Information on the activity of the institute

The institute mission

The maximum extent is 2 pages.

The history of the Institute of Molecular Genetics (IMG) of the Czech Academy of Sciences (CAS) ensues from the Department of Experimental Biology and Genetics of the Institute of Biology of the Czechoslovak Academy of Sciences, headed by Milan Hasek, co-discoverer of immunological tolerance. In 1962, the Institute of Experimental Biology and Genetics (IEBG) of the Czechoslovak Academy of Sciences was founded with M. Hasek as its director. During subsequent years, the "Czechoslovak immunogenetic school" was established; another research themes developed at IEBG were retrovirology and tumour biology. The end of the "Prague Spring" after August 1968 marked the end to this famous era – many scientists had emigrated or lost their positions.

In 1977, the Institute was reorganized and renamed IMG. Molecular biology has become the main topic of the Institute. The original research interests remained; however, they were gradually transferred to the "molecular level." The otherwise difficult seventies and eighties were highlighted by several scientific breakthroughs, especially, co-discovery of reverse transcriptase, discovery of retroviral integration into the genome of the host cell, so-called virogeny, and sequencing of one of the first viral genomes. Emphasis on the molecular biology approaches continued after 1989.

Originally, IMG was housed in two geographically distant locations in the Prague 4 and 6 districts. The separated branches were united in one modern building in 2007 constructed in the campus of research institutes of the CAS in Prague 4 Krc. In 2015, a new building of BIOCEV – the Biotechnology and Biomedicine Centre of the Academy of Sciences and Charles University in Vestec – was completed. The BIOCEV project was funded by the European Union Structural Funds and IMG was one of the main beneficiaries of financial support. The support was used to build a complex of buildings in Vestec, a small town about 6 km from the Prague 4 campus. BIOCEV hosts more than 600 researches from seven institutions, including several IMG research groups, facilities, and a large IMG-hosted national research infrastructure, Czech Centre of Phenogenomics. In the same period, two other research infrastructures, hosted by IMG, started operating in the Prague 4 Krc campus; namely, CZ-OPENSCREN and Czech-BioImaging. Besides the main parts in Prague 4 and Vestec, the Institute includes one detached research group hosted by the Institute of Organic Chemistry and Biochemistry of the CAS in Prague 6 and a poultry facility located about 35 km from Prague in the small Central Bohemian village of Kolec.

The principal mission of IMG is experimental biology research. The research is focused on the molecular bases of serious diseases (e.g., cancer, leukaemia, AIDS), biology of normal and transformed cells, immune mechanisms involved in the defence of the organism, DNA repair mechanisms, and cellular senescence. Selected retroviruses, oncogenes and tumour suppressors, cell-surface receptors, cytoskeleton, and cytoplasmic and nuclear structures are studied at the molecular level. Research also comprises processes of the regulation of gene expression and cellular signalling, epigenetics, and molecular mechanisms of fertilization. In relation to the principal mission, the Institute's main goal is to make important original discoveries in these fields and publish them in prestigious scientific journals. The strength of the Institute is the state-of-the-art equipment, which is either operated within the core facilities, service research groups, or in the large national research infrastructures. Services and sophisticated instruments are not utilized by the scientists from IMG only, but can also be used by researchers from other institutions. IMG thus significantly supports the scientific community in the Czech Republic and abroad.

Another important goal of the Institute is education of university students. More than 160 PhD, master, and bachelor students are engaged in research at IMG. The focus on scientific education and training is evident from a large number of PhD, diploma, and bachelor theses completed at IMG every year. Additionally, approximately 50 semestrial university courses are conducted by IMG scientists

every year. Teaching activities are not limited to scientific training and lecturing, but also include scientific writing exercises, teambuilding events, progress reports, interviews, and career discussions.

Finally, one important priority of the Institute is applied research. IMG currently owns approximately 40 licenses and 60 patents. Research groups and facilities cooperate with a number of companies within the framework of 26 projects (year 2019) on the possible practical use of their scientific results.

Description of the main research directions investigated by the institute

The maximum extent is 10 pages.

Research pursued at IMG combines continuation of the long-term topics developed by well-established groups and new themes brought by new group leaders. The Institute perceives the diversity of topics as its strength because it creates an inspiring environment that attracts young promising scientists. On the other hand, it is evident that the basis of important discoveries is the synergy between collaborating laboratories. Several major research directions are thus crystallizing at IMG. The main research directions and their achievements in the evaluated period have been as follows:

Cancer biology and genome maintenance mechanisms

The topic includes identification and characterization of oncogenes or tumour suppressor genes (and alteration of these genes in transforming cells), DNA repair mechanisms including DNA damage response, and the role of other factors that are responsible for cellular transformation and tumour formation.

Therapeutic resistance of cancer cells; RECQ5 helicase suppresses transcription-associated genomic instability (the team of J. Bartek, Z. Hodny, and P. Janscak)

The long-term research interests of the IMG team are mechanisms of the cellular DNA damage response in relation to human diseases including cancer and ageing. In recent years, the efforts of the team were dedicated to unravelling circumstances of DNA 'irreparability' and resulting incessant DNA damage response, which guides a cell to a specific phenotype. Among the most important results obtained in the evaluation period was the contribution to the mechanisms of therapeutic resistance of cancer cells ***(Kyjacová L, Hubáčková S, Krejčíková K, Strauss R, Hanzlíková H, Dzijak R, Imrichová T, Šímová J, Bartek J, Reiniš M, Hodný Z: Radiotherapy-induced plasticity of prostate cancer mobilizes stem-like non-adherent, Erk signalling-dependent cells. Cell Death Differ 2015, 22(6): 898-911)***.

Transcription-replication conflicts (TRCs) represent a significant source of genomic instability in cells experiencing DNA replication stress. However, the question how a replication fork restarts DNA synthesis upon a TRC remains elusive. The IMG team found that RECQ5 helicase binds to RNA polymerases I and II and suppresses transcription-associated genomic instability. This occurs by promoting resolution of conflicts between transcription and replication machineries promoting replication fork progression through actively transcribed genes ***(Urban V, Dobrovolna J, Hühn D, Fryzelkova J, Bartek J, Janscak P: RECQ5 helicase promotes resolution of conflicts between replication and transcription in human cells. J Cell Biol 2016, 214(4): 401-15)***.

Identification of the primary source of genome damage detected by sensor protein PARP1 (the team of K. Caldecott)

DNA single-strand breaks (SSBs) are amongst the most frequent DNA lesions arising in cells threatening genetic integrity and cell survival. ADP ribosylation catalysed by PARP enzymes that occurs at the site of the breaks is a ubiquitous post-translational modification involved in a number of critical physiological processes such as DNA replication and repair, cellular differentiation, and carcinogenesis. Inherited defects in ADP-ribose metabolism often cause human disease such as cancer,

immunodeficiencies, and neurodegeneration. The IMG team showed that the intermediates of DNA replication so-called Okazaki fragments are the primary source of DNA SSBs in cells. The work has important implications for cancer research, because it identifies these obligatory DNA replication intermediates as the likely source of synthetic lethality that is triggered in certain cancer cells by PARP1 inhibition ***(Hanzlikova H, Kalasova I, Demin AA, Pennicott LE, Cihlarova Z, Caldecott KW. The importance of poly(ADP-Ribose) polymerase as a sensor of unligated Okazaki fragments during DNA replication. Mol Cell 2018, 71(2):319-331)***.

Deciphering the role of the WIP1 (proto)oncogene in cancer development (the team of L. Macurek)

The IMG team previously identified clinically relevant frameshift or non-sense mutations in the *PPM1D* gene (the gene encodes WIP1 phosphatase) resulting in production of a C-terminally truncated stabilized form of WIP1. Importantly, the phosphatase regulates modification/stability of the principal tumour suppressor p53. The team developed a new transgenic mouse model that mimics the mutations observed in humans. Additionally, a cohort of human patients suffering from colon carcinoma was analysed. Moreover, the effect of WIP1 inhibition was tested using organoids derived from the colon tumours. The results showed that truncated WIP1 increased the number of intestinal polyps induced in the APCmin mouse model of induced intestinal cancer; *PPM1D/WIP1* mutations were predominantly identified in a subgroup of tumours with microsatellite instability driven by oncogenic BRAF-V600E mutation. Interestingly, tumours carrying truncated PPM1D/WIP1 were more sensitive to WIP1 inhibition, and the inhibition improved sensitivity to the commonly used chemotherapeutic 5-fluorouracil ***(Burocziova M, Burdova K, Martinikova AS, Kasparek P, Kleiblova P, Danielsen SA, Borecka M, Jenikova G, Janečková L, Pavel J, Zemankova P, Schneiderova M, Schwarzova L, Ticha I, Sun XF, Jiraskova K, Liska V, Vodickova L, Vodicka P, Sedlacek R, Kleibl Z, Lothe RA, Korinek V, Macurek L: Truncated PPM1D impairs stem cell response to genotoxic stress and promotes growth of APC-deficient tumours in the mouse colon. Cell Death Dis 2019, 10(11): 818)***.

The function of the C/EBPa transcription factor in granulopoiesis and haemato-oncological disorders (the team of M. Alberich Jorda)

Haematopoiesis is a continuous and tightly regulated process in which haematopoietic stem cells (HSCs) develop into mature blood cells. The HSC pool is limited and its integrity needs to be preserved throughout life. The IMG research group investigated the regulation of HSC maintenance/fate by C/EBPα transcription factors (C/EBPα plays a crucial role in HSC fate and the commitment of HSCs into the myeloid lineage). Using gene expression profiling and chromatin-immunoprecipitation followed by sequencing, the team identified *EVI2B* (ecotropic virus integration site 2) as a novel target gene of C/EBPα. During granulocytic differentiation, EVI2B levels are upregulated, and prevention of this upregulation results in a block of neutrophilic production in mouse and human cells. Importantly, in the acute myeloid leukaemia (AML) patient samples with mutated C/EBPa, EVI2B levels are low, thus possibly contributing to the block of granulocytic development characteristic of this disorder ***(Zjablovskaja P, Kardosova M, Danek P, Angelisova P, Benoukraf T, Wurm AA, Kalina T, Sian S, Balastik M, Delwel R, Brdicka T, Tenen DG, Behre G, Fiore F, Malissen B, Horejsi V, Alberich-Jorda M: EVI2B is a C/EBPα target gene required for granulocytic differentiation and functionality of hematopoietic progenitors. Cell Death Differ 2017, 24(4): 705-716)***.

Molecular mechanisms controlling self-renewal and transformation of intestinal and hematopoietic stem cells (the team of V. Korinek, L. Lanikova, and T. Valenta)

In the small intestine, epithelial Paneth cells secrete Wnt ligands and thus potentially form the stem cell niche that normally could maintain the epithelial homeostasis. On the other hand, in the colon, the identity of cells comprising the stem cell niche is unknown. The IMG team in collaboration with the laboratory of K. Basler (Institute of Molecular Life Sciences, Zurich, Switzerland) showed that sub-epithelial mesenchymal cells expressing transcription factor Gli1 form the “enigmatic” niche for intestinal epithelial stem cells in the colon. In addition, single-cell RNA sequencing and immunohistocytochemical analyses revealed that Gli1-expressing cells represent a heterogeneous cell

population consisting of myofibroblasts and lipofibroblasts, some of them secreting Wnt ligands. Importantly, Gli1$^+$ cells are enriched during tissue regeneration upon intestinal damage or in tumour tissue ***(Degirmenci B, Valenta T, Dimitrieva S, Hausmann G, Basler K: GLI1-expressing mesenchymal cells form the essential Wnt-secreting niche for colon stem cells. Nature 2018, 558(7710): 449-453).***

Myeloproliferative neoplasms (MPN) represent a group of disorders arising due to the genetic defect(s) in haematopoietic stem cells. While the concept of somatic driver mutations in MPNs is well established, contribution of other factors, such as germ-line variants that modulate the risk of MPN development by promoting acquisition of additional somatic mutations, is less understood. The IMG team demonstrated that germ-line (or acquired) mutations in the gene encoding Janus kinase 2 (JAK2) enhances the oncogenic JAK2/STAT signalling and causes a specific clinical course of the disease in MPN patients. In more detail, it was shown that besides well-characterized mutation JAK2 V617F frequently detected in polycythaemia vera (PV) patients, the course of the diseases may be influenced by additional JAK2 mutations that may contribute to leukaemic transformation of PV cell clones ***(Lanikova, L., Babosova, O., Swierczek, S., Wang, L., Wheeler, D.A., Divoky, V., Korinek, V. and Prchal, J.T.: Coexistence of gain-of-function JAK2 germ line mutations with JAK2V617F in polycythemia vera. Blood 2016, 128, 2266-2270)***.

Developmental biology

Several IMG research groups are pursuing developmental biology topics. Besides experimental mice, the groups use other animal models such as zebrafish, medaka, chicken, amphioxus, and several invertebrate models (e.g., jellyfish, marine ragworm).

Developmental mechanisms for the eye lens formation and neural crest induction (the team of Z. Kozmik)

Eye development is a “classical” model suitable for investigating how a spatiotemporal control of gene expression regulates cell specification. The IMG team discovered that during eye lens formation, expression of transcription factor Pax6, a "master regulator" of the eye, is regulated by Meis1 and Meis2 transcription factors ***(Antosova B, Smolikova J, Klimova L, Lachova J, Bendova M, Kozmikova I, Machon O, Kozmik Z: The Gene Regulatory Network of Lens Induction Is Wired through Meis-Dependent Shadow Enhancers of Pax6. PLoS Genet 2016, 12(12): e1006441)***.

