physiology, cell biology, biochemistry, molecular biology, molecular physiology, cell morphology and experimental physiology. Research projects at IMPG SAS require advanced experimental equipment, and therefore adequate infrastructure is crucial for their successful implementation. Infrastructure of the institute was built using resources ranging from NIH FIRCA and HHMI grants (USA) through Volkswagenstiftung (Germany), FP6 projects of the European Commission, to funding programmes of the Centres of Excellence (at the national and SAS levels), and culminating in funding by the Structural Funds of the EU in which IMPG SAS was the principal partner or partner (as summarised in Table 2.4.7). In the following text, the infrastructure that was built/upgraded in the assessed period is shown in **bold**.

In 2012-2015, IMPG SAS shared their infrastructure (confocal microscopes, electron microscope, patch-clamp setups, Typhoon imager, Accuri cytometer, ultracentrifuge) with colleagues from other institutes in the Slovak Academy of Sciences (IEE, CRI, ICh, IMB, IMMM), institutions in Slovakia (FNS UPJS Košice; CIB UPJS Košice; FChFT STU Bratislava; FPh Comenius Univ. Bratislava, Institute of Metrology, Bratislava) and abroad

(FNS Charles Univ., Prague, Czech Republic; VRI, Brno, Czech republic, FI Masaryk Univ, Brno, Czech Republic; INSERM U796, LabEX LERMIT, IFR 141, Univ. Paris Sud, Chatenay-Malabry, France; Institute Pasteur, France; Inst. Biomed. Transl. Med, Univ. Tartu, Tartu, Estonia).

The institute is equipped for studies of electrophysiological phenomena from single ion-channel molecules, through single cells and tissue slices, to in situ studies in live animals (3 + **1 planar lipid bilayer setups**, 2 + **2 patch clamp setups**, **one setup for in situ electrophysiological recording**, and a variety of accessory equipment: D/A-A/D converters, electronic and **mechanical vibration isolation tables**, **microscopes**, micromanipulators, setups for fast perfusion, **Faraday cages**, patch pipette pullers, **vibratome** for the preparation of heart and neuronal tissue slices, Langendorff apparatus for the isolation of calcium-tolerant cardiac myocytes). This infrastructure was essential for implementing six ongoing projects and eight projects completed in the assessed period.

Infrastructure built to cover fluorescence methods to study living specimens includes Leica Microsystems **TCS SP8 STED 3X STED super-resolution confocal microscope** and a TCS SP2 AOBS confocal microscope, an Amersham **In Cell Analyzer 2200** suitable for high-resolution microscopy, long-term recording and automated high-content screening, a **CMOS camera-based fluorescence system** for wide-field imaging, and an Amersham **Cytell cell imaging system** for image cytometry, an **Accuri C6 (BD) flow cytometer** and a Cassy TT (Roche) cell counting and analysing system. The confocal systems are combined with electrophysiology setup (patch clamp, field stimulation), which allows their use for dynamic measurements of calcium signals in stimulated cells. This infrastructure was essential for implementing eight ongoing projects and six projects completed in the assessed period.

For high spatial resolution, we use transmission electron microscope (JEOL JEM-1200Ex electron microscope with Gatan Dual Vision 300W CCD camera) with elemental analyser (**EDS analyser Inca**, Oxford Instruments) and with equipment necessary for sample preparation (ultra-microtome, thermostatic oven, perfusion fixation setup). Recently, we have also access to the high-throughput sub-Angstrom imaging on **FEI Titan Themis electron microscope** (Pavilion of Materials Research SAS). This infrastructure was essential for implementing four ongoing projects and three projects completed in the assessed period.

