1. The cell mediated immunity of *Drosophila melanogaster*

*Drosophila melanogaster* has been recognized as a premier genetic model system for understanding gene function, developmental networks and molecular basis for genetic disorders. *Drosophila* has blood cells or hemocytes that are important for innate immune functions as well as pattern formation, tissue remodeling and wound healing. Throughout evolution, a large number of molecules have retained their biochemical specificities and maintained analogous functions with organization in similar pathways. The immune response in *Drosophila* shows remarkable similarities with the innate immunity of vertebrates, suggesting that they share a common evolutionary ancestry. *Drosophila* lacks adaptive immunity but it can eliminate microbes in minutes with well developed innate immunity generating a concerted action of humoral and cellular mechanisms. The humoral immunity involves the secretion of inducible antimicrobial peptides by the fat body and hemocytes and induction of proteolytic cascades which lead to melanization and coagulation. The cellular reactions are mediated by hemocytes, cells, directly interacting with microorganisms and parasites. The cellular reactions are initiated immediately after the recognition of the foreign particles and manifested as phagocytosis of microorganisms and cell debris or encapsulation of tissues and parasites. In the past decade we have established the tools and methodology to define the cellular elements of the *Drosophila* immune system. These involved the generation of immunological markers for *Drosophila* hemocytes, isolation of genes encoding for the markers, the generation of transgenic stocks having marker molecules for “in vivo” detection and analysis, generation of mutant and transgenic stocks with impaired hemocyte morphology and function as well as “in vitro” culture of *Drosophila* cell lines and hemocytes. These constructs allowed also genetic screens to identify signaling pathways of hemocyte development. We are defining further the molecules expressed in a cell type specific manner with the aim to identify hemocyte subpopulations, compartments and lineages and to find out their lineage- and functional- significance.

**Supervisor:** István Andó, Institute of Genetics  
**E-mail address:** ando@brc.hu

2. Structural and functional heterogeneity of the opioid (morphine) receptor system

The membrane localized opioid and antiopiate receptors, their endogenous and synthetic ligands play a major role in the process of pain relief, principally involved in the development of opiate addiction and display heterogeneity. This group is investigating
the ligand-receptor interactions for understanding the molecular basis of multiplicity. The emerging new receptor subtypes are characterized by novel compounds and radioligands of high specificity and affinity. The ultimate goal is to develop novel analgesics (peptides or heterocyclic compounds) with reduced side effects. Monitoring the changes in the opioid system in pathological conditions, neurological disorders (including epilepsy) and interaction with other receptor systems (e.g. nociceptin, cannabinoids) is also in the focus. The experimental approaches include in vitro radioreceptor binding assays, structure activity relation analysis and functional biochemical studies on transmembrane signalling. The experiments are carried out with different animal tissues, purified or genetically modified receptors, cultured mammalian cell lines. Applicants with degree in chemistry, biology, medicine, molecular biology are welcome; experience in laboratory animal handling is preferred but not obligatory.

Supervisors: Anna Borsodi, Sándor Benyhe
E-mail address: borsodi@brc.hu, benyhe@brc.hu

Selected references:

3. The potential of molecular gene silencing techniques using exogenous synthetic nucleic acids in plant systems

Short synthetic nucleic acid stretches can inhibit gene expression by interfering with translation by a number of mechanisms. Typically 16-23 nucleotide long, antisense oligonucleotides that are complementary to a section of the target mRNA, can prevent translation either by physically blocking the process or by cleaving the target. Additionally, oligonucleotides can alter the splicing pattern of pre-mRNA. Double-stranded oligoribonucleotides and catalytically competent single-stranded nucleic acid stretches (ribozymes, DNAzymes) also results in cleavage of the target mRNA. Even
with no RNA as target, oligonucleotides can be selected as aptamers to bind to any protein to inhibit its activity. These modes of actions mentioned above and several others are well-known and extensively used in human and animal genomics and even for drug development. Although in principle, applications of this kind in plant systems are possible, only very few examples were published in this field up till now.

Based on our results achieved with antisense oligonucleotides, we aim to apply the listed oligonucleotide species in different plant systems in order to exploit the potential of the mentioned, novel molecular inhibitory pathways. Our research is focused on two main topics: i/ Search for new, efficient oligonucleotide delivery methods for plant cells (molecular carriers, lipophyl derivatization) ii/ Increasing the inhibitory efficiency and selectivity, widening the field of applications by introducing chemical modifications. As an advantage, a well equipped nucleic acid synthesis laboratory and at the same time a variety of plant biology test systems are at our service. Both monocots (cereals) and dicots (tobacco, arabidopsis) showing experimental or economical significance serve as test objects in our work. Our final goal is to achieve an efficient functional genomic tool, which is widely applicable in plants and requires no genomic transformation.

**Supervisor:** Sándor Bottka, Central Laboratories
**E-mail address:** bottka@brc.hu

### 4. Studying gravitropic regulation in Arabidopsis thaliana roots

Gravity is a constant force which directs plants from vertical to horizontal orientation after gravity vector change. Gravistimulation in plants results in four consecutive steps including gravity perception, formation of signal(s) in perceiving cells, the intra and intercellular transduction of signal(s), which is followed by disproportioned cell division between upper and lower sides of the affected organs. Most higher plants have two gravity perceiving organs, one of these is the root cap in which the columella cell layers are known to be specifically sensing changes in gravitational status of plant. The other gravity perceiving tissue is the endodermis of hypocotyl and inflorescence stem. The most studied physiological signal molecule involved in gravitropic response is the auxin. The asymmetrical auxin redistribution causes differential elongation of organs. Several genes coding for components of auxin influx and efflux carriers have been identified and characterized in Arabidopsis thaliana. Components of plasma membrane located PIN-FORMED (PIN) family complex are able to facilitate the efflux of auxin from cells and are distributed asymmetrically in auxin transport competent cells.