The neural crest (NC) is crucial for the evolutionary diversification of vertebrates. NC cells are induced at the neural plate border by a coordinated action of several signalling pathways, including Wnt/β-catenin. NC cells are normally generated in the posterior neural plate border, whereas the anterior neural fold is devoid of NC cells. Using the mouse model, the team showed that active repression of Wnt/β-catenin signalling is required for maintenance of neuroepithelial identity in the anterior neural fold and for inhibition of NC induction ***(Mašek J, Machoň O, Kořínek V, Taketo MM, Kozmik Z: Tcf7l1 protects the anterior neural fold from adopting the neural crest fate. Development 2016, 143(12): 2206-16)***.

Ex vivo growth and manipulation of haematopoietic stem cells obtained from the zebrafish model (the team of P. Bartunek)

The IMG team established *in vitro* and *in vivo* systems to study the self-renewal and differentiation of embryonic, haematopoietic, and neural stem cells. Cytokines, genetic engineering tools and small molecules were employed to manipulate these cells from various vertebrate model organisms. Zebrafish became a popular model organism to study the genetic underpinnings of haematopoiesis. However, the main disadvantage of this model was unavailability of culture conditions to study haematopoietic cells *ex vivo*. The team optimized culture conditions and generated recombinant zebrafish cytokines that enable growth and differentiation of zebrafish haematopoietic cells in cultures for the first time ***(Svoboda O, Stachura DL, Machonova O, Zon LI, Traver D, Bartunek P: Ex vivo tools for the clonal analysis of zebrafish hematopoiesis. Nat Protoc 2016, 11(5): 1007-20)***. The cytokines and additional tools are either available through *Addgene* or directly distributed by the IMG laboratory.

Contribution of retrotransposons to gene expression remodelling and gene evolution (the team of P. Svoboda)

The IMG team studies evolution of genes and their regulation mainly in the context of the female germline in mice. During the 2015-2019 period, among interests of the team were long non-coding RNAs (lncRNAs) and comparative analysis of mammalian maternal transcriptomes with a particular focus on the contribution of retrotransposons to gene expression in the germline and its evolution. This work yielded the most significant article of the group, which identified the largest contribution of a single retrotransposon family to gene expression remodelling and gene evolution discovered so far ***(Franke V, Ganesh S, Karlic R, Malik R, Pasulka J, Horvat F, Kuzman M, Fulka H, Cernohorska M, Urbanova J, Svobodova E, Ma J, Suzuki Y, Aoki F, Schultz RM, Vlahovicek K, Svoboda P: Long terminal repeats power evolution of genes and gene expression programs in mammalian oocytes and zygotes. Genome Res 2017, 27(8): 1384-1394)***.

Molecular retrovirology

Retrovirology has been the most traditional research area at IMG. The research topic remains strong and productive, as documented by the following results published by **the team of J. Hejnar**.

The main model of the IMG team is represented by avian leucosis viruses. Moreover, the team studies the genetics and genomics of chicken, the natural host of the avian leucosis viruses. The team showed that transcriptionally active proviruses were found close to the active promoters and enhancers, and proviruses in other locations were mostly silenced. This is an important finding indicating that retroviral vectors aimed for gene therapy in humans have to be designed with altered integration preference so that they integrate into intergenic regions. At these positions, the proviruses should be protected from DNA methylation and transcriptional silencing ***(Senigl F, Maman Y, Dinesh RK, Alinikula J, Seth RB, Pecnova L, Omer AD, Rao SSP, Weisz D, Buerstedde JM, Aiden EL, Casellas R, Hejnar J, Schatz DG: Topologically Associated Domains Delineate Susceptibility to Somatic Hypermutation. Cell Rep 2019, 29(12): 3902-3915.e8)***.

The expertise related to the epigenetic control of retroviral infection was employed in the studies of retroviral integration in mammals. The IMG team and its collaborators examined the dynamics of DNA methylation of HIV-1 proviruses. The study clearly showed that the epigenetic control is an important mechanism of transcriptional silencing of HIV-1, which creates a latent reservoir of proviruses in infected patients ***(Trejbalová K, Kovářová D, Blažková J, Machala L, Jilich D, Weber J, Kučerová D, Vencálek O, Hirsch I, Hejnar J: Development of 5' LTR DNA methylation of latent HIV-1 provirus in cell line models and in long-term-infected individuals. Clin Epigenetics 2016, 8: 19)***.

Mining the newly released mammalian genomes provided an excellent opportunity to identify molecular fossils – rare copies of old endogenous retroviruses preserved from ancient infections of the evolutionary lineages. The team developed original bioinformatic tools and methods for discovering such endogenous retroviral copies and described the evolution and diversification of lentiviral copies in recent dermopteran species ***(Hron T, Farkašová H, Padhi A, Pačes J, Elleder D: Life history of the oldest lentivirus: characterization of ELVgv integrations in the dermopteran genome. Mol Biol Evol 2016, 33(10): 2659-69)***. The team also described the first endogenous deltaretrovirus (HTLV-related retrovirus) discovered in the genome of Miniopterus bats and constructed the tree of this retrovirus family. This contribution was of "heuristic" importance and shed light on genome evolution, "endogenization" of retroviruses, and virus-host co-evolution ***(Farkašová H, Hron T, Pačes J, Hulva P, Benda P, Gifford RJ, Elleder D: Discovery of an endogenous Deltaretrovirus in the genome of long-fingered bats (Chiroptera: Miniopteridae). Proc Natl Acad Sci U S A 2017, 114(12): 3145-3150)***.

Finally, the IMG team contributed significantly to the field of transgenesis in chicken. The team developed an original strategy of orthotopic male germ line transplantation into the testes of recipients ***(Trefil P, Aumann D, Koslová A, Mucksová J, Benešová B, Kalina J, Wurmser C, Fries R,***

Elleder D, Schusser B, Hejnar J: Male fertility restored by transplanting primordial germ cells into testes: a new way towards efficient transgenesis in chicken. Sci Rep 2017, 7(1): 14246).

Molecular and cellular immunology

Immunology represents one of the most important IMG research areas. In recent years, it has shifted from the "classical" (transplantation) immunology mainly to molecular immunology, with emphasis on the mechanisms of immunoreceptor signalling, and detailed analysis of the specific cell types involved in the immune responses.

Virtual memory T-cell production mechanisms (the team of O. Stepanek)

The main team focus is on the T-cell-mediated adaptive immune responses and T-cell diversity. Virtual memory T-cells are foreign antigen-inexperienced T-cells that have acquired memory-like phenotype and constitute 10-20 % of all peripheral $CD8^+$ T-cells in mice. Their origin, biological roles, and relationship to naïve and foreign antigen-experienced memory T-cells are incompletely understood. By analysing T-cell receptor repertoires and using retrogenic monoclonal T-cell populations, the team described the molecular mechanisms driving formation of virtual memory T-cells ***(Drobek A, Moudra A, Mueller D, Huranova M, Horkova V, Pribikova M, Ivanek R, Oberle S, Zehn D, McCoy KD, Draber P, Stepanek O: Strong homeostatic TCR signals induce formation of self-tolerant virtual memory CD8 T cells. EMBO J 2018, 37(14))***.

PSTPIP2 has a central position in the signalling network of neutrophil activation (the team of T. Brdicka)

The main focus of the IMG team is on the biology of membrane adaptor proteins in leucocytes. Membrane adaptors are transmembrane (or membrane-associated) proteins that have no enzymatic activity. However, their intracellular parts contain various interaction motifs, which recruit signalling enzymes and other proteins to the proximity of cellular membranes. The team is interested in different aspects of adaptor protein function, starting with molecular and biochemical properties and ending with physiological functions in living organisms and roles in diseases. One of the membrane adaptors that was identified by the team was PSTPIP2. Interestingly, PSTPIP2 deficiency in the mouse model resulted in autoinflammatory disease chronic multifocal osteomyelitis, characterized by sterile inflammation of hind paw and tail bones and surrounding soft tissues. Detailed analysis of this phenotype demonstrated that neutrophils from PSTPIP2-deficient mice showed generalized hyper-responsiveness to multiple stimuli acting through different receptors, indicating the role of PSTPIP2 in neutrophils ***(Drobek A, Kralova J, Skopcova T, Kucova M, Novák P, Angelisová P, Otahal P, Alberich-Jorda M, Brdicka T: PSTPIP2, a protein associated with autoinflammatory disease, interacts with inhibitory enzymes SHIP1 and Csk. J Immunol 2015, 195(7): 3416-26)***.

Molecular mechanisms of the autoimmune polyendocrine syndrome; early embryo haematopoiesis (the team of D. Filipp)

The IMG team was focused on central and peripheral T-cell tolerance and autoimmunity, and embryonic haematopoiesis. Autoreactive T-cells aided by autoantibodies cause an organ-specific autoimmune disease in multiple organs, but the disease pathogenesis is poorly understood. One example is the autoimmune polyendocrine syndrome type (APS-1), a rare autosomal recessive disorder caused by loss of central immunological tolerance due to mutations in the autoimmune regulator (*AIRE*) gene. Capitalizing on joint expertise and collaborations with leading European investigators, the team described the molecular and cellular mechanisms behind gut-related immunopathology of APS-1. The results provided important clues for development of new diagnostic biomarkers and therapeutic options for gut autoimmunity diseases ***(Dobeš J, Neuwirth A, Dobešová M, Vobořil M, Balounová J, Ballek O, Lebl J, Meloni A, Krohn K, Kluger N, Ranki A, Filipp D: Gastrointestinal autoimmunity associated with loss of central tolerance to enteric α-defensins. Gastroenterology 2015, 149(1): 139-50)***.

The team identified Toll-like receptors (TLRs) and their adaptor proteins as functionally important molecules during early stages of embryonic development. Using genetic labelling in live animals, the team demonstrated that the *Tlr2* locus is indeed activated at early stages of embryonic development in emerging haematopoietic progenitors. Notably, when Tlr2-positive progenitors were genetically labelled at embryonic day 8.5, they were able to give rise to erythroid, myeloid, as well as lymphoid haematopoietic lineages that persisted in the peripheral blood of adult animals. The results indicate that Tlr2 can be utilized as a reliable marker of early haematopoietic precursors ***(Balounová J, Šplíchalová I, Dobešová M, Kolář M, Fišer K, Procházka J, Sedlacek R, Jurisicova A, Sung HK, Kořínek V, Alberich-Jorda M, Godin I, Filipp D: Toll-like receptor 2 expression on c-kit cells tracks the emergence of embryonic definitive hematopoietic progenitors. Nat Commun 2019, 10(1): 5176)***.

Mechanisms of mast cell chemotaxis (the team of Petr Draber)

The long-term research interest of the IMG team lies in the molecular mechanisms governing signal transduction from plasma membrane immunoreceptors, specifically the high-affinity IgE receptor (FcεRI), to the cytoplasm. In relation to new functions of non-T cell activation linker (NTAL) adaptor protein, discovered at IMG, in chemotaxis of mast cells, the team discovered the role of RHOA/ERM/β1-integrin and PI3/AKT signalling pathways in this process ***(Halova I, Bambouskova M, Draberova L, Bugajev V, Draber P: The transmembrane adaptor protein NTAL limits mast cell chemotaxis toward prostaglandin E_2. Sci Signal 2018, 11(556): eaao4354)***.

Molecular genetics, genomics, and disease modelling

The theme represents a research direction with a long tradition at IMG; the main topics include elucidation of the phenomenon of mouse subspecies male hybrid sterility, cancer transcriptomics, and pathological mechanisms of rare diseases.

Involvement of PRDM9 in hybrid sterility and in meiotic chromosome synapsis (the team of J. Forejt)

The main topic of the IMG team is the role of meiotic recombination and homologous chromosome synapsis in infertility of interspecific hybrids and in the origin of species. Hybrid male sterility is the most studied but still poorly understood form of reproductive isolation, which restricts gene flow between incipient species. The phenomenon is an essential prerequisite for successful speciation. In 2009, the group identified *Prdm9* as the first hybrid sterility gene in vertebrates (Mihola et al. Science 2009). In the evaluated period, the team mainly focused on detailed analysis of the role of Prdm9 in meiotic recombination. To investigate the relation between Prdm9-controlled meiotic arrest and asynapsis, random stretches of consubspecific (belonging to the same subspecies) homology were inserted into several autosomal pairs in sterile hybrids. Interestingly, 27 or more megabases of consubspecific homology fully restored synapsis in a given autosomal pair, indicating that two or more double-strand breaks within symmetric hotspots per chromosome are necessary for successful meiosis ***(Gregorova, S., Gergelits, V. Chvatalova, I., Bhattacharyya, T., Valiskova B., Fotopulosova V., Jansa, P., Wiatrowska, D., Forejt, J*,: Modulation of Prdm9-controlled meiotic chromosome asynapsis overrides hybrid sterility in mice. Elife 2018, 14(7): e34282)***.