The above methods are complemented with infrastructure for classical biochemistry (1 + **1 UV/VIS spectrophotometers** equipped for a wide range of kinetic and steady-state measurements, electrophoresis/Westen blotting, radioactive, chemiluminescent and fluorescent detection on Amersham Typhoon 9210 and Imager 600) as well as for molecular biology (**2pc Bio-Rad CFX96 for Real Time PCR**, Eppendorf Mastercycler for RT-PCR). The institute is also equipped for cell culture of primary cultures and cell lines (**2 laminar flow cabinets**, 2 + **2 CO_2 incubators**) and cell transfection by lipofection or **electroporation** (**Neon Transfection System,** Invitrogen). Adenoviral transfection techniques are in the process of implementation. This infrastructure was essential for implementing eleven ongoing projects and six projects completed in the assessed period.

The research conducted at the institute requires significant computing infrastructure. At the Institute, there are dedicated **computer workstations** for the development and use of mathematical models (Wolfram Research **Mathematica**), computer simulations of molecular and cellular processes (**MATLAB**), molecular modelling (**UCSF Chimera**), as well as software for image analysis, 3D reconstruction and deconvolution (Leica **LAS X**, SVI **Huygens**). The laboratories are well equipped with **computers** of the adequate quality and with commercial software (Windows platform) for the **acquisition and analysis of electro-physiological data**, **acquisition of optical data**, and recording of electron-microscopy data. For tasks requiring higher computing power we have access to the supercomputer **Aurel** (IBM) at the Computing Centre of the Slovak Academy of Sciences. A dedicated **file server** for long-term data storage is backed up off-site at the Computing Centre SAS. This infrastructure is essential for implementing all projects at IMPG SAS.

Owing to the relocation of the institute to new premises in the **Pavilion of Biomedical Sciences**, sufficient laboratory space is available and has all the required permissions from the Regional Authority for Public Health and State Veterinary and Food Authority. IMPG SAS

has sufficient facilities such as ultracentrifuges, **deep freezers** and **fume hoods**. We have access to the **cold rooms and warm rooms** of the Pavilion of Biomedical Sciences. The **animal facility** of the Pavilion of Biomedical Sciences that is in the last stages of completion will have sufficient capacity and infrastructure for the required number of experimental animals (including transgenic animals) and for the required **surgical procedures**. Recently, we have used the animal facility of the Institute of Experimental Pharmacology and Toxicology SAS. For experimental interventions on animals, we have instrumentation for recording the extent of voluntary exercise of laboratory rodents and access to **ultrasonography/ECG** and **Langendorff perfusion apparatus** for small laboratory rodents at the Institute for Heart Research SAS. This infrastructure is essential for for implementing all projects at IMPG SAS.

2.8.4. Description of how the results and suggestions of the previous assessment were taken into account

According to the last accreditation, IMPG SAS was not committed by any specific suggestion or task that must be performed by the organisation prior to the next regular evaluation.

The institute paid attention to continuing the activities that were assessed as positive: to perform hypothesis driven research and create original concepts; to publish in high quality journals; to maintain international scientific collaborations; and to preserve the quality of PhD education. We also managed to keep a favourable number of citations per research article.

Level of external funding: Despite absence of a call from the Scientific Research and Development Agency in the year 2013, funding from SRDA increased from 161,568 €/year to 203,625 €/year. We have substantially increased the funding for IMPG SAS from the Structural Funds from 32,077 €/year to 656,704 €/year. However, the level of funding from international sources decreased from approx. 140,000 €/year to 42,341 €/year since the international projects in this period comprised a lower level of funding for salaries and stipends.

The average funding from VEGA increased from 71,358 €/year in the previous period to 94,161 €/year in the current period.

Recruitment of postdoctoral scientists: In addition to the three existing Stefan Schwarz scholarships, we have obtained two scholarships from SAS /EU sources - one SAS scholarship and one SASPRO scholarship. In May 2015, we have created two postdoctoral positions by using the resources from the streamlined economic section of the institute.