We have isolated and characterized some genes that control positive and negative gravitropism in Arabidopsis thaliana. Function of identified genes will be characterized with special emphasis on primary root gravitropic processes. We are looking for candidates to participate in the further analysis of this regulation. Physiological processes like influence of different inhibitors of gravitropic response will be studied using Arabidopsis mutants and transgenic plants with altered gravitropic responses. Study the influences of these genes on PIN proteins is also planned.
Methods used: We use molecular, genetical and physiological (mainly microscopic- e.g. LSM) techniques to characterize genes and gene function.

Preference: Knowledge of molecular biology methods (DNA, RNA isolation, Northern blot analysis), experience in basic methods of protein chemistry (gel electrophoresis, Western blot analysis) and/or microscopic field is preferred.

Supervisor: Ágnes Cséplő, Institute of Plant Biology
E-mail address: cseplo@brc.hu

5. Functional analysis of extracellular matrix proteins in tissue regeneration and tumorigenesis

Aim: Extracellular matrix provides physical support to the cells, delineates pathways for cell migration during differentiation and tissue regeneration and provides the necessary milieu for the normal cell metabolism and development. Previously we identified by molecular cloning matrilin-2, component of a filamentous network in many tissues. We have found that expression of the gene is upregulated during muscle regeneration in mice and rats. We have also found that efficiency of tumor induction and growth is largely affected by presence or absence of matrilin-2 in transgenic mice. It is not known yet, what is the exact function of matrilin-2 in maintaining the integrity of muscle. It is also yet to be discovered how the cells interact with matrilins, whether they have special receptors. The function and interaction of matrilin-2 with other matrix components will also be studied in vitro and in transgenic mouse.

Methods: recombinant DNA technology, cell culturing, immunohistochemistry.

Previous knowledge in cell biology, histology, nucleic acid biochemistry or protein analysis is helpful.

Supervisor: Ferenc Deák, Institute of Biochemistry
E-mail address: matrix@brc.hu

6. Cell cycle regulation by proteolysis

Key transitions in the eukaryotic cell cycle are regulated by ubiquitin-dependent proteolysis mediated by an unusually large ubiquitin-protein ligase complex known as the anaphase-promoting complex or APC. Together with other enzymes, the APC catalyses the assembly of poly-ubiquitin chains on mitotic regulatory proteins and thus targets them for degradation by the 26S proteasome. Due to the irreversible nature of protein degradation by sequentially removing regulators, the APC generates directionality in the cell cycle and ensures proper timing and coordination of mitotic events. Our aim is to determine the role of the APC in regulating late mitotic events in the genetically well tractable experimental organism, Drosophila melanogaster. The entry point to this project is a large-scale screen of P element insertion mutants we undertook to isolate mitotic genes in Drosophila.
Methods:
We use genetic, molecular and cell biological techniques and exploit the complete genome sequence of *Drosophila* in order to identify conserved subunits, new substrates and regulators of the APC.

Preference:
Applicants with experience in *Drosophila* genetics and working with DNA and proteins.

**Supervisor:** Péter Deák, Institute of Biochemistry  
**E-mail address:** deakp@brc.hu

7. *Medicago* structural and functional genomics

Leguminous plants (soybean, bean, pea, alfalfa, lentils) comprise one of the most important agricultural taxa worldwide providing a major source of proteins for humans and animals. Similarly to most crops they are able to establish root endomycorrhizae with soil fungi which contribute to the phosphorous nutrition of the plant; on the other hand they have a unique feature that is forming symbiosis with soil bacteria to reduce and utilize atmospheric nitrogen.

The main focus of our team has been the identification and function of plant symbiotic genes, especially using forward genetics or recently other genomic tools. Our aim is to improve our knowledge about the genes and their protein products, as well as their interaction during this important plant-bacterium symbiosis for further possible exploitation of this biological process. For this, besides classical and molecular genetic work, our laboratory uses the wide varieties of techniques of molecular biology, and our research experience covers structural genomics, forward genetics, plant tissue culture, transformations, yeast two hybrid system, protein expression and purification. Our group also has a long-standing research activity on different legume genetic systems: alfalfa (*Medicago sativa*) and the model *Medicago truncatula*. Current projects include DNA chip hybridizations and further investigation of the resulted candidate genes and their protein products. There are available resources also for reverse genetic approach for the ultimate validation of these candidate genes. These ongoing projects are open for ITC students to join.

**Supervisor:** Gabriella Endre, Institute of Genetics  
**E-mail address:** endre@brc.hu

8. Fertilization-induced gene expression changes in wheat egg cells

The project aims to identify genes expressed in wheat egg cells right after fertilization. During the one year course, the candidate will be involved in the cloning and characterization of candidate genes, the bioinformatic analysis of DNA sequence information and gene expression verification by real-time qPCR. Candidate genes will be
functionally tested in microinjected wheat egg cells. Proven skills in English and a basic laboratory practice are required.

**Supervisor:** Attila Fehér, Institute of Plant Biology  
**E-mail address:** fehera@brc.hu

**9. The link between cellular signaling and plant development**

The project aims to identify elements of a signal transduction cascade involving a plant-specific group of protein kinases and small GTP-binding proteins. These proteins are supposed to be involved in the organization of cell shape and the orientation of cell divisions that basically contribute to plant form and function. During the one year course, the candidate will be involved in the characterization of transgenic *Arabidopsis* plants, protein-protein interaction studies in vitro, in yeast and in planta, molecular cloning and protein analyses. Proven skills in English and basic laboratory practice are required.

**Supervisor:** Attila Fehér, Institute of Plant Biology  
**E-mail address:** fehera@brc.hu

**10. Genotype-dependency of somatic embryogenesis**

The project aims to investigate factors, first of all the organization of the chromatin that contribute to the highly genotype-dependent expression of somatic embryogenesis. The experimental work includes the treatment of plants with various chromatin remodeling chemicals and monitor somatic embryo induction and the related gene expression pattern. Proven skills in English and basic laboratory practice are required.