Recovery of male fertility by a loss of meiotic epigenetic factor PRMD9 (the team of Z. Trachtulec)

Infertility is a major health issue, as it affects about 186 million people in reproductive age worldwide. In mouse, the deficiency in Prdm9 results in complete meiotic arrest of both sexes of all tested “classical” mouse strains. The IMG team investigates the effects of chromatin marks, especially histone methylations, accompanying the sites of programmed meiotic double-stranded DNA breaks (and other meiotic epigenetic modifications) on the quantity and quality of germ cells as well as on offspring production in several animal species. Strikingly, using genetic manipulation and cross breeding, the team showed that in some (specific) genetic backgrounds, the Prdm9-deficient mice are fertile. One of the possible mechanisms of infertility suppression could be more efficient DNA repair of relocated recombination sites to crossovers. The results imply that drugs (or conditions) inducing

increase in DNA breaks could improve fertility in humans ***(Mihola O, Pratto F, Brick K, Linhartova E, Kobets T, Flachs P, Baker CL, Sedlacek R, Paigen K, Petkov PM, Camerini-Otero RD, Trachtulec Z: Histone methyltransferase PRDM9 is not essential for meiosis in male mice. Genome Res 2019, 29(7): 1078-1086)***.

Cancer transcriptomics, Scrimer, Ancient mitochondrial genomes database (the team of M. Kolar)

The focus of the service-research group is genomics, transcriptomics, bioinformatics and database development. The team was involved in a long-term collaborative project focused on identification of specific genetic markers in cancer tissue isolated from patients with head and neck squamous cell carcinomas and skin cancer ***(Kodet O, Lacina L, Krejčí E, Dvořánková B, Grim M, Štork J, Kodetová D, Vlček Č, Šáchová J, Kolář M, Strnad H, Smetana K Jr: Melanoma cells influence the differentiation pattern of human epidermal keratinocytes. Mol Cancer 2015, 14(1): 1)***.

With the next-generation sequencing methods, it has become possible to obtain genome-wide sequence data even for non-model species. Currently, there is no available software for automated design of PCR and genotyping primers from next-generation sequence data. The group developed the Scrimer "pipeline" that automates multiple steps: adaptor removal, read mapping, selection of single nucleotide polymorphisms (SNPs) and multiple primer design from transcriptome data ***(Mořkovský L, Pačes J, Rídl J, Reifová R: Scrimer: designing primers from transcriptome data. Mol Ecol Resour 2015, 15(6): 1415-20)***.

The group also generated an open database of ancient mitochondrial genomes. It is the most comprehensive published database focused entirely on human populations from prehistoric and early historic times. The database brings the full "mitogenome" sequences together with extensive metadata and advanced search and mapping tools. The database is used by geneticists, anthropologists, archaeologists, and other researchers from all over the world, having over 10,000 unique users in 2019 ***(Ehler E, Novotný J, Juras A, Chylenski M, Moravcík O, Paces J: AmtDB: a database of ancient human mitochondrial genomes. Nucleic Acids Res 2019, 47(D1): D29-D32)***.

The group also published many articles in collaboration with other groups from the Institute (see the group summary).

Molecular mechanisms of the Netherton syndrome (the team of R. Sedlacek)

Although thematically distinct, all research of the IMG team is based on the usage of mouse models as a tool to reveal gene functions in the complexity of the whole organism. The topics include ubiquitin ligases, skeleton and tooth development, transcription factors, proteases, and rare disease models. One of the major focuses of the team were kallikrein-related peptidases (shortly kallikreins; Klks). The team generated a set of single or compound Klk knockout mice allowing deciphering the functional proteolytic network in the skin (the disrupted genes were *Klk5*, *Klk7*, *Klk8*, *Klk11*, *Klk13*, and *Klk14*). The Netherton syndrome (NS) is a rare hereditary disease characterized by hair and skin anomalies and increased susceptibility to atopic eczema. To generate a mouse model of NS, a mutation identified in the NS individuals in the coding sequence of the *Spink5* gene (the gene encoded protease inhibitor LEKT1) was introduced into the mouse genome. Subsequently, Spink5 mutant mice in combination with Klks-deficient animals were used to identify the NS pathological mechanisms. Interestingly, simultaneous disruption of the *Klk5* and *Klk7* genes suppressed the pathological effect of mutant LEKT1, indicating possibilities of therapeutic intervention in humans suffering from NS ***(Kasparek P, Ileninova Z, Zbodakova O, Kanchev I, Benada O, Chalupsky K, Brattsand M, Beck IM, Sedlacek R: KLK5 and KLK7 ablation fully rescues lethality of Netherton syndrome-like phenotype. PLoS Genet 2017, 13(1): e1006566)***.

Analysis of neurotransmitter-mediated signalling (the team of J. Blahos)

The IMG team was focused on the role of signalling initiated by the interaction between neurotransmitters, namely endocannabinoids, and the glutamate G-protein coupled receptors (GPCR). They used molecular biology, pharmacology, and genetic tools to uncover the signalling mechanisms

and function of metabotropic glutamate receptors (mGluRs). The team identified SGIP [Src homology 3-domain growth factor receptor-bound 2-like (endophilin) interacting protein 1] as a novel partner of CB1R (type 1 cannabinoid receptor). SGIP1 is functionally linked to clathrin-mediated endocytosis and its overexpression in the hypothalamus leads to energy regulation imbalance resulting in obesity. The team reported that SGIP1 prevents the endocytosis of activated CB1R and, consequently, alters signalling via the receptor ***(Hájková A, Techlovská Š, Dvořáková M, Chambers JN, Kumpošt J, Hubálková P, Prezeau L, Blahos J: SGIP1 alters internalization and modulates signalling of activated cannabinoid receptor 1 in a biased manner. Neuropharmacology 2016, 107: 201-14)***.

Genotype-phenotype association study of the Bardet-Biedl syndrome (the team of O. Stepanek and M. Huranova)

Besides its major topic related to T-cell biology, the group studies the molecular mechanisms of ciliogenesis, particularly the role of an octameric ciliary transport complex called the 'BBBsome'. Alterations in the BBSome composition (or structure) are associated with the Bardet-Biedl syndrome (BBS), a recessive hereditary disease causing multiple organ anomalies. Since there is a link between the function of the BBSome and the immune/haematopoietic system, research topics in the groups are interlinked. The team applied a meta-analysis approach to study the genotype-phenotype association in humans using a proprietary database of all reported BBS patients. The analysis revealed that the identity of the causative gene (and the character of the mutation) partially predicts the clinical outcome of the disease. Besides its potential use for clinical prognosis, the analysis revealed functional differences of particular BBS genes in humans ***(Niederlova V, Modrak M, Tsyklauri O, Huranova M, Stepanek O: Meta-analysis of genotype-phenotype associations in Bardet-Biedl syndrome uncovers differences among causative genes. Hum Mutat 2019, 40(11): 2068-2087)***.

Biology of the cell nucleus, cytoskeleton, and cellular flagellum

Biochemistry and cell biology of the cytoskeleton and cytoskeleton-associated proteins represent one of the "traditional" topics of the Institute. However, two newly formed groups (led by M. Gregor and V. Varga) brought new impetus to this theme. The topic of the nucleus organization and splicing mechanisms are studied in groups of P. Hozak and D. Stanek, respectively.

The structure and functions of the nuclear lipid islets (the team of Hozak)

Different processes are spatially and temporarily organized in cell nuclei and many nuclear functions are critically dependent on this order. The IMG team pioneered a novel and original concept of involvement of phosphatidylinositol 4,5-bisphosphate (PIP2) in gene transcription and nucleolar organization. The team aimed to map structural and regulatory molecules of the nucleus with relation to the intranuclear phosphoinositides. The team described a novel type of nuclear structure – nuclear lipid islets (NLIs). They are of 40-100 nm in size with a lipidic interior, and PIP2 molecules comprise a significant part of their surface. Most of NLIs have RNA at the periphery. Consistent with that, RNA is required for their integrity. The NLI periphery is associated with Pol II transcription machinery, including the largest Pol II subunit, transcription factors and nuclear myosin 1 (NM1/NMI). Importantly, the PIP2-NM1 interaction is important for Pol II transcription ***(Sobol M, Krausová A, Yildirim S, Kalasová I, Fáberová V, Vrkoslav V, Philimonenko V, Marášek P, Pastorek L, Čapek M, Lubovská Z, Uličná L, Tsuji T, Lísa M, Cvačka J, Fujimoto T, Hozak P: Nuclear phosphatidylinositol 4,5-bisphosphate islets contribute to efficient RNA polymerase II-dependent transcription. J Cell Sci 2018, 131(8): 211094)***.

Regulatory sequences requirement for splicing of long non-coding RNAs (the team of D. Stanek)

The IMG team was primarily focused on RNA splicing, particularly on the formation of spliceosomal small nuclear ribonucleoproteins (snRNPs) and RNA splicing regulation. The team also studied splicing of non-coding RNAs and elucidated a "puzzling" fact why long non-coding RNAs (lncRNAs) are less efficiently spliced than protein-coding pre-mRNAs. The team discovered that the

splicing efficiency of lncRNAs is more dependent on the 3' splice site strength than pre-mRNAs, which suggested that lncRNAs are more dependent on basic splicing signals. Indeed, further analysis confirmed that lncRNAs contain less binding sites for splicing enhancers SR proteins. The results indicated that lncRNAs lack the cooperative interaction network that enhances splicing, which rendered their splicing outcome more dependent on the optimality of splice sites ***(Krchnáková Z, Thakur PK, Krausová M, Bieberstein N, Haberman N, Müller-McNicoll M, Stanek D: Splicing of long non-coding RNAs primarily depends on polypyrimidine tract and 5' splice-site sequences due to weak interactions with SR proteins. Nucleic Acids Res 2019, 47(2): 911-928)***.

The expression and function of γ-tubulin isoforms in neuroblastoma cells (the team of Pavel Draber)

The main research interest of the IMG team were the molecular mechanisms governing the regulation of microtubule nucleation and organization in normal and pathological conditions. The organization of dynamic microtubules, formed by αβ-tubulin dimers, is controlled by microtubule organizing centres (MTOCs). One of the critical components of MTOCs is γ-tubulin, which along with γ-tubulin complex proteins (GCPs) forms nucleation complexes necessary for microtubule nucleation. The team mainly studied the regulation of γ-tubulin nucleation complexes by signal transduction molecules (kinases and phosphatases) and newly discovered centrosomal adaptor proteins (GIT/βPIX). The team showed that enhanced expression of γ-tubulin isoform 2 in neuroblastoma cells was triggered by oxidative stress induced by mitochondrial inhibitors and that γ-tubulins associate with mitochondria ***(Dráberová E, Sulimenko V, Vinopal S, Sulimenko T, Sládková V, D'Agostino L, Sobol M, Hozák P, Křen L, Katsetos CD, Dráber P: Differential expression of human γ-tubulin isotypes during neuronal development and oxidative stress points to a γ-tubulin-2 prosurvival function. FASEB JOURNAL 2017, 31(5): 1828-1846)***.

Analysis of the eukaryotic flagellum composition (the team of V. Varga)

The IMG team was focused on the protein composition and formation of eukaryotic flagella and cilia. These closely related and evolutionarily conserved organelles are – due to their motility, sensory and signalling functions – essential for many organisms. In humans, cilia are found on the surface of a vast majority of cell types and their malfunctions are manifested by a wide range of symptoms, including developmental abnormalities, sterility, chronic respiratory problems, blindness, and polycystic kidney disease. The team aimed to elucidate poorly understood aspects of basic biology of the cilia and flagella, in particular those related to their cytoskeleton. The model systems were parasitic protozoan Trypanosoma brucei and ciliated mammalian cells. The group identified a number of novel constituents of the flagellum tip, sub-localizes them and characterizes their contribution to the flagellum functions ***(Varga V, Moreira-Leite F, Portman N, Gull K: Protein diversity in discrete structures at the distal tip of the trypanosome flagellum. Proc Natl Acad Sci U S A 2017, 114(32))***.

The role of plectin in biliary tree architecture and stability in cholestasis (the team of M. Gregor)

The main focus of the IMG team in the past five years has been cytoskeleton-dependent regulation of cell-cell contacts in simple epithelia, regulation of cell-matrix adhesions, and cytoskeleton (and adhesion)-mediated signalling in epithelial-mesenchymal transition, cell migration, and invasiveness. Using a liver-specific knockout mouse model in combination with an "array" of cell biology techniques (e.g., CRISPR/Cas9 targeted cell lines, traction force and atomic force microscopy, magnetic tweezer rheology, cell stretching, and FRET-based tension sensors), the team analysed the liver-specific role(s) of cytoskeletal linker protein plectin. The team demonstrated that plectin plays an essential role in the adaptation of liver tissues to cholestasis (cholestasis is a condition where the bile flow from the liver is blocked or reduced}. In cholestasis experimental models, plectin deficiency led to biliary epithelial instability, and mutated mice failed to activate a cholestasis-induced adaptive response ***(Jirouskova M, Nepomucka K, Oyman-Eyrilmez G, Kalendova A, Havelkova H, Sarnova L, Chalupsky K, Schuster B, Benada O, Miksatkova P, Kuchar M, Fabian O, Sedlacek R, Wiche G, Gregor M: Plectin controls biliary tree architecture and stability in cholestasis. J Hepatol 2018, 68(5): 1006-1017)***.