- **Supplementary information and/or comments on management, research infrastructure, and trends in personnel development**

3. Research strategy and future development of the institute for the next five years (2016-2020) (Recommended 3 pages, max. 5 pages)

3.1. Present state of the art in both the national and the international contexts

Molecular physiology of cardiac calcium signalling

Basic research in cardiology is moving towards the molecular-biological aspects of myocardial function. Understanding the physiological processes at the molecular and subcellular levels provides guidance to this effort. Complex data generated by this research necessitate their integration and validation through the use of computer models. The topic of cardiac excitation-contraction coupling developed due to an interdisciplinary approach that requires prolonged training of specialists coming from different disciplines of natural sciences. The team at IMPG SAS consists of physiologists, biophysicists, chemists, engineers and information scientists who develop their curriculum through international experience. In recent years, a solid methodological and intellectual basis for internationally competitive research of structure-function relationships at the level of cardiac muscle cells and molecules related to E-C coupling was built. This includes the isolation of functional cardiac myocytes, measurements of intracellular calcium signals at high spatial and temporal resolution by confocal microscopy integrated with patch-clamp technique for membrane ion channel studies, planar lipid bilayer techniques for study of single intracellular RyR channels, electron microscopy with ultrastructural analysis and quantitative morphometry, mathematical modelling for model-based data analysis and simulations, and bioinformatics methods for structure/function analysis of the involved molecules. In the recent past, we have contributed to the field by highly rated papers in leading physiology and biophysics journals that clarified structural and mechanistic aspects of ion channel gating, calcium signalling and cellular energetics in cardiac myocytes.

Molecular basis of neuronal excitability

Central nervous system (CNS) illnesses, such as depression, anxiety, post-traumatic stress disorder (PTSD), schizophrenia, drug and alcohol addiction are coupled with altered neuronal function including excitability. Direct examination of such changes in identified brain neurons is critical for understanding the corresponding pathophysiology. In vivo electrophysiological examination uses precise anatomic location to reach specific neuron types. In vitro investigations are based on the enzymatic isolation of neurons from a defined brain region, on visual identification based on the neuronal markers and/or anatomy of individual neurons, or on the visual localisation of specific types of neurons in brain slices. For all the mentioned disorders, animal models are developed or are being developed. Such models and experimental methods are also crucial for the early preclinical assessment of the efficacy of CNS drugs and for the development of new CNS medications. The teams at IMPG SAS use in vivo and in vitro electrophysiological examination of certain types of central nervous system (CNS) neurons. Currently, voluntary wheel running (VWR) rats present an established model for voluntary physical activity. A rat model of prenatal stress and infection is in a pilot phase of investigation. In recent years, we established solid neuropsychopharmacology research in our institute. Our achievements include: characterisation of a specific contribution of L-type calcium channel isoforms to neuronal excitability, establishment of an *in vitro* model of neuronal injury, description of the critical role of serotonin-dopamine interactions in the onset of therapeutic effect of antidepressant treatment, role of serotonin-norepinephrine interactions in antidepressant and mood-stabilising effect of atypical antipsychotic drugs, putative role of brain histamine and adenosine in pathophysiology and the treatment of depression and schizophrenia, and role of brain monoamines and neuropeptides in the beneficial mood effect of physical exercise.

Multidrug resistance development in leukaemia cells

Depressed sensitivity to several drugs (multidrug resistance) that occurs in cancer cells (including leukaemia cells) represents a real obstacle in effective cancer therapy and leads to impairments in patients' prognosis. Several diverse but well defined mechanisms are known to be responsible for depressed cell sensitivity to different drugs. Overexpression of P-glycoprotein and/or other membrane drug transporters is the most often observed molecular causality of multidrug resistance. Detailed description of regulatory pathways involved in control of expression/drug efflux activity of these transporters is, therefore, the focus of multidrug resistance research worldwide. Besides the drug efflux activity of P-gp as the major drug transporter active in multidrug resistance, this protein also plays an additional role as a regulatory protein with anti-apoptotic function, seemingly independent of its transport activity. This is responsible for the additional resistance of neoplastic cells expressing P-gp also to several other drugs that are not substrates for P-gp transport. Currently, new modern instrumental infrastructure enables us to use a large variety of cell and molecular biology methods. In addition to the standard methods of biochemistry and molecular biology, our team uses cell cytometry, confocal microscopy, electron microscopy combined with EDS analysis, and online monitoring of cells using the InCell apparatus. The approach to this topic at IMPG SAS is based on evidence based research with clear logic relations between all the laboratory activities. Members of our team are publishing results in internationally recognised scientific journals in which reasonable citation response is obtained.