**Supervisor:** Attila Fehér, Institute of Plant Biology  
**E-mail address:** fehera@brc.hu

**11. Cellular Imaging Laboratory is looking for SUMO wrestlers**

At the Cellular Imaging Laboratory, we are strongly committed to the development and application of modern cell biology methods that will enable us to understand the complex organization within and between cells [1]. Our lab’s special interest is the functional analysis of cell division-related proteins using both human cancer cells and tumor-like callus tissues of plants. In human cancer cells, we study the role of SUMO (Small Ubiquitin related Modifier) proteins using confocal laser scanning microscopy and biochemical methods [2, 3].

SUMO family proteins function by becoming covalently attached to other proteins as post-translational modifications. The functional consequences of SUMO attachment vary greatly from substrate to substrate, and in many cases are not yet understood at the
molecular level. Loss of regulated control on sumoylation causes defects in maintaining cellular homeostasis and therefore may give rise to various human diseases including cancer development and progression. Recent studies have revealed that the SUMO system is also involved in cancer metastasis. We are interested to identify novel SUMO target substrates, their intracellular localization and function. In addition to tissue culture equipment and molecular biology-biochemistry tools, our modern imaging center is equipped with state-of-the-art confocal laser scanning microscopes, a fluorescence stereo microscope, a real-time imaging workstation and powerful image analysis computers with imaging software. With these advanced microscopes we can perform protein localization and mobility analyses (FRAP, FLIP), three dimensional and time course dynamic analyses of live cells, tissues and organisms.

Highly motivated, enthusiastic candidates are expected to take part in this project. At the end of the training course, the applicant will benefit from acquired experience in modern techniques related to advanced cellular imaging and fluorescence microscopy methodologies in addition to techniques such as sterile handling of human cancer cell cultures, molecular cloning, immunoprecipitation, protein electrophoresis, subcellular fractionation and flow cytometry.

Supervisor: Ferhan Ayaydin, Central Laboratories
E-mail address: ferhan@brc.hu

Selected Publications:


Highly organized molecular macroaggregates are found in many hierarchically organized biological systems: chromosomes, viruses, stacked membranes, tissues, cytoskeletal and other actin-based structures. However, our understanding concerning their self-assembly, molecular organization, structural dynamics and physiological functions is still rudimentary. The major aim of our research is to identify and characterize anisotropic biological macroassemblies with the aid of a novel, differential polarization laser scanning microscope designed and constructed in our laboratory. With our DP-LSM we can image the following differential polarization quantities: linear and circular dichroism (LD&CD), birefringence (LB), fluorescence detected dichroisms (FDLD&FDCD), anisotropy (r) and degree of polarization (P) of the fluorescence emission. These DP quantities and the reconstituted 2D or 3D images, as it has been shown on several
examples, provide important and unique information on the molecular architecture of various biological membranes, cellular organelles and tissues. The ITC fellow, biophysicist or cell biologist, would join the team of DP-LSM Laboratory, and participate in various projects, including international collaborations, on the identification and characterization of anisotropic structures in various biological objects. Candidates interested in technical questions will have the opportunity to participate in the work to further improve this novel and recently patented instrument.

For more information:

**Supervisor:** Győző Garab, Institute of Plant Biology
**E-mail address:** gyozo@brc.hu

13. Biological thermo-optic effect. Structurally flexible macroassemblies in thylakoid membranes

Earlier we have shown that loosely stacked lamellar aggregates of the main chlorophyll a/b light harvesting complex of photosystem II (LHCII) possess the ability of undergoing light-induced reversible structural reorganizations that affect the long-range chiral order of their chromophores; they closely mimic the behavior of the thylakoid membranes, where the changes turned out to be largely independent of the photochemical activity of the membranes, and operate above the saturation of photosynthesis, a potentially very important, unique feature that appears to play a role in the protection of plants against excess excitation. Detailed analysis of the transients revealed that these structural transitions are driven by a novel, biological thermo-optic mechanism: fast thermal transients arising from dissipated excitation energy, which lead to elementary structural transitions in the close vicinity of the dissipation centers, due to the presence of ‘built-in’ thermal instability in the (macro) assembly of complexes. We would like to elucidate the nature and more precise mechanism of the thermo-optically induced reorganizations in different antenna systems, and establish the physiological significance of these, previously unknown regulatory mechanism.

The ITC fellow, physicist or biologist, is expected to take part in this research, in the frame of an EU supported Research Training Network (INTRO2).

For more information:

**Supervisor:** Győző Garab, Institute of Plant Biology
**E-mail address:** gyozo@brc.hu
14. Artificial light harvesting antenna complexes

The intensity of sunlight is dilute, i.e. the photon flux density is low - even in strong sunlight the optimal operation of the photosynthetic machinery cannot be ensured without a light harvesting antenna system, of ~200-500 chlorophylls on average per photochemical reaction center. Also, efficient capture of solar energy, by an antenna system, is crucial in artificial solar devices.

The antenna should possess the following properties: (i) cover a large spectral range (i.e. contain various chromophores), (ii) possess a high absorption cross section (i.e. large number of pigments per light converting unit and a high extinction coefficient) (iii) be able to transfer excitation energy sufficiently fast to a light-conversion unit in order to avoid unwanted loss and photodamage processes (i.e. short distances between the antenna pigments and directionality of transfer to the light-conversion units) (iv) have photoprotection (carotenoids) and photostability and protection against oxidation by the light-converting unit.

Artificial antenna systems, composed of native, isolated complexes and embedded in lipid (multi)layers, or nanostructures self-assembling from native or synthesized porphyrin molecules might satisfy these requirements. The ITC fellow will have the opportunity to learn a wide range of preparative and biophysical techniques that are related to this important research area.