Structural biology

The topic is covered by **the team of P. Maloy Rezacova**. The main interest of the team lies in structural studies of various proteins of biological or medicinal interest using protein crystallography. The structural knowledge is used to understand the protein function and (in some projects) also in modulating the protein function by design of specific inhibitors. In a structure-based drug discovery project, the team targets human enzymes, and the knowledge of protein structures provides a platform for rational design of specific inhibitors. Since the laboratory expertise is unique within the Czech Republic, the team also participated by its structural biology expertise in many other projects.

The team contributed to structural analysis of important interactions of lens epithelium-derived growth factor LEDGF/p75. LEDGF/p75 is a transcriptional co-activator that contributes to the regulation of gene expression by tethering other factors to actively transcribed genes on chromatin. Its chromatin-tethering activity is "hijacked" in two important disease settings: HIV and mixed lineage leukaemia. The basis for the biological regulation of LEDGF/p75's interaction to binding partners has remained unknown. During the evaluated period, the team uncovered molecular features crucial for interaction with LEDGF/p75 with several binding partners ***(Tesina P, Čermáková K, Hořejší M, Procházková K, Fábry M, Sharma S, Christ F, Demeulemeester J, Debyser Z, De Rijck J, Veverka V, Řezáčová P: Multiple cellular proteins interact with LEDGF/p75 through a conserved unstructured consensus motif. Nat Commun 2015, 6(6): 7968)***.

In another project, the team focused on design of novel and original inhibitors targeting a therapeutically relevant isoenzyme of human carbonic anhydrase (CA). A series of more than 70 sulfamides incorporating carborane clusters were developed. The lead compounds from this series inhibited CA with Ki values in the low nanomolar or subnanomolar range, with some inhibitors being more than 1000-fold more selective for tumour-specific CA isoform (CAIX) than CAII present in normal tissue. Importantly, the compounds demonstrated favourable *in vitro* toxicological and pharmacokinetic profiles and reduced the tumour size in mice ***(Grüner B, Brynda J, Das V, Šícha V, Štěpánková J, Nekvinda J, Holub J, Pospíšilová K, Fábry M, Pachl P, Král V, Kugler M, Mašek V, Medvedíková M, Matějková S, Nová A, Lišková B, Gurská S, Džubák P, Hajdúch M, Řezáčová P: Metallacarborane Sulfamides: Unconventional, Specific, and Highly Selective Inhibitors of Carbonic Anhydrase IX. J Med Chem 2019, 62(21): 9560-9575)***.

Cooperation within international research area

The institute will indicate a cooperating institute in national and international context, the form of cooperation, main outputs/results on the level of institute and a way of providing the cooperation.
The maximum extent is 2 pages.

At the international level, IMG has established and continuously extended scientific cooperation with the Max Planck Institute of Molecular Cell Biology and Genetics (MPI-CBG) in Dresden, Germany. Intense contacts were greatly facilitated by the geographic proximity of both Institutes. In the evaluation period, the Dresden Prague Science Exchange (DPSX) seminar series featured scientific speakers from Dresden and Prague visiting the respective city (six speakers visited Prague; five IMG speakers visited Dresden). As part of a rapidly developing collaboration, PhD students from Prague and Dresden participated in the annual PhD conferences held at both institutions. Furthermore, the faculties of IMG and MPI-CBG met at a two-day scientific retreat in Liblice (altogether 54 participants). The management of both institutes tried to "institutionalize" the cooperation within the Horizon 2020 WIDESPREAD Teaming program. The joint project 'Advanced Research Incubator in Biosciences' succeeded in the first phase of the evaluation (year 2017). As part of second phase project preparation, numerous bilateral meetings at different levels were held. The scientific topics and prospective areas for future collaboration were discussed at meetings of group leaders from Prague and Dresden (more than 10 meetings were held in 2017-2018). Moreover, meetings of the

administrative staff (15 meetings) and heads of research facilities (14 meetings) were organized. Finally, representatives of both institutes met with prospective industrial partners from the Czech Republic or Germany that could be involved in commercialization of obtained scientific results (seven meetings). Although the Teaming project did not receive European funding in the second phase of the evaluation, the co-operation of the institutes continues (student exchanges, etc.).

At the national level, the most important form of cooperation of the Institute was within the BIOCEV project. The BIOCEV project was supported from the Operational Programme Research & Development for Innovations using the European structural and investment funds (approx. 100 mil €). The EU funds were used to establish a joint scientific Centre of Excellence. In summary, the project comprised construction of a complex of research buildings of more than 26,000 sq. metre floor space, equipped with state-of-the-art instruments and technologies for biotechnological and biomedical research. IMG is the official guarantor of the project and recipient of the funding. Additional five institutes of the CAS and two faculties of Charles University are involved in the project. The construction period of the BIOCEV project was finalized in December 2015 and since then, the Centre is fully operational and hosts approximately one third of IMG personnel. Additional details are given in the section “Joint research centres with universities”.

Cooperation, whether national or international, at the level of research groups, large national infrastructures hosted by the Institute or within the AV 21 Strategy programme is described in the relevant sections of the report.

HR policy of the institute

Qualification structure, staff structure from the viewpoint of the international representation, description of the recruitment process, way of evaluation of researchers and teams, qualification growth, support in gaining DSc. degree, number of gained DSc. degree, support of researchers in gaining them and providing background for committees assessing DSc. dissertation, earned awards related to the institute including HR Award, international mobility, measures to support work-life balance.
The maximum extent is 5 pages.

The organizational structure of IMG is based on Act No. 341/2005 Coll. on Public Research Institutions. The main bodies of the Institute are the Director, the IMG Council, and the Supervisory Board. The Director is a statutory body and takes decisions on all key issues that are not in the scope of the Council, Supervisory Board, or the founder (Czech Academy of Sciences). The IMG Council is composed of elected representatives of the scientific community (both internal and external) and takes decisions related to the research directions of the Institute. The IMG Council proposes new group leaders to the Director, approves the annual budgets and reports, and discusses proposals for research and development projects. The Supervisory Board supervises the economy and asset management. Strategic planning is ensured by the Director, in cooperation with the Council and the International Advisory Board (IAB). IAB, which acts as an advisory body, was established in 2014 and currently has five members, internationally renowned scientists representing diverse fields of biological research (e.g., cancer biology, immunology, RNA biology, and genomics). Importantly, in 2017 the IAB members performed “on site” evaluation of five research groups established in frame of the BIOCEV project. The operational side, which is led by the Deputy Director for Administration, includes the Administrative and Technical Service, e.g., Economic and Information Technology (IT) Departments, Building Maintenance. IMG core facilities are led by the Head of Research Services. Additionally, IMG operates four large research infrastructures. The infrastructures carry out research and provide open access to unique instrumentation, expertise and research services (details are given in the corresponding part of the document).

Group leaders

The research part of IMG includes 26 research groups and two research-service groups; the latter groups carry out research, but at the same time provide services for research groups and external

users. The Institute has a “flat” research structure without intermediaries, with heads of the groups reporting directly to the Director. Group leaders are highly independent; the Director and the Council essentially do not interfere with their running the groups and personnel policy (unless there are financial problems connected with the institutional support of the groups). Group leaders decide which research directions they would pursue, how and when they would publish their results, how they build their research team. The reverse of this independence lies in the fact that the group leaders must secure most of the funds for the functioning of the group. Due to the long-term underfunding of the CAS Institutes from the state budget, grant funds often make up more than 80 % of the financial resources used by the research groups annually. The grant "agenda" thus significantly burdens the functioning of most groups. The constant threat of losing money also affects the scientific direction and personnel policy of the groups and (indirectly) of the entire Institute.

In relation to the career development of research group leaders, the career path goes from the ‘junior group leader’ to the ‘senior group leader’. Junior/senior group leaders are selected in open calls. The selected new group leader has the opportunity to build the new group according to his/her own plans. At the end of the year 2019, there were four junior groups at the Institute. In addition, the Institute has established a new programme called ‘IMG Fellows’ for recruitment of young researchers with extensive international postdoctoral experience. As the financial support from the Institute for these groups is minimal, it is expected that the Fellows are able to secure grant support for their small independent groups. In the evaluation period, two IMG Fellow groups were established.

Both, junior and IMG Fellow groups are evaluated (3-5 years after recruitment) by IAB and if they succeed, they advance to the senior or junior group status, respectively (the status is accompanied by corresponding institutional funding). One “exception from the rule” was promotion of the IMG Fellow group of O. Stepanek, who was awarded a European Research Council (ERC) Starting Grant in 2018 and his group gained the junior status after internal evaluation by the Director and IMG Council. Evaluation of three junior groups and one IMG Fellow group was planned for May 2020. However, due to the anti-covid-19 measures, it was postponed until 2021.

Senior group leaders (in fact, all scientists since employment contracts of group members are tied to the contract of the group leader) have contracts for a maximum of five years. The extension depends on external and internal evaluation. The external evaluation by CAS takes place every five years. Internal evaluation is done by the Director and IMG Council. They decide whether the contract of the group leader will be extended and thus whether the group will continue. The perspectives of a group may be discussed (and decided) by the Director and Council even during the period between the general evaluations. The main criterion is excellence in science, but additional activities (e.g., teaching, grant support, student supervision) are considered as well.

The Institute attempted to internationalize the scientific environment and in the evaluated period organized competitions for the positions of new junior and senior group leaders. However, most foreign winners of the competitions did not accept the offered position in the end (probably due to the relatively low financial offers on the side of the Institute). Thus, of the current research group leaders, only three have no Czech origin. However, in 2018, under an agreement with the University of Sussex, UK, IMG established a group led by an outstanding and internationally recognized scientist in the field of DNA repair mechanisms, Keith Caldecott. The resulting “Guest Group” is mainly financed by the ERC Advanced Grant and enables continuous exchange of researchers between the Czech Republic and UK. Moreover, due to the thematic focus of the new group, the topic of genomic DNA integrity and DNA damage signalling at IMG was significantly strengthened.

The Institute also takes care of turnover of research groups in order to maintain high quality of research and age-balanced community of group leaders. The two main routes to closing groups are inadequate performance and retirement. The Institute has well-defined rules for terminating groups whose leaders are about to retire. Each group leader approaching the official retirement age (65 years) negotiates the plan for closing the group during the next three years. The rule does not apply to the group of the acting director. For excellent research groups, the integration of the leader and (some) employees into another thematically related research group is encouraged. Thus, the original scientific theme is not discontinued. In the years 2015-2019, two senior groups were terminated. It should be

noted that out of a total of 28 research/research-service groups, 23 were established after year 2006, i.e., after moving into the new building of the Institute in the Prague 4 Krc campus or into the BIOCEV Centre in Vestec.

Postdoctoral and Research Fellows, and other employees

Recruitment of new employees combines active recruitment and open search for suitable candidates. Recruitment of employees into research groups is managed by group leaders. Open search includes internet tools (both local and international, including research job posting sites operating worldwide) and advertisement in other media, including professional publications and periodicals, etc. The selection criteria are based on previously demonstrated professional performance strictly in accordance with the valid legislation, i.e., not discriminating as to the gender, race, religion, or nationality.

PhD student recruitment and management

Students are an important part of the "life" of the Institute. More than 110 PhD students are conducting their PhD research at IMG; 15-25 students are accepted annually. While some students continue their PhD research after acquiring the MSc degree at the Institute, IMG places strong emphasis on recruiting talented students from elsewhere. IMG is a training place having legal contracts with several universities (mainly Charles University and the University of Chemistry and Technology), which officially administer studies and award the PhD degree. However, IMG developed its own arrangements, which provide a strong "added value" to the PhD training and build a strong sense of an IMG PhD community despite the fact that students register in several different PhD programmes (mainly developmental and cell biology, immunology, molecular biology, virology and genetics).

The Institute organizes a PhD selection system, which begins with online applications and culminates in the IMG Interview Day held every March since 2008. All prospective students apply online and are pre-screened; the most promising candidates (20-40) are invited for interviews, where they present and discuss their research in English in front of three-member committees, which then rank them. Additionally, each applicant has an interview with group leaders of choice and get time to talk to IMG PhD students. This allows systematic recruitment of the best applicants while giving them a clear idea what to expect from conducting PhD studies at IMG. Announcements about open PhD positions are distributed through different "channels"; universities in the former "Eastern bloc" countries are frequently "targeted" to recruit talented students who do not go "further west" as many Czech students.

The number of international PhD students steadily grows; e.g., in 2015, 45 students were interviewed, 27 of them were from abroad. IMG also provides additional career development training to PhD students. Apart from *ad hoc* career development activities taking place at IMG, all new PhD students go through a weekend retreat organized since 2010. This is an "initiation" training course, which includes publication and grant writing workshops, teambuilding activities, and career discussions aimed to prepare students for the PhD study and experimental work. Subsequently, interviews with PhD students are conducted at the end of their second year and annually since their fourth year to follow their progress and give them some advice if needed. All PhD students are encouraged to spend some time abroad. Recently, the Institute was awarded mobility grant supporting working stays, usually for six to nine months of eight PhD students (or younger scientists) abroad and one postdoc for ten months from abroad to the Czech Republic.

The established PhD committee summarizes (and updates) the experience in the IMG PhD Administration Handbook, a manual distributed to the IMG administration and group leaders. The Handbook provides detailed overview for all parties of PhD-related matters and fosters building common, self-sustaining policies and "PhD culture" at the Institute. This systematic international recruitment lays good foundations for internationally competitive research at IMG and seems unique among the institutes of the CAS. That fact that the PhD community is thriving at IMG can be demonstrated at the annual one-day IMG PhD conference organized entirely by PhD students since 2008.