3.2. Research strategy of the institute in the national and the international contexts, objectives and methods

Outline of general strategy

In agreement with the general trend to integrate fragmented research in Slovakia we are actively involved in formation of a new scientific centre with the aim to enhance the productivity of involved institutes. Together with the Institute of Animal Biochemistry and Genetics (IABG SAS), the Institute launched an initiative to establish a new legal entity. Both institutes signed a Memorandum of Understanding on the formation of the Centre of Biosciences of the SAS. The main motivation for this initiative was to stimulate horizontal integration of research to share the infrastructure and methodologies established in partner institutes. Reaching a reasonable, well-manageable size, the new institution is intended to provide further strengthening of the interdisciplinary character of research, improvement of the efficiency and the quality of research, increased competitiveness within the European Research Area, and in effective applications for international research projects. We also expect a substantial improvement of the managerial processes and decrease of the administrative load on research scientists. The time schedule of the integration process assumes the creation of the Centre of Biosciences by 1 January 2017. In the future, the Centre will also be open to other institutes which currently have the observer status.

We are prepared to explore the potential of the newly built biomedical and technological facilities on the SAS campus that include the super-sensitive electron microscope FEI TITAN Themis, infrastructure for physiological experiments at IHR SAS and surgical facilities at the Pavilion of Medical Sciences. We will further develop our formal collaborations (institutes of SAS - IMB, IHR, IEE BMC, IEPT, ICh, PolI, universities - FMed, FPharm, Comenius University in Bratislava, FChFT STU, University Paris-Sud, France, Albert-Ludwig-University in Freiburg, Germany, National Academy of Med. Sci. Ukraine, and South Ural State Univ., Chelyabinsk, Russian Federation) and informal collaborations (FNS, UPJS Kosice, Med. Univ. Vienna, Austria, Univ. Tartu, Estonia, Ohio State Univ., USA, Univ. Cardiff, Wales, Inst. Org. Chem. and Biochem. Acad. Sci. Czech Republic, Brains On-Line BV and Univ. Groningen, the Netherlands, Univ. Kurume, Japan) to coordinate our efforts and participate in EU and other international projects when possible.

The vision for development of our Institute in the future can be summarized by the following headlines:

- Research topics are relevant in the context of world-wide research; research output is internationally excellent and of reasonable quantity
- The institute is an attractive place for talented and dedicated students, postdocs, and early carrier researchers with international experience
- The institute is a reputable partner of international and domestic research institutions and universities

Molecular physiology of cardiac calcium signalling

The objective of cardiac calcium signalling research at IMPG SAS is to understand the calcium dynamics in cardiac excitation-contraction (E-C) coupling from the structural and functional aspects. The idea behind this is that the phenomena accompanying E-C coupling are by a large part determined by the spatial and temporal variability of the underlying molecular machinery. The spatial and temporal aspects are convolved via reaction-diffusion processes leading to local variation of the interaction between ligands and their receptors. Structural adaptation of the myocytes to the changing demands of the organism adds to the range of effects. The observed variability may reflect the limits of functional states of the studied processes. Several critical aspects of regulation of the key player of E-C coupling, the ryanodine receptor (RYR2), linked to various cardiac disease states, are not fully understood. Recently, the methodological repertoire of our teams was extended for molecular biology approaches to complement functional studies with studies of the relevant protein interactions, especially super-resolution STED fluorescence microscopy. We will focus on identifying the structural basis of ryanodine receptor regulation by cytosolic and luminal calcium, and on the morphological and functional changes of calcium signalling occurring in response to physiological (postnatal development, voluntary exercise) and pathological stimuli (myocardial injury induced by experimental models of cardiac disease).