**Supervisor:** Győző Garab, Institute of Plant Biology  
**E-mail address:** gyozo@brc.hu

15. Role of lipids and carotenoids in the structural stability of photosynthetic protein complexes

We are to investigate the structural integrity and stability of photosynthetic protein complexes in cyanobacterial mutants deficient in lipid or carotenoid biosynthesis. It is well studied that phosphatidylglycerol and the unsaturated membrane lipids affect photosynthetic processes. Under stress conditions the quantity and quality of carotenoids are changing in the vicinity of photosynthetic protein complexes. We are to investigate the structural background of these physiological effects by using biophysical methods like DSC (Differential scanning calorimetry), FTIR (Fourier-transformed infrared spectroscopy) and CD (circular dichroism). We determine the protein composition of photosynthetic complexes in the mutant cells by 2D-BN/SDS PAGE.

**Supervisor:** Zoltán Gombos  
**E-mail address:** gombos@brc.hu

**Selected references:**
16. Role of phosphatidyglycerol in cell division

We are going to generate mutant cyanobacterial strains which are lacking protein subunits of division ring. We are to combine phosphatidyglycerol mutation with GFP fused constructions. *Synechococcus* PCC7942 strain is used for producing FtsZ, MinE, MinD and SepF mutants. Min proteins are signals for the location of division ring and SepF is the binding protein between the ring and membranes. We study the effect of phosphatidyglycerol deficiency on division ring formation and mutant phenotype. The division mutants would be characterized physiologically.

**Supervisor:** Zoltán Gombos  
**E-mail address:** gombos@brc.hu

**Selected references:**
Laczko-Dobos et al.: Role of phosphatidyglycerol in the function and assembly of Photosystem II reaction center, studied in a *cdsA*-inactivated PAL mutant strain of *Synechocystis* sp. PCC6803 that lacks phycobilisomes. *BBA-Bioenergetics*, 1777:1184-1194 (2008)

17. Identification of lipolytic enzymes involved in remodeling of glycolipids

Our earlier studies demonstrated the retailoring of an artificial phosphatidyglycerol in *Synechocystis* PCC6803 cyanobacterial strain. Most of the enzymes involved in this process are not known in cyanobacteria. By homology search and using fluorescent inhibitors we are to determine these proteins and corresponding genes. We inactivate the genes in order to study the role of these enzymes. The mutants would be also characterized physiologically.

**Supervisor:** Zoltán Gombos, Institute of Plant Biology  
**E-mail address:** gombos@brc.hu

**Selected reference:**
18. Carcinogenesis and mutagenesis; replication of damaged DNA in yeast and human cells

The stalling of DNA replication machinery that occurs as a consequence of encountering unrepaired DNA damage is a challenging problem for cells. To rescue the stalled replication fork, different DNA damage bypass mechanisms have evolved that promote replication through DNA lesions. In humans increased error-prone bypass of DNA lesions causes increased mutagenesis, and as a consequence, a rise in the incidence of cancers. Error free-bypass processes, by contrast, keep mutagenesis low and reduce cancer frequencies.

ITC positions are available in our laboratory to study the regulation and mechanisms of damage bypass by yeast and human translesion synthesis DNA polymerases and DNA helicases. The main players are Pol eta, which when defective causes the cancer-prone syndrome, the variant form of Xeroderma pigmentosum, Pol iota, Pol kappa, Rev1, and other tumor suppressor proteins such as human SHPRH and HLTF, which are playing roles in melanoma and colon cancer development, respectively. Projects include: determination of mechanisms of action of these damage bypass proteins and study of physical and functional interactions of these enzymes with components of the DNA replication and cell cycle checkpoint machinery. In addition, the manner by which the polymerase switch occurs at the lesion site, and the mechanisms by which ubiquitin and SUMO conjugation modulates DNA damage bypass are being actively pursued.

Applicants should be prepared to carry out research on a highly competitive research field in a stimulating research environment and after an initial period, to take part in our international (mainly American) collaborative research works. Only enthusiastic highly motivated applicants will be accepted.

For additional details visit our website at www.brc.hu/lajoslab

Supervisor: Lajos Haracska, Institute of Genetics
E-mail address: haracska@brc.hu

Selected publications:


19. Tracing Reactive Oxygen Species In Plants

Background
Endogenously produced reactive oxygen species (ROS) are inevitable consequences of any oxygenic life form. ROS are essential for several biological functions, but may also accumulate as damaging pro-oxidants when the activity or amount of cellular antioxidant is lowered. In this way, the assessment of ROS is a key factor of stress studies. ROS are short lived and present at extremely low concentrations which requires special techniques for their identification. In higher plants or in photosynthetic micro-organisms, ROS detection is specially challenging, due to the presence of extreme redox and pH conditions, and the special optical properties of pigments.

The Project
A long-term project of our laboratory is to identify primary ROS sources and link these to either defence mechanisms or damage pathways. The corner stone of this work is the development of ROS trapping, by refining and adapting existing methodology to the special conditions of stressed plant tissue and also by the development of new ROS probes. The latter is done in collaboration with the Department of Organic and Medicinal Chemistry, Pécs University (Hungary) and our task is the testing of potential new probes for their reactivity, selectivity to various ROS in vitro, followed by analysing stability, toxicity and localisation in vivo. The last stage of the study is the application of the selected probes in vivo, in plants under stress. Although the project is focused on ROS detection, in order to be able to link ROS to the advancement of stress, the applicant will, to some extent, be also involved in parallel measurements of functional and structural damage in plants.

Applicants should have basic knowledge on the biochemistry and biophysics of photosynthesis in higher plants. Background in organic chemistry, as well as experience in EPR or fluorescence spectroscopy will be preferred. Good command of English and strong motivation are mandatory, pre-selected applicants will be interviewed either in person or in a telephone conference.