Awards, prestigious memberships, fellowships and grants

IMG researchers belong to the best in the Czech Republic as evidenced by a number of recently received awards and commemorations: the Czech government award "Czech Head" granted to Jiri Forejt (2016), silver commemorative medal of the Czech Senate granted to Jiri Hejnar (2015), Neuron Endowment Fund Award granted to Jana Dobrovolná (2015) and Petr Kasparek (2017) and the Novartis Discovery Award granted to Lenka Kyjacova (2015). Jiri Hejnar also received the Praemium Academiae for extraordinary scientific achievements (2018). Helena Fulkova was granted the Otto Wichterle Award Czech Academy of Sciences (2015); Vladimir Varga was granted the five-year J. E. Purkynje Fellowship of the Czech Academy of Sciences (2016) and the EMBO Installation Grant (2017). Lukas Cermak received the prestigious Marie Skłodowska-Curie Fellowship from the EU Commission (2018). Petr Svoboda obtained a prestigious five-year ERC Consolidation Grant (2015); Ondrej Stepanek was awarded a five-year ERC Starting Grant (2018) and the EMBO Installation Grant (2016). Two IMG scientists (Vaclav Paces, Jiri Forejt) are members of the Learned Society of the Czech Republic. Four Institute scientists (Jiri Bartek, Vaclav Paces, Jiri Forejt, Petr Svoboda) are EMBO members.

As appreciation for highly qualified scientists of a distinguished scientific personality who achieved original and important results in a certain scientific field, the Academy awarded the scientific title "Doctor of Science" (DrSc., and since 2003, DSc.). At present, the Institute has three holders of the DrSc. title (Petr Draber, Jiri Forejt, and Pavel Hozak).

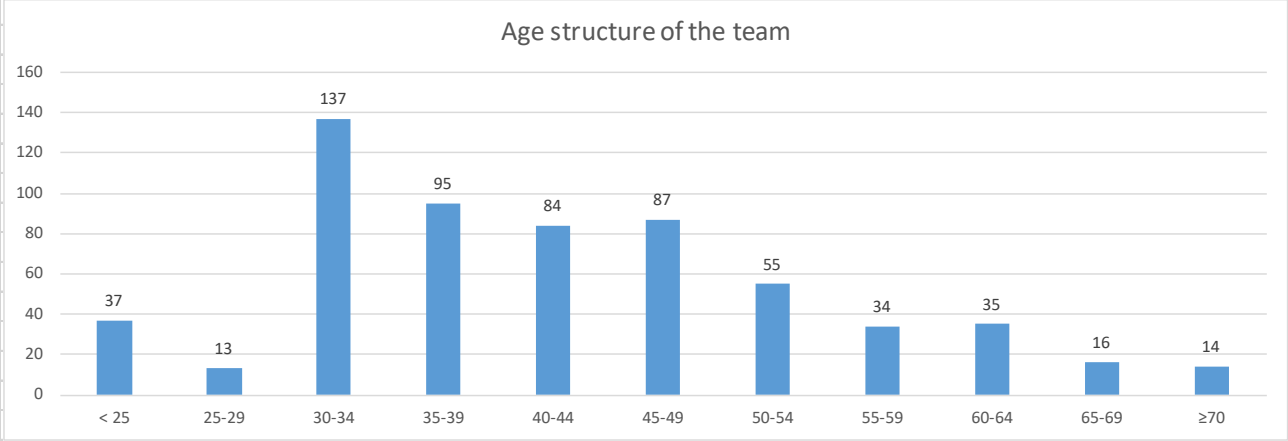
General conditions, benefits for employees

The Institute has a well-established classification system of professional ranks (including salaries). Excellent employees achieving outstanding results can be promoted to a higher rank. The promotion is based on the recommendation of the institutional Attestation Committee and signed by the Director. The Institute actively supports women in science and has pro-active family policy. Apart from flexible working hours, one of the important steps in this direction was foundation of an IMG day care/kindergarten, which makes easier return of IMG employees from parental leave. The day care/kindergarten is also an invaluable benefit when recruiting new researchers. Additionally, IMG offers its own guesthouse located on the campus in Prague 4 Krc. The Institute also offers a canteen and cafeteria, gym and squash court, and subsidizes theatre tickets. IMG organizes a St. Nicholas party with games and theatre performance for children of the employees.

Age structure of the institute

Related to 31 December 2019

Age category	< 25	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	≥70
Number of members	37	13	137	95	84	87	55	34	35	16	14



Strengths and weaknesses of the institute

The maximum extent is 2 pages.

Strength

Research focus

Research topics of IMG groups have high general interest; they are important in the context of international research. The topics have clear biomedical relevance. IMG has become the leading Czech institution utilizing vertebrate models to study pathological situations and developmental processes.

Skilled and motivated employees

The vast majority of current group leaders have spent a significant portion of their scientific "life" in excellent foreign laboratories. This fact, although common in the western developed world, is still to some extent exceptional in the Czech scientific environment. The international “perspective” influences the composition of the research staff of individual laboratories. This creates an attractive environment for young promising scientists and students, whether from the Czech Republic or abroad. Additionally, the system for admitting PhD students and overall organization of PhD studies at IMG generated a strong and emancipated PhD student community that is truly international. Technical and administrative personnel is well-trained and competent.

Well-defined organizational structure

IMG management is straightforward with efficient flat-structure organization and transparent financing of research groups. The Institute (gradually) introduced a system of continuous establishing and disbanding research groups resulting in adequate “turnover” of research groups/topics (the majority of laboratories were established after 2006). Research and administrative issues are discussed at weekly meetings of group leaders. Additionally, each group presents its projects at regular Wednesday Institute seminars and annual conferences. IAB has been successfully established and participated in research group evaluation.

Excellent working environment

IMG is located in modern buildings situated on the Academy campus in Prague 4 Krc or in the BIOCEV Centre in Vestec. The Institute runs state-of-the-art-equipped core facilities. Additional (specific) services are provided by the hosted Infrastructures; the Institute owns a unique collection of mouse, chicken, and fish strains and a wide portfolio of cell lines. The Institute is becoming one of the national “hubs” for biomedical imaging techniques. The IT Department ensures administration of the computer network, institutional servers, and storage including data backup. The IT Department provides installation and registration of computers and printers to the network, hardware purchases and consultancy. The IT Department also operates the audio-visual equipment in the conference hall.

High-quality publications

The Institute places emphasis on quality, not quantity of publications, discouraging publications in low-impact journals. The published articles are often based on long-term international collaborations.

Collaboration with universities, excellent reputation

Thanks to the frequent presentation of the results by public media, IMG is recognized as one of the top Czech research institutes. Many seminars, lectures, and conferences organized by IMG are attended by scientists and PhD students from other institutes of the CAS or universities. IMG scientists annually conduct many courses for master or bachelor students at universities. This fact not only increases the visibility of the Institute, but at the same time helps to create a personal connection

between universities and IMG. Additionally, IMG opened efficient communication channels that include up-to-date web pages and social media.

Weaknesses

A small number of group leaders who come from abroad

Even though our personnel are relatively international (when compared to other Czech institutions), IMG is still not enough international according to the common standards in similar institutions from the "old" EU member states or US. The main difference is a minimum number of group leaders of non-Czech origin. During the evaluation period, the Institute attempted to eliminate this weakness. The Director, in cooperation with the IMG Council, announced several open calls for group leaders in various categories (IMG Fellow, senior or junior group leader). Preselected candidates were invited for an interview (public lectures of the candidates were part of the selection procedure). The positions were subsequently offered to new potential group leaders, the vast majority of whom were of foreign origin. However, none of the foreign researchers accepted the final offer. The problem is probably the relatively low financial possibilities of the Institute (in comparison with foreign institutions), which makes the offered positions less attractive for excellent scientists of foreign origin.

Limited direct funding from the institutional budget

This point is closely related to the facts described above. Due to the long-term policy of the government of the Czech Republic, emphasis is placed on the project funding of research. Consequently, the majority of research groups are dependent on short-term (usually three-year) grants from a few providers. In addition, the resources that are allocated to the Institute as a direct subsidy from the state budget stagnate or are increased only minimally every year. The absolute amount of institutional support for research groups has not changed since 2012. Consequently, the financial offer to newly recruited group leaders cannot match the level of funding provided by western European research institutions. In recent years, the Institute addressed the unsatisfactory situation and attempted to obtain substantial financial resources within the 'Era chair' and 'Teaming' applications of the Horizon 2020 programme (between 2015-2018, two Era chair and two Teaming applications were submitted on an ongoing basis). Obtaining these resources would allow establishing several new research groups with excellent financial support for a period of up to seven years. However, these applications have not been successful and the unsatisfactory situation continues.

Relatively low number of publications in the most prestigious scientific journals

Although the Institute is gradually improving the publication output, the amount of articles in the top-level journals is still below expectations, i.e., it is lower when compared to the respected world research institutions. The "phenomenon" is linked to the above-mentioned funding "scheme" accompanied by the unfortunate policy of grant agencies that place emphasis on the "quantity", i.e., the total amount of articles per one financed project, rather than the scientific content of the studies. Consequently, the principal investigators are forced to publish rather frequently and there is not time enough to undergo the often long-term revision process so typical of the most prestigious journals.

Assessment of the strategy plan of the institute for the period of 2015-2019

The maximum extent is 2 pages.

Completion of the BIOCEV Centre and its full operation

A major factor influencing IMG was completion and running of the BIOCEV Centre. The construction works were finished in the end 2015 and IMG research groups started to work in the Centre. Thanks to the interconnection of research programs and projects supported by a robust research infrastructure, BIOCEV is not only a place of intensive cooperation between the research

groups of the CAS and Charles University, but also enables establishment of new groups. In fact, six of the eight IMG research groups located in the Centre were newly established since 2015.

Consolidation and development of the internal organization

The Institute completed the system of internal division of research groups (senior/junior groups, IMG Fellows). The division corresponds to the system of allocation of institutional finances and rules for evaluation of the quality (prospect) of the groups. Additionally, laboratories that are largely focused on (some) technology development and usage (e.g., sequencing techniques, testing of biologically active compounds) have been newly categorized as 'service-research groups'. The basic feature of these groups is that besides their own research activity, they provide services to other IMG research groups or external researchers. Finally, four large national research infrastructures started to operate at IMG providing services to the Czech and European scientific communities.

Research focus

The main IMG research focus remained on cancer biology (molecular oncology), molecular immunology, functional genetics and genomics, and cell biology. Although IMG research priorities remained "rooted" in basic science documented by questions: *How do the cells read information stored in their genome? How do the cells communicate, and how do they build tissues?* IMG researchers extended their expertise to animal modelling of human diseases including cancer, sterility, and hereditary disorders. Another area that was rapidly evolving at IMG was cell biology. The IMG has established state-of-art microscopy and cell sorting units. Importantly, sophisticated instrumentation and trained staff impacted research in all groups of the Institute.

Group leader recruitment, research group evaluation

To strengthen the IMG research topics, seven new group leaders were recruited during the years 2015-2019. The prospects of four of the new groups were already evaluated by IAB (or internally); additional evaluation was postponed due to the anti-covid-19 measures until 2021.

Support of young researchers

A high priority for work with human resources was given to support young (<40) group leaders and research associates/postdocs. It had a form of mentoring and advising on lab management, human resource management (each IMG Fellow/junior group leader has its mentor selected from leaders of senior groups), and applying for funding. A number of prestigious grants and fellowships obtained by young group leaders and postdocs are the proof that the support is functional and effective. IMG continued supporting young researchers with families. IMG runs and subsidizes day care/kindergarten, researchers from abroad (including their families) can stay for a period up to 18 months in the IMG guesthouse.

Implementation of recommendations from past evaluation

The maximum extent is 2 pages.

As part of the previous evaluation (which took place in 2015, evaluation period: 2011-2014), the Institute was evaluated by two commissions (commissions Nos. 6 and 9.). The final statements of both commission were very positive, e.g., "The Director and the managing Board should be congratulated on providing an excellent working environment and motivation for young researchers. The Institute of Molecular Genetics should continue to participate in the world-class research" – commission No. 6; "The commission concludes that the position of IMG is internationally competitive and, in some parts, leading. The commission felt that IMG is a "Flagship" institution of Czech science and a particular asset to the Czech Academy of Sciences)" – commission No. 9.

Commission No. 6 recommendation: "IMG should maintain the good monitoring of team leaders and of the research quality, and continue the involvement in high-risk-high-benefit projects. The excellent strategy to invest resources into talented young researchers (from a not too large Czech scientific budget!), and to send them to spend time in the best world laboratories (e.g. in US, England, France, Australia), has shown very good results in highly efficient budget spending".

Commission No. 9 recommendation: "The commission recommends a yearly retreat (1-2 days), where the entire faculty can discuss emerging fields and technologies that may influence the overall strategy. The commission also recommends that the Institute discuss ways to strengthen the cooperation with clinicians. Otherwise, keep going with the same winning formula!".