The principal funding resources for the next period are two projects from Slovak Research and Development Agency (APVV 14-032, APVV-SK-FR-2015-0007), one SASPRO scholarship (0063/01/02), and 6 VEGA projects awarded to members of teams. The state-of-the-art methods, including confocal and super-resolution microscopy, patch-clamp, planar lipid bilayers, electron microscopy, quantitative image analysis, mathematical modelling, simulation, and bioinformatics will be used together with biochemical methods and structural biology for the characterisation of ion channel structure/activity relationship, myocyte ultrastructure, calcium signals, membrane excitability, and to understand the compensatory mechanisms by which myocytes adapt to specific loads.

The involved teams include three senior scientists over 60, five independent/senior researchers aged 35-50 and three PhD students. We expect to benefit from the return of two young scientists from postdoctoral stays abroad. This would enable progress and the continuity of modern research in this field of research after the expected retirement of the most senior scientists in the forthcoming years. The senior researchers involved in this field of research have a very strong background in ion channel biophysics, calcium signalling, cell morphology and mathematical modelling and simulation. Our ability to bring new innovative ideas has been already manifested in a number of successfully completed research projects and in the quality of our publications.

Molecular basis of neuronal excitability

The objective of our future research in neurophysiology is to investigate calcium transporting ion channels in neurons and in heart. In neurons, we will concentrate on pharmacological and non-pharmacological regulation of their excitability and on the analysis of mechanisms of action of antidepressants and mood regulators. We will also investigate excitability alterations caused by external influences, either positive, e.g. a physical exercise, or negative, e.g., an inflammation, with the aim to address the possible replacement of drug therapy by a positive external intervention (exercise) and/or possible alleviation of negative

influences (inflammation) by drug treatment. We will develop new animal models for certain CNS disorders, such as pre- and post-natal exposure to stress, infection and/or ionizing radiation. In parallel to neuronal cells, we will use recombinant ion channels for the characterisations of some highly specific signalling mechanisms.

For these aims, we will use in vivo extracellular single-unit assessment of the generation of action potentials in amino acid-, monoamine-, and neuropeptide-secreting neurons and in vitro whole-cell patch clamp assessment of electrophysiological characteristics of single neurons either acutely isolated, in primary culture, or in slices. For recombinant channels, we will employ the transfection of HEK 293 or CHO cells with plasmids containing corresponding cDNAs. These methods are routinely used in our laboratory. We are currently working on the development of further cutting edge neurophysiological techniques: in vivo patch clamp electrophysiology combined with local iontophoretic intra- or extracellular microinjection of potential CNS drugs to investigate their efficacy; and in vivo and in vitro evaluation of morphological and physiological properties of dendritic spines.

The research in our laboratory is supported by one grant from the Slovak research and development agency (APVV-15-0388), by the Scholarship Award of the Slovak Academy of Sciences, by a DAAD grant (DAAD/SAV), and by 3 VEGA grants. A proposal for a NATO Science for Peace and Security grant, submitted jointly with the Institute of Radiology of the National Academy of Medical Sciences of Ukraine, is under consideration. We are now preparing to join an international consortium entitled “Long Life without Stress” (with universities from Russia, the Netherlands, USA, and Israel.

The team working on neuronal calcium signalling is relatively small. Senior leader of the team has D.Sc. degree obtained for her work on calcium channels. Another team member will submit his D.Sc. thesis in the field of neuropsychopharmacology in 1-2 years. This scientist is in his early 40s, so long-term continuity is ensured. The rest of the team are young PhD students or post-docs. As the membrane excitability is determined not only by diverse ion channels but also by the lipidic environment in which the channels operate, we plan to address this topic in the near future with the help of specialists from IABG SAS. The merger of our institutes should greatly facilitate such exchange.