Supervisor: Éva Hideg, Institute of Plant Biology
E-mail address: ehideg@brc.hu

Selected publications:

20. Regulation of plant cell division cycle by the retinoblastoma-related protein pathway

The mammalian retinoblastoma susceptibility gene product known as the first tumor suppressor protein (pRB), has central role in the regulation of cell cycle, differentiation and apoptotic pathways of specific cell types. Discoveries of the past decade showed that the elements of the RB regulatory network also exist in higher plants and proposed to have a wide range of cellular functions including the control of cell cycle and developmental events as well. Results of studies on plant RB-related proteins (RBRs) have demonstrated that they have interactors as D-type cyclins, viral proteins, transcription factors etc. that display amino acid sequence homology and biochemical binding properties analogous to their mammalian homologues. Exact functions of some plant RBR partners has not been clarified in details yet; since phosphorylation-dephosphorylation cycle plays a pivotal role in the activity of retinoblastoma protein, the recently isolated PP2A phosphatase B" regulatory subunit interacting partner has the clear potential of fundamental modification of RBR function. Moreover, this protein can discriminate between the two RBR species present in monocot plants, thus giving the opportunity for differential modification of the phosphorylation status of retinoblastoma-related proteins in cereals. A NAC transcription factor bearing the characteristic LXCXE motif of RB-binding and showing strong association with both rice RBR species can provide information on important plant-specific retinoblastoma function, since members of this transcription factor family can be found only in plants. Research project on the regulation of plant retinoblastoma protein function by these RBR interactors involves the analysis of the changes in the RBR phosphorylation pattern during plant development, hormone and stress treatment, generation of overexpressing and RNAi rice transgenic plants and biochemical assays on purified proteins.

After successful completion of the ITC fellowship, the project can be extended to a PhD fellowship.

**Supervisor:** Gábor V. Horváth, Institute of Plant Biology
**E-mail address:** hvg@brc.hu

21. The roles of reactive carbonyl detoxifying mechanisms in the stress tolerance of cereals

The productivity of plants is greatly affected by environmental stresses such as drought, low temperature or soil salinity. Since the generated reactive oxygen species (ROS) and their toxic products, as reactive carbonyl compounds (RCC) significantly can increase
cellular damages caused by different stress conditions, improvement of scavenging capacity of cells can lead to increased stress tolerance. Plant aldo-keto reductases are important factors for such function since they have a wide range of enzymatic activity on lipid peroxidation-derived reactive aldehydes and their detoxification capacity can limit the harmful effects of such stress-derived compounds. Moreover, the specific members of this NADPH-dependent aldo-keto reductase superfamily (AKR) are able to catalyze the production of sugar alcohols (like sorbitol or mannitol). The products of these reactions can act as radical scavengers even at low concentration and their accumulation as osmolytes can lead to improvement of osmotic adaptation. Our aim is to isolate and characterize aldose/aldehyde reductases from rice, wheat and barley focusing on their detoxification functions and sugar alcohol producing activity. The project will concentrate on the not yet characterized activities of plant AKRs: namely their role in methylglyoxal detoxification and decreasing the formation of the advanced glycation end products, AGEs. The detoxification functions of plant AKRs will be assayed by using recombinant proteins in vitro and in transgenic rice and barley plants in vivo using the GFP/DsRED differential expression method.

Methods: recombinant DNA technology, expression and purification of recombinant proteins, enzyme activity measurement, plant cell culture, Agrobacterium-mediated plant transformation, particle bombardment, fluorescent microscopy.

Previous experience in recombinant DNA techniques, protein analysis and plant transformation would be very helpful.

Supervisor: Gábor V. Horváth, Institute of Plant Biology
E-mail address: hvg@brc.hu

22. The role of membrane lipids in low temperature stress processes in wheat

Cell membranes are the primary targets of freezing injury. To avoid cold stress induced damages, higher plants modify the structure and the lipid composition of their membranes.

Besides structural lipids, the synthesis of signalling-lipids – messengers in certain, low-temperature induced plant processes - is also induced. Signalling-lipid production is regulated by lipid-hydrolysing enzymes. These enzymes play a pivotal role in the production of lipid messengers.

In our study we focus mainly on the roles and functions of major membrane-constituent phospholipids, and modes of action of phospholipid signalling in response to low temperature stress. By comparing the lipid components of frost resistant and sensitive crop plants accumulated during the stress and abscisic acid treatment, we hope to find a correlation between the changes in the lipid content and the level of tolerance. Furthermore, studying precise genetic stocks, such as substitution and recombinant lines, or even mapping populations, the genes, involved in the metabolism of lipids will be localized, and finally mapped.
23. Transcriptional regulation of cell type-specific gene expression

We aim at identifying DNA elements and transcription factors involved in tissue- or developmental stage-specific regulation of gene expression. Our traditional model tissue is cartilage, forming the vertebrate embryo skeleton, which is replaced by bone during development. Here we investigate the regulation of matrilin-1 gene expression. Matrilin-1 is found only in cartilage. We have identified the role of the main control regions in transgenic animals, transiently transfected cell cultures and by in vitro DNA-protein interaction. The aim of the present study is to identify tissue-specific protein factors contributing to assembly of active transcription complexes and to reveal the significance of chromatin-modifying enzymes in the regulation of the gene.

Methods: recombinant DNA technology, transient expression in cell culture, in vitro DNA-protein interaction studies, immunohistochemistry, transgenesis.

Previous experience in recombinant DNA techniques, protein analysis or histology would be very helpful.

Supervisor: Ibolya Kiss, Institute of Biochemistry
E-mail address: kiss@brc.hu

24. Biochemistry, molecular biology and biotechnology of thermotolerant hydrogenases

Hydrogenases are metal containing enzymes that catalyze the formation and decomposition of molecular hydrogen. Hydrogenases are significant enzymes in methanogenesis (biogas production), nitrogen fixation, denitrification, corrosive sulfate reduction, biological solar energy conversion, alternative fuel storage systems, and other processes of potential biotechnological importance. During several years of research on hydrogenases we have found that a few hydrogenases, isolated from certain marine photosynthetic bacteria, show outstanding stability under a variety of conditions. Unlike other hydrogenases, these enzymes are thermotolerant, oxygen resistant, and resistant to various proteases as well. These properties make them very suitable for biotechnological applications.