The Institute was very pleased with the positive evaluation of the commissions. **Ad commission No. 6 recommendation.** As follows from the evaluation for the period 2015-2019, IMG not only maintained, but also further developed the system for the recruitment of new group leaders. Foreign experience is necessary to gain the position; the Institute clearly supports the overall internationalization of the working environment, including stays and internships of employees and students abroad. **Ad commission No. 9 recommendation.** The Institute has a long tradition of organizing annual two-day retreats. However, with the gradual increase in the number of employees (IMG currently employs more than 600 people, of whom more than 300 are in research groups and services), the provision of these events has become very organizationally and financially demanding. Moreover, after opening of the new building in Prague 4 Krc, the Institute gained enough space to organize similar events directly in the main building of IMG. It is evident that the absence of retreats did not limit the mutual communication within the Institute. Scientific and/or organizational issues are discussed regularly on different occasions. These include the Annual Conferences, the meetings of all employees at the start of the new year, the meetings of PhD students and their tutors at the beginning of the new school year, and the weekly meetings of group leaders. Additionally, a number of smaller retreats were organized in connection with the preparation of the Teaming projects (some of these retreats were attended by colleagues from the Max Planck Institute in Dresden). Many research groups of the Institute (e.g., groups of M. Alberich Jorda, Gregor, Z. Hodny, L. Macurek) established cooperation with clinical departments; in many cases this cooperation was "covered" by joint grants. Importantly, the Institute has created legal frameworks for establishing such cooperation. In particular, it concerns creation of rules for handling clinical specimens, negotiation of such collaborations with the managements of the hospitals and clinics, and handling sensitive data in accordance with the General Data Protection Regulation, etc.

Strategy plan of the institute as a whole for the period of 2020–2024

The maximum extent is 2 pages.

Organizational changes

Due to the continuing uncertainty in institutional funding, the management of the Institute decided to reduce the property "exposure" of IMG in the BIOCEV Centre. Following an agreement with the management of the CAS and the Institute of Biotechnology of the CAS (IBT; IBT is the only one of the participating institutions directly located in BIOCEV), part of the premises and buildings in Vestec will be transferred from the ownership of IMG to IBT. The IMG will remain in possession of a large building (SO02), workplace of most of the institute's employees in the BIOCEV Centre. The building also houses the animal facility and all facilities of the infrastructure Czech Centre of Phenogenomics. With this organizational change, the Institute will significantly reduce its financial obligations arising from the operation and maintenance of the BIOCEV Centre. At the same time, there will be no reduction in the number of IMG employees in Vestec and the cooperation with the Centre's partners will continue.

Research directions, new research groups

The ongoing renewal of the institute's groups should continue, based on the transparent funding and career progression set in previous years. New junior/IMG Fellow research groups (2-3) will be established via open calls.

The research priorities for the next five years will remain the same, experimental biology research using vertebrate animal models. Recent advances in stem cell biology led to establishing organoids as a three-dimensional self-organized *in vitro* model of tissue organization and renewal. Organoids are able to recapitulate multiple biological aspects of the original tissue (cell composition and spatial organization, cell-to-cell interactions, cell differentiation). Thus, the organoids emulate the model system at the border between cell cultures and experimental organisms. Importantly, organoids might be used for screens of biologically active compounds or to generate disease models. Although several IMG groups already employ the organoid technology, the IMG management decided to strengthen this direction of research by recruiting new research groups using (and further developing) the technology.

The Institute has a long tradition in the use of the chicken model; outbred hen strains are continuously maintained at the experimental farm in Kolec. In 2018, the management of the Institute examined the sustainability of this model at IMG. The Director set up a commission to evaluate the scientific benefits of the chicken model and the economic aspects of its use. Based on the detailed report of the commission, the management decided to continue running the experimental poultry farms in the future. The fact that the preparation of transgenic hens (for scientific or practical use) has been made more efficient has also contributed to this decision. However, the use of the existing facility should be expanded by establishing a new research group using the chicken model.

Research cooperation with universities

Based on excellent cooperation within the BIOCEV project, the Institute will establish closer cooperation with the First Medical Faculty of Charles University. The research topic and future research directions will be presented and discussed during the first joint conference organized in summer 2021. Moreover, funding opportunities, especially in the field of (pre)clinical research, for joint research projects will also be identified.

Cooperation among the institutes of the CAS, application results

Based on the gradual topical convergence of institutes in the Prague 4 Krc campus (it is rather surprising that this convergence had not occurred in the past), joint laboratories/facilities will be built. In 2021, a joined Laboratory of Mass Spectroscopy (operated by IMG and the Institute of Physiology of the CAS) will be opened. We expect building and organization of other shared facilities (e.g., preclinical testing laboratory using animal models). Our priority is to maximize sharing of available equipment, know-how, and advanced technology. Additionally, our effort is to coordinate other activities such as recruitment of PhD students and joint seminars, courses, and lectures. Due to the increasing emphasis on results with possible practical use, the Institute participated in establishment of the Technology Transfer Office (TTO) operating within the Prague 4 Krc campus. The main agenda of the TTO will be to identify and further develop results with commercial potential. Additionally, the TTO will participate in securing adequate funding through programmes of the Technology Agency of the Czech Republic or Czech government institutions.

International and young research “friendly” work environment

IMG will continue supporting the international working environment and young researchers with families. A high priority for work with human resources will be given to strong career development support for young group leaders and outstanding postdocs. The support will mainly include mentoring and advising on laboratory management, human resource management, and applying for funding.

Research for practice

Identification of research results with application potential

System of identification of research results with application potential at the institute, their records, administration of intellectual property and how it pays attention to knowledge and technologies transfer.
Maximum extent is 1 page.

Knowledge and technology transfer in general

Knowledge and technology transfer at the IMG consists of expert studies for Czech and foreign academic and industrial partners, licensing and contract research services (all commercialized in an amount of more than 20 million CZK per year). Utilization of the IMG intellectual property and infrastructures is considered among the most important missions of the Institute. In the evaluation period, the commercialization activities via licensing, contractual and collaborative research (without specialized services) reached the amount exceeding 1,610,000 Eur.

Result disclosure and author motivation

IMG established a system for identification, analysis and evidence of results with possible commercial or other applicability. The system implements a passive and an active approach to the disclosure. The passive disclosure is based on the author's duties and responsibility according to a valid internal directive on technology transfer (TT) and intellectual property protection (IPR). It consists of the author's and supervisor's result analysis (prior to any publication) with a subsequent (optional) consultation at the IMG TTO level. The active result disclosure is based on the TTO employee's active communication with the researchers (authors) via individual meetings and presence at the weekly IMG group leader meetings. IMG uses "a motivational approach" towards the result disclosure and IPR, which consists of three pillars: (1) all the IPR costs and patent applications in the Czech Republic are covered by the internal IMG funds; (2) the authors have a possibility to utilize an internal commercialization fund to cover costs of proof-of-concept activities; (3) one half of any possible financial income associated with the IP commercialization goes directly to the laboratories of the IP authors and to the authors themselves. In case of contractual research, the laboratory responsible for providing it keeps half of the margin.

IP analysis and administration

Foreground knowledge determination and IP analysis, i.e., patent search and business evaluation, are part of the (optional) consultation at the IMG TTO. The TTO uses Espacenet as a patent engine and Global Data as a business analysis engine. Other tools for business analysis include the Commercialization Council (CC), which also supports stop/go decisions on proof-of-concept activities financed from external sources (e.g., projects funded by the Technology Agency of the Czech Republic) and an external contractual business analyst, e.g., i&i Prague (i&i Prague is a private Czech biotech venture financed by percentage of the profit from potential net sales of a commercialized technology). The CC is the Director's consulting body with most seats held by external consultants with biotech business or finance expertise; the IP identified for further protection and development is primarily protected by application to the Czech Industrial Property Office. A general strategy for any IPR is to have it partnered within three years since the priority with a Patent Cooperativity Treaty (PCT) at place for the meantime. Currently, IMG has three PCTs, eight international applications and 11 international patents, and approximately two dozen Czech patents either granted or awaiting granting.

Strategy AV21

Participation in research programmes of Strategy AV21.
Maximum extent is 2 pages.

IMG participates in the research programme Strategy AV21 supported by CAS. The programme aims to promote cooperation across various scientific fields and institutions. Three research topics are currently under investigation as part of the Strategy AV21 research programmes: 'Wellbeing in Health and Disease' (QUALITAS; VP07) and 'Preclinical Testing of Potential Pharmaceuticals' (VP18).

Research topic: Genetic Factors Contributing to Human Disease (QUALITAS)

This topic aims to initiate collaboration of the teams from IMG (coordinated by L. Macurek) with clinical oncologists and geneticists (coordinated by Z. Kleibl, Charles University) and promote screening of potential novel cancer-predisposing genes. The ultimate goal of this initiative is improvement of genetic counselling in the Czech population. The support from Strategy AV21 was used to perform pilot and high-risk screenings of cancer candidate genes. In the next step, the preliminary results will be used for grant applications. This strategy has already proven to be efficient, as the pilot study focused on developing an assay for evaluation of oncogenic CHEK2 variants now continues as a large study supported by a grant from the Ministry of Health. In addition, results from the original study have already been implemented in the guidelines for counselling of CHEK2 variants in the Czech population. Furthermore, next-generation sequencing was used to identify variants in several new cancer candidate genes including *FANCG*, *RAD18*, *MRE11,* and *RAD50* in breast and ovary cancer patients. In parallel, cell-based assays were developed to evaluate the function of the identified variants. Based on preliminary data, detailed analysis of selected cancer candidate genes will be performed in the future.

Research topic: Organ Culture Centre (QUALITAS)

This topic within the framework of AV21 Strategy focuses on the establishment of organoid cultures recapitulating normal development and diseases of the (1) intestinal tract (group of V. Korinek), (2) liver (group of M. Gregor), (3) eye retina (group of Z. Kozmik) and (4) haematopoietic disorders (group of L. Lanikova). One of the purposes of creating the Centre was to establish closer cooperation with clinical workplaces, such as Department of Hepatogastroenterology, Laboratory of Experimental Hepatology, and Institute for Clinical and Experimental Medicine, Prague (led by M. Jirsa). Currently, all four subprojects reached the proof-of-concept phase when model organoid cultures are being established. The long-term goal is not only to characterize the molecular and pathophysiological mechanisms of the diseases studied, but also to identify biomarkers useful for diagnosing and monitoring the course of the disease. When the disease is successfully modelled at the organoid level, it will be possible to test targeted therapy by pharmacological intervention, cell transplantation or gene manipulation.

Research topic: Preclinical Testing of Potential Pharmaceuticals

This programme, which is coordinated by the Institute of Physiology of the CAS, involves participation of four Academy institutes that have joined together in the Centre of Preclinical Testing of Potential Pharmaceuticals (CPT; http://www.prekliniky.cz). The main objective of CPT is to perform preclinical testing of compounds that were successful in investigative research and thus contribute to the development of novel drugs for treating serious life-threatening diseases and difficult-to-treat disorders. The involvement of the Academy institutes in preclinical testing of potential therapeutics brings two basic advantages (synergies) that appear absolutely uncommon in the context of the Czech biomedical research: (1) use of the capacity of basic research instruments and equipment; (2) facilitated transfer of basic research outputs into the commercial sphere and clinical practice. This creates a unique opportunity for the Academy institutes to participate in applied research of great social import. Within CPT, IMG is responsible for sub-programme 2.5. Histopathological Testing/Tissue Testing of the studied animals (group of R. Sedlacek). IMG is the testing site for histopathology, clinical biochemistry, haematology, specific toxicity assays, imaging methods in immunology and neurophysiology, neuropsychopharmacology, cardiology, and behavioural tests [all in the regime of "good laboratory practice" (GLP)]. IMG has already concluded contracts with research institutes and companies, and the interest in collaboration is growing. In the evaluated period, three studies were

conducted in the GLP regime (one is already completed, two are still running) with a drug-producing commercial subject. The studies involved histopathological analysis of tissues in relation to evaluation of safety of vaccines. In a “non-GLP” regime, IMG participated in a study of pharmacokinetics of potential therapeutics, toxicity testing of agents usable for treatment of metabolic syndrome, one dialectological study, and the possible side effects of the studied therapeutics using behavioural tests were assed. Using mouse models, a number of potential anticancer therapeutics (or therapies) were tested. The tests also included immuno-radiotherapy and therapeutics targeted to the tumour microenvironment.

Cooperation with regions of the Czech Republic

Maximum extent is 1 page.

The BIOCEV Centre and its activities not only concern research, but also significantly contribute to the development of the Central Bohemian Region (CBR), which in terms of European development is referred to as "underdeveloped". The CBR surrounds Prague and due to the ‘convergence objective’, investment from structural funds into research institutions located in the Prague area was not possible. IMG cooperates with the Science and Technology Advanced Region (STAR), which is non-profit and consists of a strong community of research organizations, companies, investors and enthusiastic “patriots” living and operating in CBR. The mission of STAR is to help establish an international research and innovation area. STAR is a pioneer among micro-regional initiatives building an innovation “ecosystem” in Central Europe and creating a better environment for science, innovative technology companies and the quality of life of its inhabitants. Within STAR, IMG cooperates with a number of private companies (DIANA Biotechnologies, EXBIO, VIDIA, SOTIO). IMG/BIOCEV provides not only services to the industrial sphere, but its representatives are members of the Competitiveness Council of CBR, an advisory body of the Regional Council. In addition to scientists and students, the Institute employs a large number of other staff and technicians and thus contributes to increasing employment in CBR.