Multidrug resistance development in leukaemia cells

In the field of multidrug resistance research, our objective is to contribute to understanding the association between the expression of P-gp in neoplastic cells and alterations of cellular regulatory pathways including phosphorylation and glycosylation of proteins and their degradation associated with protein quality control. Our future research will be oriented on a detailed study of: i. molecular causalities responsible for development of multidrug resistance associated with P-gp expression in leukaemia cells; ii. on mechanisms involved in P-gp function as drug transporter and antiapoptotic regulatory protein; and iii. on interplay between drug transporter mediated multidrug resistance and different cell regulatory pathways, including protein phosphorylation, protein glycosylation and others.

Our team is fully equipped for research oriented on the study of mechanisms of multidrug resistance development using neoplastic cell culture. The formation of a common organisation with IABG SAS will amplify our methodology with the important methods of lipidome analysis and specialised recombinant technologies using microbial producers.

The topic of MDR has been studied at IMPG SAS for more than 25 years. All the team members are skilled in the methodology of biochemistry, cellular and molecular biology that are essential for further successful research. Most members of the team are familiar with the methods of fluorescent cytometry and confocal microscopy. Two members are also competent in transmission electron microscopy and EDS. The collective is led by a scientist (DSc. degree) who coordinated research oriented on P-gp associated MDR in two consecutive projects of SRDA. Her DSc. dissertation was based on the topic of P-gp mediated MDR. The team includes a further internationally recognised (DSc. Degree) scientist, two independent scientists (IIa, PhD. degree; one of them under 35 years), three researchers (PhD degree) and two PhD students.

Our research is supported by two active projects of Slovak research and development agency (APVV-14-0334, APVV-15-0303) and 3 projects of the VEGA grant agency. We are also involved in three other SRDA projects that are partially oriented on MDR.

SWOT analysis

STRENGTHS: • Clearly defined research areas • Quality of the infrastructure • Stable personal matrix guaranteeing 3 PhD study programmes • Participation in education at universities • Young scientists with postdoctoral or research experience abroad • High quality publications with adequate citation response • Collaboration between teams	**WEAKNESSES:** • Small institute vulnerable to instabilities from fluctuations • Relatively low number of publications • Low number of international projects • Insufficient resources for the stimulation of existing and recruitment of new researchers • Limited ability to retain the most talented young scientists at IMPG SAS
OPPORTUNITIES: • Formation of a larger organisation by integration with IABG SAS and other related organisations • Participation in projects of European structural Funds • Recruitment of high-quality young scientists • Acquiring funds for research outside of the national budget • Collaboration with the commercial sphere (biomedical organisations, pharmaceutical and biotechnological companies)	**THREATS:** • Unstable conditions of research funding in Slovakia • Fluctuations in continual generational exchange • "Brain drain" • Problematic sustainability of the infrastructure

Project proposals submited to 7RP or H2020	2012	2013	2014	2015
Institute as coordinator	0	0	0	0
Institute as participant	1	0	0	0

4. Other information relevant for the assessment

In autumn 2014, the institutes of SAS started preparations for their transformation to public research institutions. The transformation projects included plans for the fusion of smaller institutes into larger organisational units. The academic community of the institute did not reach an agreement with the director Olga Krizanova on this issue. O. Krizanova preferred focussing research within biomedical disciplines closer to the clinic, while a major part of the academic community preferred orientation on molecular and cellular physiology and biophysics inspired by medical problems. The list of potential partner institutes only partly overlapped between both bodies. O. Krizanova instead of starting negotiations preferred leaving the institute together with a small group of collaborators. As a result, 11 employees of IMPG SAS were delimited into the Centre of Molecular Medicine SAS (MMC SAS). The staff of IMPG SAS after the delimitation amounted to 42. The Institute of Molecular Physiology and Genetics SAS now follows the concept accepted by the majority of the academic community and is preparing for the fusion of the institute with another partner institution (see chapter 3).