Research project involves molecular biological and genetic approaches, 2D-PAGE, genome sequencing.

Supervisor: Kornél Kovács, Institute of Biophysics
E-mail address: kornel@brc.hu
25. Intensification of biogas production by microbiological means

Decomposition of wastes anaerobically to form biogas is one of the earliest applications of biotechnology. We have studied the microbiological and biochemical aspects of the process for several years and identified weak points where significant improvement of the biogas production efficacy can be achieved. A major rate-limiting step of the overall biogas formation reaction chain is interspecies hydrogen transfer and the availability of reducing power for methanogens in the complex microbiological populations. We have shown that an alteration of the bacterial population balance to facilitate interspecies H₂ transfer brings about pronounced beneficial effects: an increase of the biodegradation rate and biogas productivity. When compared to the currently employed technologies, the practical advantages include lower operational costs (smaller digesters and/or shorter retention times; more biogas) and decreased environmental stress upon discharging the digested material.

Supervisor: Kornél Kovács, Institute of Biophysics
E-mail address: kornel@brc.hu

26. Molecular basis of the blood-brain barrier function

By forming a single cell layer lining the blood vessels of the brain, cerebral endothelial cells (CECs) constitute the principal component of the blood-brain barrier (BBB). Tight junctions (TJ) and adherens junctions (AJ) play a key role in the maintenance of the barrier function. Despite considerable experimental efforts the molecular organization and regulation of cerebral interendothelial junctions is less well understood. Our project is focused on the role of interendothelial junctions under pathological conditions. The experiments will be carried out on an in vitro model of the BBB based on the culture of cerebral endothelial cells. Using different molecular, biochemical and immunofluorescent techniques we will investigate the changes in the expression, localization, interaction and posttranslational modifications of the junctional proteins (occludin, claudins, ZO-1, ZO-2, cadherins, catenins) in CECs in response to pathological conditions like oxidative stress and inflammatory stimuli. Proteomic analysis will be applied to find endothelial proteins involved in these pathological processes. Furthermore, planned experiments are designed to elucidate the role of different signaling pathways, protein phosphorylation and proteolysis in the pathomechanism of endothelial dysfunction. Applicants interested in basic biomedical research with affinity to modern molecular and biochemical techniques are welcome.

Supervisor: István A. Krizbai, Institute of Biophysics
E-mail address: krizbai@brc.hu

27. Role of the blood-brain barrier in brain metastasis formation
Brain metastases of malignant tumors are life threatening pathologies with limited therapeutic options. Therefore suppressing or reducing the risk of metastasis formation could be one of the most effective approach in the therapeutic strategies besides surgical removal of the primary tumor. Since the CNS lacks a lymphatic system, the only possibility for cancer cells to reach the brain is via the blood stream. Metastatic cells invading the CNS thus have to pass the blood-brain barrier (BBB). The tumors giving CNS metastases with the highest frequency are the malignant melanoma, lung cancer and breast cancer. By using an in vitro model of the BBB the project is focused on the elucidation of molecular mechanisms by which cancer cells cross the BBB. Different molecular, biochemical and immunofluorescent techniques will be applied to elucidate the role of various signaling mechanisms, proteolytic enzymes and brain derived factors in the transmigration of metastatizing cancer cells. Applicants interested in disease oriented basic biomedical research with affinity to modern molecular and biochemical techniques are welcome.

**Supervisor:** István A. Krizbai, Institute of Biophysics  
**E-mail address:** krizbai@brc.hu

**28. Connecting environmental stress signaling to plant E2F-RBR growth regulatory pathway**

The Molecular Regulators of Plant Growth is a newly established group in the Institute of Plant Biology. The major interest of the group is to understand the molecular mechanisms, which regulate plant growth. We cloned a family of genes from the model plants *Arabidopsis thaliana* called E2F transcription factors; their function is to coordinate cell proliferation with cell growth and differentiation. Environmental stresses such as drought could change the activity of E2F complexes, which lead to repress growth. We are seeking to understand how and why under stress conditions plants stop growing, and what is happening at the cellular level. We are specifically interested how signaling pathways link to the E2F growth regulatory pathway and influence its activity.

The main experimental techniques to be employed include, but not limited to those in the areas of molecular biology (gateway cloning, PCR, Q-RT-PCR, reporter constructs, chromatin immunoprecipitation, identification of E2F target genes by using ChIP-seq analysis), protein biochemistry (western blot, immunoprecipitations, protein complex purifications and their analysis by mass spectometry to identify their components as well as their post-translational modifications) plant cell biology (transient protoplast transfection analyses, fluorescence microscopy, confocal laser scanning microscopy), generation and analysis of transgenic *Arabidopsis* plants, research are focusing on the roots and the leaves.

The project is run in collaboration with the Bögre lab (Royal Holloway University of London), DeVeylder lab (University of Gent) and Scheres lab (University of Utrecht).

**Supervisor:** Zoltán Magyar, Institute of Plant Biology  
**E-mail address:** magyarz@brc.hu
Selected publications:
Magyar Z. Keeping the balance between proliferation and differentiation by the E2F transcriptional regulatory network is central to plant growth and development. Plant Growth Signalling edited by László Bögre and Gerrit Beemster 2008; Springer; Plant Cell Monographs; Vol.10; pp 89.