Additional cooperation with regions of the Czech Republic is indicated in the section describing large research infrastructures.

Cooperation with universities

Overview of semestrial lectures, seminars and courses

Name of the university	Number of semestrial lectures, seminars, and courses 2015-2019		
	Bachelor	Master	Doctoral
Charles University, Prague	64	103	54
University of Chemistry and Technology, Prague	6	49	4
Czech Technical University, Prague	2	8	0
University of Ostrava	0	5	0
Palacky University, Olomouc	0	4	4
Comenius University, Bratislava	3	0	0

Supervision of students

Type of study	No. of supervisors	No. of consultants	Theses defended 2015-2019
Bachelor	41	4	52
Master	59	10	72
Doctoral	84	16	57

Joint research Centres with universities

Name of the joint research Centre, its mission, organizational structure, funding and its most important outputs/results relevant to the institute.
Maximum extent is 1 page.

BIOCEV (https://www.biocev.eu)

Cooperation with Charles University, Prague and five other institutes of the CAS. **Mission:** BIOCEV builds upon three pillars of the knowledge triangle: teaching and education, research and development, and transfer of research results into practice. The cooperation is based on the Partnership Agreement; research is organized in five research programmes: Biomaterials and Tissue Engineering, Cellular Biology and Virology, Development of Diagnostic and Therapeutic Procedures, Functional Genomics, Structural Biology and Protein Engineering. As of 31 December 2019, the BIOCEV Centre employed 882 people (519.43 FTE), of whom 482 are scientists (289.66 FTE), working in a total of 56 scientific groups of the Centre or in the core facilities and research infrastructures. **Results:** Since the beginning of the BIOCEV project, 841 scientific reports have been published with the dedication to the Centre. Currently, 176 specifically funded projects are running in the Centre, of which nine are international.

Centre for Tumour Ecology - Research of the cancer microenvironment supporting cancer growth and spread (https://cne.cuni.cz/en/)

Cooperation with Charles University based on the common project. **Mission:** To achieve better insights into cancer progression and to develop new tools for such discoveries (e.g., specific imaging probes). **Results:** one publication by the end of 2019.

Centre of competence for molecular diagnostics and personalized medicine (https://www.imtm.cz/moldimed)

Cooperation with the Palacky University in Olomouc. **Mission:** To achieve a critical mass of experts, institutions, and knowledge in research, development, protection of IP, certification, technology transfer, and commercialization of *in vitro* diagnostics, in order to create a market-oriented flexible national network in the area of diagnostic, prognostic and predictive biomarkers and to enable further development of personalized medicine.

Centre of Excellence - Centre of RNA biology

Cooperation with Charles University and CEITEC/Masaryk University. **Mission:** To integrate interdisciplinary approaches that involve scientific exchanges across disciplinary boundaries to provide a complex understanding of biological mechanisms involved in RNA biology. **Results:** one manuscript is currently under revision in Nucleic Acids Research.

Research services

Research services: library, database, collections and others

Maximum extent is 2 pages.

IMG operates several core facilities. Importantly, the Facilities support not only the IMG research community, but as they are run in the open access mode, the Facilities are used by many researchers from other institutions.

The Genomics and Bioinformatics Core Facility operates instruments for functional genomics and provides next-generation sequencing and single-cell transcriptomics services including consultations on project considerations and experimental design. The facility also performs primary bioinformatical analyses. The service is provided to the research groups at the Institute, to other academic institutions, and also to commercial entities. The core facility is equipped with an Illumina NextSeq 500 next-generation sequencer, two single-cell technologies (10x Genomics Chromium Controller and Bio-Rad ddSEQ), two real-time PCR cyclers (Roche LC480), two legacy microarray platforms (Affymetrix GeneChip System and Illumina BeadStation 500) and an EnVision Plate Reader (PerkinElmer). The laboratory also operates instruments for assessment of the quality and quantity of processed samples (Nanodrop spectrophotometer, Qubit fluorometer, capillary electrophoreses Agilent Bioanalyzer 2100, and Agilent Fragment Analyzer 5200). Two ultrasonicators (Covaris ME 220 and Bioruptor) are available as shared equipment. The Facility is an integral part of the Laboratory of Genomics and Bioinformatics.

The Light Microscopy Core Facility is a state-of-the-art research facility equipped with a wide range of high-end microscopy technologies and image-processing tools. Most of the instrumentation in the facility is available on the self-service basis, for trained users. User access to the facility is supported via the “Czech-BioImaging open access” programme both for in-house and external scientists. The available technologies range from simple wide-field and confocal fluorescence microscopes to more advanced systems such as light-sheet, confocal spinning disc and superresolution techniques SMLM, SIM and STED. In addition, the Facility personnel provides expertise on final image processing and analysis, including image registration, routine deconvolution, tracking, image segmentation, analysis of photo-kinetic experiments, mathematical modelling and simulations of biological processes.

The Electron Microscopy Core Facility provides expertise and ‘cutting edge’ equipment for a broad range of biological sample preparation and ultrastructural imaging techniques. The sample preparation techniques include routine chemical fixation and resin embedding, cryofixation using high-pressure freezing technique, freeze-substitution, plunge-freezing, cryosectioning, and immunolabelling, including simultaneous detection of multiple targets by our self-developed methods. High-pressure freezing machines, two automatic freeze-substitution machines, freeze-fracture and replica making device, cryo-ultramicrotomes, Leica EM GP2 for automated plunge-freezing, as well as additional wet lab equipment are available. The core facility is equipped with two transmission electron microscopes (TEM) installed in November 2019 – a standard instrument for routine observation and an advanced 200 kV instrument providing the possibility of high-resolution TEM, STEM, 3D electron tomography, cryo-electron microscopy and EDS elemental analysis and mapping. The Facility provides open access to our technologies and expertise via Czech-BioImaging and Euro-BioImaging infrastructures.

The Flow Cytometry Core Facility provides methodological and instrumentation background for flow cytometry. The facility is equipped with two flow cytometers with high-throughput automated sampler and two polychromatic high-speed cell sorters. The Facility includes a magnetic separator for

automatic rapid sorting of cells. Cytometers and magnetic separator are available for trained users on a self-service basis. Sorting in polychromatic high-speed cell sorters is performed by operators.

The Monoclonal Antibodies and Cryobank Core Facility (the Facility has two units located in the Prague 4 Krc campus and BIOCEV in Vestec) provides generation of mouse monoclonal antibodies including immunization, ELISA testing, (sub)cloning of selected hybridomas, sample freezing, production of cell culture supernatants, and isotype determination of the produced antibody. Further services comprise testing of cell culture supernatants for the presence of mycoplasms. The cryobank serves for long-term storage of samples in liquid nitrogen. The current cryobank capacity is 320,000 samples, with further possible extension. The cryobank stores cell lines, hybridomas, mouse sperm, and mouse embryos. The storage containers (LABS40K – Taylor-Wharton and 24K) are connected to the exterior liquid nitrogen container and supplied automatically. The entire cryobank system is secured by a backup energy source in case of power failure. All operations, diagnostics and monitoring of the level of liquid nitrogen in the storage containers are fully automated and controlled. Parameters (temperature, humidity, O2 concentration) and safety both in the cryobank and in the individual storage containers are followed by the monitoring system with GSM and web interface outputs.

The X-ray Irradiation Facility is equipped with an X-RAD 225XL Biological Irradiator for regulated radiation of cells and mice. The instrument is used by trained personnel as self-service.

The Histological Laboratory provides equipment for tissue dehydration, creation of paraffin blocks, tissue sectioning, deparaffination and antigen retrieval. The most important laboratory equipment consists of a set of four Leica devices – tissue processor, paraffin embedding station, and two microtomes. The facility is based on semi-self-service – tissue dehydration is collective and handled by the staff, all the other steps are carried out by each user individually independently and without time limitations.

The Media and Glass Washing Units in the Prague 4 Krc campus and BIOCEV offer preparation of tissue culture media and solutions, preparation of bacteriology media and plates, sterilization of solutions and material, glass and plastic washing, and decontamination of hazardous waste.

Other (specific) services are provided by large research infrastructures hosted by IMG; details are given in the following paragraphs.

Administration of research infrastructures

Research infrastructures mean a unique devices or platforms which provide the research community with resources and services for performing top research and development and which are established for use by also other research organizations and other users under transparent conditions defined in advance. Definition of research infrastructure is based on IPn methodology for research infrastructures evaluation, http://www.msmt.cz/file/33846_1_1/ p. 4-5, the required description includes the main criteria of the evaluation by IPn methodology or on Article 2(91) of Commission Regulation (EU) No 651/2014.
Brief description of the infrastructure, service portfolio, principles of the access to the infrastructure, characterisation of the users´ community, data about utilisation including the ratio of external and internal users, characterisation of the results achieved based on their utilisation, involvement in international cooperation, development strategy.
Maximum extent is 5 pages.

IMG established and hosts three new large research infrastructures that are part of the European Strategy Forum on Research Infrastructures (ESFRI) and are also listed as national research infrastructure of the Czech Republic. The Infrastructures work under open an access mode. Thus, they provide services not only to the Czech but also European research community.

Czech-BioImaging (https://www.czech-bioimaging.cz/) is a large national research infrastructure, consisting of 14 closely cooperating facilities, for biological and medical imaging. Its aim is to allow permanent access to cutting-edge imaging technologies and expertise in imaging to scientists who do not have them available at their own institutions, to increase awareness and knowledge of biological and medical imaging, to support mutual cooperation of scientists and sharing best practices and knowledge.

Czech-BioImaging provides open access to a wide range of biological and medical imaging technologies: e.g., advanced light microscopy, fluorescence microscopy, super-resolution microscopy, electron microscopy, correlative light and electron microscopy, sample preparation, neuroscience imaging, magnetic resonance, magnetic particle imaging, image analysis and development of new methods. Prior to the usage, the Czech-BioImaging experts help users in preparing and executing their projects at the Czech-BioImaging nodes. Moreover, the Czech-BioImaging provides introductory hands-on training to its users and organizes regular courses on biological and medical imaging, data acquisition and analysis. Besides the training activities, the Czech-BioImaging organizes workshops, seminars and technical demonstrations of new imaging techniques.

In the first four years of operation, almost 3,000 users used the open access, of whom 5.5 % were from foreign institutions. Most Infrastructure users come from academia. Users from home institutions included CAS institutes involved in Czech-BioImaging, as well as other institutes of the CAS and universities from the Czech Republic and abroad. A large group of users consists of employees of medical facilities. Private users account for less than 3 %. Foreign users come to the Infrastructure mainly from countries of the European Union (Slovakia, Hungary, Croatia, Poland, Great Britain, Netherlands, Slovenia, Germany, France, Serbia), but the Czech-BioImaging Infrastructure has also been used by scientists from Australia, Brazil, Israel, Japan, Canada, or the US.

The relevance of the national imaging research Infrastructure is evidenced by the existence of many original articles in highly impacted scientific journals (Nature, Nature Communications, Science, Cell Metabolism, Nature Cell Biology, Journal of Hepatology, etc.), which were produced using the instrumentation associated with Czech-BioImaging. Several results from applied research are also listed as patents and software. In 2016: 27 publications, three software packages and three patents were generated; 2017: The Infrastructure team created one software and participated in a total of 57 publications; 2018: The team was involved in 71 research articles; 2019: 78 publications and one software were produced using the equipment and resources of the Infrastructure. The published results cover a wide range of scientific areas, in particular cell and molecular biology, structural biology, genetics, environmental sciences, biophysics, biomaterials, microbiology, parasitology, preclinical imaging, neuroscience, pathology and many others that demonstrate the attractiveness of the Infrastructure to a broad scientific community branches.

Institutions involved in Czech-BioImaging already participate in a number of research projects, including international ones. IMG participates in the project of the Centre of Competence focused on electron microscopy, which also includes the Biology Centre of the CAS, the Institute of Scientific Instruments of the CAS, and several companies and other institutes of the CAS (beside those involved in Czech-BioImaging). The project is focused on the development of new methods of sample preparation and new strategies for data acquisition and analysis in electron microscopes and is funded by the Technology Agency of the Czech Republic.

Finally, Czech-BioImaging was also the basis for the creation of two Czech “nodes” of Euro-BioImaging ERIC, thus connecting the Czech scientific community more closely with foreign countries. Czech-BioImaging will, in cooperation with Euro-BioImaging ERIC, further expand and strengthen its cooperation with foreign scientists; an increase in users from abroad is also expected.

The National Infrastructure for Chemical Biology CZ-OPENSCREEN (https://www.openscreen.cz/en) operates the most advanced research Infrastructure for basic and applied research in the fields of chemical biology and genetics in the Czech Republic; the Infrastructure provides open access to its external users. The other partner institutions of CZ-OPENSCREEN are Palacky University, Olomouc, Masaryk University, Brno, and the University of Chemistry and Technology, Prague. The main mission of CZ-OPENSCREEN is (1) to identify new molecular probes and develop new tools for research; (2) to identify chemical compounds as candidates for development of new potential therapeutics. Unlike commercial platforms, CZ-OPENSCREEN also focuses on non-validated molecular targets, signalling pathways, and so-called neglected diseases. Users of CZ-OPENSCREEN mainly include biologists, chemists, and data users.

CZ-OPENSCREEN offers comprehensive services for biologists such as standard biological and biochemical assays, consultancy and development of new assays, high-throughput screening (HTS), profiling of chemical compounds on a panel of cell lines, and medicinal chemistry optimization of newly identified biologically active compounds. CZ-OPENSCREEN is systematically building a library of both commercial chemical compounds as well as compounds synthesized in the Czech Republic. It provides access to its systematically built unique library to external users. An integral part of the services is cheminformatics support, such as data analysis and storage, development of new analytical tools and database systems.

CZ-OPENSCREEN has a very strong background in software development for cheminformatics. Data about chemical probes (chemical probes are small-molecular compounds commonly used in biological experiments) and their qualities are often scattered over various data sources, which makes the search for the “right” chemical tool a time-consuming task. To alleviate these problems, the Infrastructure bioinformaticians developed the Probes & Drugs (P&D) portal ***(Skuta C, Popr M, Muller T, Jindrich J, Kahle M, Sedlak D, Svozil D, Bartunek P.: Probes & Drugs Portal: an interactive, open data resource for chemical biology. Nat Methods. 2017, Jul 28;14(8):759-760)***. The portal is an up-to-date public resource for chemical biology that should simplify the well-informed selection of high-quality chemical tools for biological screening. The P&D portal is currently the most comprehensive source of both well-described non-commercial and pre-picked commercial compound libraries and it is one of the three main resources in this field used by the research community.

The Infrastructure provides services either in the open access mode, where the costs are fully or partially covered by the Infrastructure, or in the so-called full-cost mode, where the user pays all the costs of the project. Due to a variety of services offered in the fields of chemical biology, medicinal chemistry, cheminformatics, data mining, and HTS testing, there are several options of access when users submit their project proposals and requests. The Infrastructure is used mainly by external users from academic institutions and universities, but a significant part is also made up of users from hospitals, industry, and the private sector [e.g., small and medium enterprise (SMEs)]. Current users are organic and medicinal chemists, cell and structural biologists, molecular and developmental biologists, biochemists, microbiologists, and pharmacologists. In upcoming years, the Infrastructure will be fully open to innovative approaches and projects addressing various issues of chemical biology, as evidenced by the aforementioned spectrum of the users.

CZ-OPENSCREEN collaborates with a number of other research infrastructures and institutions, hospitals and small companies. These collaborations resulted in numerous outputs, such as scientific publications and patents (https://openscreen.cz/en/papers).

In upcoming years, the Infrastructure will modernize the technological instrumentation, by both upgrade of the current or purchase of new instruments. This modernization will significantly improve the quality of services offered to the users and will also increase the competitiveness of the Infrastructure. The future focus will be on more intensive connection of individual infrastructure sites, in particular closer collaboration in terms of joint projects, creation of a new (common) library of

chemical compounds, student exchanges, and collective presentation of the Infrastructure towards users.

CZ-OPENSCREEN represents a national node of EU-OPENSCREEN ERIC. This pan-European infrastructure for chemical biology was established by the decision of European Commission in 2018 and the Czech Republic belongs to the founder states. Within EU-OPENSCREEN ERIC, CZ-OPENSCREEN will operate the European Chemical-Biological Database (ECBD), in which all the data generated by Partner sites of the EU-OPENSCREEN consortium will be stored. The new legal framework of EU-OPENSCREEN will facilitate cross-border cooperation within the EU-OPENSCREEN Distributed Research Infrastructure and offer researchers from around the world access to a wide range of state-of-the art technologies in an open access mode. Importantly, the integration of CZ-OPESNCREEN into the European consortium EU-OPENSCREEN ERIC has contributed to its international visibility, which will be essential for establishing future international collaborations and access to the Infrastructure by foreign users.

Czech Centre for Phenogenomics (CCP) (https://www.phenogenomics.cz/) is the largest biomedical research infrastructure and the main site in the Czech Republic with the expertise and capacity for large-scale generation of genetically modified mouse and rat models, and their advanced and standardized phenotyping. This expertise, together with high breeding capacity under specific pathogen-free (SPF) conditions and cryo-archiving and recovery services, provides open access to services and expertise at a level comparable to the leading research institutions in the Europe.

CCP is a founding member of INFRAFRONTIER GmbH (the pan-European infrastructure) and the global International Mouse Phenotyping Consortium (IMPC). The main IMPC goal is to build the first comprehensive functional catalogue of a mammalian genome. CCP occupies more than 10,000 sq. meters of space split between two research locations with academic biomedical research institutions: the BIOCEV Centre in Vestec and campus in Prague 4 Krc. CCP can provide breeding capacities for rodent animal models and effectively satisfy needs of the large research community. The new building in the BIOCEV Centre with more than 7,000 sq. metres has become the headquarters of the Infrastructure providing the primary site for model generation and phenotyping (and other specialized services). Both locations have animal breeding capacity managed in the way that the models could be easily transferred between these two locations.

CCP with more than 110 employees mostly engaged in services is organized in three main modules: Transgenic and Archiving Module (TAM) provides a broad range of transgenic and archiving services including gene targeting using classic technologies or using the latest technology of programmable endonucleases, generation of transgenic animals, as well as rederivation/reanimation, and cryo-archiving of mouse strains. TAM collaborates closely with the Animal Facility Module (AFM), which is responsible for all housing and breeding services of mice and rats; Phenotyping Module (PM) provides standardized phenotyping characterization of all models established or imported into CCP. The PM module constitutes a compendium of technologies and expertise for investigating major physiological systems of the body. The technologies accompanying specific services are grouped into these units: histopathology, metabolism, clinical biochemistry and haematology, cardiovascular function, lung function, embryology, whole body imaging and dysmorphology, neuro-behaviour and sensory function. CCP also has an appropriate administration unit to manage all operational tasks.

CCP collaborates with a number of researchers from IMG or other research institutions, hospitals and small companies. These collaborations resulted in numerous scientific publications (https://www.phenogenomics.cz/research-and-education/publications/).

Pan-European ELIXIR Bioinformatics Research Infrastructure (https://www.elixir-czech.cz/)

Life science experiments generate an immense volume of data. It is necessary to store the data, make them accessible, and safe. The mission of ELIXIR CZ is to create a sustainable infrastructure for storing, processing, and analysing data in the Czech Republic. The uniqueness of ELIXIR CZ lies in the expertise provided by specialized groups at Czech research institutions members of the ELIXIR CZ consortium. Jointly they create a bioinformatic platform offering services for a wide research community in the open access mode. IMG forms one of the nodes of the ELIXIR CZ consortium. The node curates and maintains the database of mitochondrial sequences coming from ancient DNA samples (AmtDB) and the database of human endogenous retroviruses (HERVd).

Outreach activities

Research popularisation

Media strategy, courses and lectures for general public, popularisation publications, educational films, videos, television and radio programmes, children and youth educational activities and other activities in the interest of general public relevant to the institute.
Maximum extent is 2 pages.

Since outreach activities are described in detail in the material supplied by each IMG group, here we describe only the outline of these activities. IMG has taken several steps towards greater openness to the general public in previous years. The Institute presents its research and results in a more understandable way using not only the traditional methods (TV interviews, press releases, etc.), but also modern ways of communication such as social networks. IMG also released new promotional materials (“Roll Ups”, information leaflets, etc.) and laboratory notebooks in a new, more attractive form (Figure 1). Recently, the IMG Annual Book 2017-2019, summarizing information about the Institute, was released. Taking into account the economic and ecology aspects, the Annual Book is available online only (https://www.img.cas.cz/files/2020/06/Scientific-report-2019.pdf).

Figure 1 *New IMG Roll Ups, Information leaflet and Laboratory Notebook*

Online communication and media

Social networks with daily updated content became an important part of IMG communication with general public. The social network profiles were established in 2018 on Facebook (360 followers), Twitter (510 followers) and Instagram (260 followers) with the content focused on general public (Facebook), general public/scientists (Twitter), and young audience/potential PhD students (Instagram).

IMG regularly prepares official press releases representing our latest scientific achievements (usually several per month) for media purposes. Research group leaders are often guests in various interviews or authors of popular (educational) articles, commentaries or blogs, for example:
https://www.img.cas.cz/files/2019/06/P.Svoboda-tema-14.6.2019.pdf
https://www.idnes.cz/technet/veda/pestovani-lidskych-bunek-a-organu.A190816_152013_veda_vse
https://www.img.cas.cz/files/2019/04/Pe.Draber-tyden-22.4.2019.pdf
http://blog.aktualne.cz/blogy/vaclav-horejsi.php

Offline communication, educational activities

IMG participates in several events organized annually by the CAS, for example *Otevřená Věda (Open Science)* or *Týden Vědy a Techniky AV ČR* (*Science and Technology Week of the CAS*; Figure 2). IMG researchers organize the (traditional) course *Advances in molecular biology and genetics* (Figure 3). Typical attendees of the Course are the first and second year PhD students from biomedical programs. The main aim of the two-week lecture course is to inform the participants about the recent progress in the fields of molecular biology, genetics and biomedicine together with selected new biotechnology approaches.

Figure 2 *Science and Technology Week of the CAS 2019*

Figure 3 *Participants of 43rd 'Advances in Molecular Biology and Genetics course' organized by IMG*

Publishing activity concerning scientific books and periodicals

Maximum extent is 2 pages.

Scientific books published by the IMG researchers in the evaluation period

Advances in Chemical Biology. Praha: OPTIO CZ, 2019 - (editor Bartůněk, P.), s. 166-173. ISBN 978-80-88011-03-3

Advances in Disease Models. Praha: OPTIO CZ, 2019 - (editor Bartůněk, P.), s. 303-310. ISBN 978-80-88011-06-4

Introduction to RNAi and miRNA pathways. Praha: Karolinum, 2019 - (author Svoboda, P.), s. 1-339. ISBN 978-80-246-4372-4

Organized conferences and workshops

Conferences and workshops organized by institute.
Maximum extent is 1 page.

Events (co)organized by IMG researcher(s) and located at IMG

Conferences, symposia, and workshops
2016: International meeting of ENIGMA consortium
2017: International symposium Hallmarks of Cancer: Focus on RNA; Metabolism from Cells to Mouse Workshop; 8th EMBRN International Mast Cell and Basophil Meeting; EU-OPENSCREEN Bioprofiling workshop
2018: Joint Workshop of the Society for Histochemistry and the COST Action "An integrative action for multidisciplinary studies on cellular structural networks; FEBS Advanced Lecture Course and 33rd European Cytoskeletal Forum Meeting on Biology and Pathology of the Cytoskeleton: The Crossroads of Three Cytoskeletal Systems
2019: Nuclear Architecture, Lipids, and Phase Separation Workshop; EMBO workshop Awakening of the genome: The maternal-to-zygotic transition; The 2nd Czech Cilia Meeting; 8th International Symposium on Kallikreins and Kallikrein-Related Peptidases

Practical courses
2016: Application of microCT technique for biological applications; Programmable nucleases course; Mouse cryopreservation workshop
2017: Anatomical Basis of Mouse Multimodal Imaging Course; 2nd Programmable Nucleases Course
2018: New innovative technology in rodent body temperature telemetry; Use of microCT technique for biological applications; 3rd Programmable nucleases (CRISPR/Cas9); Mouse vs Human Comparative Morphology: Essentials for accurate interpretation of Precision Medicine models; CCP Programing in R: Basics and Graphs
2019: MicroCT technique for biological applications; CCP Phenogenomics Conference

Events (co)organized by IMG researcher(s) and located outside the Institute

Conferences, symposia, and workshops
2015: 23rd Czech Cytoskeletal Club (Vranovska Ves, Czech Republic)
2016: 12th EFIS-EJI Tatra Immunology Conference (Strbske pleso, Slovakia); 13th Transgenic Technology meeting (Prague, Czech Republic); EMBO Workshop "Wnt meeting 2016 (Brno, Czech Republic); 12th International Congress of Cell Biology - Minisymposium "Microtubules in health and

disease" (Prague, Czech Republic); 16th International conference on crystallization of biological macromolecules (Prague, Czech Republic); National Bioinformatics Conference ENBIK2016 (Loucen Castle, Czech Republic)
2017: 29th International Workshop of Retroviral Pathogenesis (Liblice, Czech Republic); EMBO workshop Awakening of the genome: The maternal-to-zygotic transition (Dresden, Germany); The 22nd Annual Meeting of the RNA Society (Prague, Czech Republic)
2018: 12th EFIS-EJI Tatra Immunology Conference (Strbske pleso, Slovakia); The 22nd International Chromosome Conference (Prague, Czech Republic); EMBO workshop Noncoding RNAs in embryonic development and cell differentiation (Rehovot, Israel); The 43rd FEBS Congress, 2018 (Prague, Czech Republic); National Bioinformatic Conference ENBIK2018 (Skalský dvůr, Czech Republic)
2019: Conference Seeing is believing, Czech-BioImaging conference (Lednice, Czech Republic); The EMBO Young Scientist Forum (Prague, Czech Republic)

Practical courses
2016: FEBS practical courses: Advanced methods in protein crystallization (Nové Hrady, Czech Republic)
2018: FEBS practical courses: Advanced methods in protein crystallization (Nové Hrady, Czech Republic)
2019: EMBO practical course: Mouse genome engineering (Dresden, Germany)