29. Functional analysis of an actin cytoskeleton regulator in Drosophila

The actin cytoskeleton plays an essential role in a wide variety of cellular processes. To fulfill these functions, actin dynamics is tightly regulated both in space and time. Most of this regulation is executed by actin binding proteins. Amongst these, the actin nucleation factors play a critical role by promoting the formation of novel actin filaments. Members of the Formin protein family identify actin assembly factors that assist the formation of unbranched actin structures. We are interested in the functional analysis of a Drosophila formin, dDAAM. Previously we have shown that this protein is required for axonal growth and recently, we found that it also plays a role in muscle development. We have good evidences that both of these functions are evolutionary conserved. Currently, we are studying the cellular and molecular mechanisms by which dDAAM contributes to CNS development and muscle formation in flies, and potentially, in higher animals as well. In order to do so, we apply a number of different approaches including Drosophila genetics, molecular biology, immunohisto-chemistry, confocal microscopy and biochemistry.

Applicants with interest in Drosophila developmental biology, in particular, CNS and muscle development, are very welcome to join our lab for the 2010/11 ITC course.

Supervisor: József Mihály, Institute of Genetics
E-mail address: mihaly@brc.hu

30. Optical micromanipulation in biology

By optical micromanipulation it is possible to manipulate individual biological objects: cells, molecules. We use such techniques for the investigation of mechanical properties of biological particles.

In addition, we further develop the optical micromanipulation techniques where a higher level of control is possible.

Knowledge and interest in biophysics is needed.

Supervisor: Pál Ormos, Institute of Biophysics
E-mail address: pomros@brc.hu
31. The membrane protein folding problem-experimental and theoretical approaches

Protein insertion, folding and assembly in membranes is a key part of many life processes. Native folding of proteins clearly happens in a tiny segment of their huge conformational space, since there is no time to sample it extensively. How certain membrane proteins are able to insert, fold and assemble in the lipid bilayer, in some cases even pass it through, often in the absence of cellular folding machines is one of the biggest challenges in biophysics both experimentally and computationally. Specific interactions between the protein and lipids of the target membrane play a crucial role yet to be explored in detail. Non-bilayer forming lipids are of particular and growing interest. The successful candidate will study the membrane-protein folding problem on the lipid-protein system of choice experimentally, primarily with ultra high-sensitivity differential scanning calorimetry and spin label electron paramagnetic resonance, fluorescence and possibly Fourier transform infrared spectroscopies and/or theoretically. The data will be used for physical modelling of the folding, insertion and assembly processes and to develop potentials for fast simulations.

Requirements:
Background in physics, biophysics or (computational) chemistry is favorable. Candidates with experience or interest in one or more of the above techniques and/or computer programming are especially welcome.

Supervisor: Tibor Páli, Institute of Biophysics
E-mail address: tpali@brc.hu

32. The vacuolar proton-ATPase: spectroscopy based structural studies of a membranous molecular motor

The vacuolar proton-ATPase (V-ATPase) is a membranous molecular motor, which uses energy from ATP hydrolysis to drive proton transfer (it works in the opposite sense as the better known F-ATPase). Our long-term objective is to reveal the mechanism of this enzyme and to identify specific inhibitor binding sites/conditions that has a direct medical relevance. The protein and its subunits will be studied in native yeast vacuolar membranes or as reconstituted into phospholipid membranes after purification. Mutants with key residue replacements will be expressed and purified as well. Techniques involve spin label electron paramagnetic resonance, Fourier transform infrared and fluorescence spectroscopies as well as microcalorimetry. Molecular modeling will be used both to interpret structural data and dynamics consistently and to aid designing inhibitors and new experiments.

Requirements:
Background in molecular biology or biophysics is favorable. Candidates with experience or interest in molecular biology or in the above techniques are welcome.

Supervisor: Tibor Páli, Institute of Biophysics
**E-mail address:** tpali@brc.hu

### 33. Bioinformatics of drug interaction networks

Large-scale screening methods have recently enabled the systematic mapping of synergistic and antagonistic interactions between drug compounds (i.e., the non-additive effects of two compounds). Understanding the mechanisms underlying drug interactions and predicting new drug interactions could facilitate the discovery of novel multi-target agents and could help combat antimicrobial resistance. Our project aims at combining large-scale antibiotic interaction data from *E. coli* with chemical, chemo-genomic and functional genomic information to elucidate the general properties of synergistic and antagonistic drug interactions using data mining and bioinformatics tools. Interested applicants should have basic skills in computer programming and statistics.

**Supervisor:** Balázs Papp, Institute of Biochemistry  
**E-mail address:** pappb@brc.hu

For more information, visit our website at: www.brc.hu/sysbiol

### 34. Cellular and molecular biology of hormone induced neuro-glial plasticity

It is well documented that gonadal steroids exert organizational effects on developing neuronal connectivity and induce plastic changes on neuronal contacts in adults. Such effects are involved in the generation of sexually differentiated behaviour and neuroendocrine functions. This project is focused on the study of cellular and molecular events related to synaptogenesis and synaptic plasticity in the sexually dimorphic areas of the central nervous system. It proposes a study on the effect of physiological and experimental modifications of the levels of gonadal steroids on the arcuate nucleus and the olfactory bulb according to the following objectives:

1. the identification of estrogen-sensitive synaptic contacts in these brain areas and their responses to estrogen during normal development and function.
2. the identification of neuronal membrane components mediating the synaptic effects of sex steroids and the interaction of estrogen with adhesion molecules.

The candidate will be in charge of the immunocytochemical, in situ hybridization and Western blot studies devoted to the identification of the chemical nature of neurons that show a sex dimorphic pattern. The successful applicant is supposed to have previous knowledge in basic light and electron microscopic techniques.

**Supervisor:** Árpád Párducz, Institute of Biophysics  
**E-mail address:** parducz@brc.hu
35. Network models in biology

Biological systems are characterized by a variety of complex interactions. Network models provide a common framework for understanding the behaviour of various biological systems, and are also useful for designing classification and information retrieval strategies.

The Bioinformatics Group of the Szeged Biological Center (BRC) is interested in studying the efficiency and the stability of networks, using computational models including directed or undirected graphs. The goal is to understand how these networks evolve in order to fit various conditions and to understand how information propagates in them.

We are looking for motivated students who have a background or good practical experience in mathematics, computer sciences or artificial intelligence with an interest in studying large networks (graphs), as well as a willingness to apply their knowledge to biological problems. Good programming skills are required and an interest in wide analogies between different scientific fields is appreciated.

The proposed project is part of the International Training Course organized at the BRC, it is offered for a one year period (with a possible Ph.D. extension). The course is in Szeged, Hungary, a good command of English is required, knowledge of Hungarian is not necessary.

Supervisor: Sándor Pongor, Central Laboratories
E-mail address: pongor@brc.hu, pongor@icgeb.org

Selected publications:
Netotea S, Pongor S: Evolution of robust and efficient system topologies. Cell Immunology, 122,244,8083(2007)

36. Stability of bacterial communication systems

Multi-species communities, consortia are a predominant form of life in the bacterial world. Members of such communities co-operate with each other via sharing signaling molecules and secreted factors that enable them to solve various tasks in a concerted fashion, such as infecting and colonizing a host organism, spread on surfaces, etc. One of such mechanism is quorum sensing that relies on a well define set of regulatory genes.

The Bioinformatics Group of the Szeged Biological Center (BRC) is studies the cell-to-cell communication networks of bacteria using agent-based models that communicate via diffusible chemicals or other signaling mechanisms. Our goal is to understand how the agents can form stable communities and how changes of the regulatory mechanism influence the stability of the forming community.
We are looking for motivated students who have a background or strong interest in agent-based models, have programming skills and are open to learn new biological problems and their analogies with technical communication networks. The project is a collaboration with experimental scientists, so an interest in or experience with simple bacteriological lab methods is appreciated.

The proposed project is part of the International Training Course organized at the BRC, it is offered for a one year period (with a possible Ph.D. extension). The course is in Szeged, Hungary, a good command of English is required, knowledge of Hungarian is not necessary.

**Supervisor:** Sándor Pongor, Central Laboratories  
**E-mail address:** pongor@brc.hu, pongor@icgeb.org

**Selected Publication:**

### 37. Synthetic biology: experimental validation of systems biology models of *E. coli*

Synthetic biology is the deliberate design of biological systems and living organisms using engineering principles. Using approaches of synthetic biology, we are focusing on the rational large-scale remodeling of the *Escherichia coli* K-12 genome. *E. coli* K-12 is a model organism of basic research, the workhorse of molecular biology, and the platform of choice for the production of DNA, metabolites and many proteins of therapeutic or commercial interest. In spite of being one of the best understood model organisms, roughly third of its ~4300 genes have no experimentally verified functions assigned to them. Moreover, as *E. coli* evolved in the intestinal tracts of animals, it has many genes that are not relevant to practical applications and some that may be detrimental. Our goal is to experimentally construct an improved, core/minimal genome *E. coli* to serve both as a reduced-complexity model organism, and as a programmable cellular chassis for biotechnological applications. In the process of gradually streamlining the genome (*Science* 2006, 312: 1044-1046), we are investigating the effect of genome architecture and gene content on the adaptation and evolution of the cells. The particular project for ITC students involves specific genetic modifications of wild-type and reduced *E. coli* genomes in order to validate and improve systems biology models of the cell.

**Supervisor:** György Pósfai, Institute of Biochemistry  
**E-mail address:** posfai@brc.hu

### 38. Application of microarray technologies for miRNA expression and genomic methylation pattern analysis
Microarrays are novel and extraordinary tools for functional molecular biology providing a rapid and comprehensive approach to simultaneously monitor the different mutations in the genome, expression level of thousands known and uncharacterized genes, and protein expression differences between diverse biological samples in a comparative way at different system levels (genome, transcriptome, proteome). Since 2000 the Laboratory of Functional Genomics successfully applied the microarray technique for genomic, transcriptomic and proteomic research.

In the present project proposal the ITC student candidate would apply DNA microarrays for miRNA expression and genomic methylation pattern analysis of human clinical samples (cancer tissues) as well as samples from model organisms (rat, mouse).

**Supervisor:** László G. Puskás, Central Laboratories
**E-mail address:** pusli@brc.hu

**Selected references:**

### 39. Hydrogenomics, hydrogen metabolomics

Hydrogen the cleanest and one of the most promising energy carriers of the future can be produced by biological tools. Hydrogenases are the metalloenzymes which are primarily involved in the hydrogen metabolism of a cell. From practical point of view, there are few alternative strategies for biohydrogen production. One is based on the *in vitro* application of the hydrogenase enzymes, while an alternative technologies use whole cells capable to produce hydrogen. In both cases stable, "hydrogen evolving" enzymes are required.

When the whole cell approach is applied, a potential bottleneck of the hydrogen productivity is the electron supply of the hydrogenases. There are metabolic/redox processes providing electrons for the hydrogenases, while other routes consume electrons, thus representing competitive channels for the electrons. Therefore, understanding the bioenergetic, metabolic context of the hydrogenases is necessary to disclose the redox and metabolic pathways releasing or requiring electrons. For realization of these aims, the genome of the strain of interest must be known and functional genomics tools will be used to analyze the role of the various potential pathways likely related to the hydrogen metabolism. Finally, artificial strains with better hydrogen evolving capacities are to be constructed.

**Supervisor:** Gábor Rákhely, Institute of Biophysics
**E-mail address:** rakhely@brc.hu
40. Nitrogenase based biohydrogen production

Bacterial nitrogenases are metalloenzymes dedicated for fixation of molecular nitrogen. There are many bacteria capable to assimilate molecular nitrogen, including nitrogen fixing and numerous photosynthetic bacteria. The nitrogen fixation requires energy/ATP and during the process substantial amount of hydrogen is formed. In photosynthetic bacteria, the ATP demand of the nitrogen assimilation can be sufficed from the light energy, therefore these cells are suitable for light driven hydrogen evolution. Moreover, nitrogen fixation takes place under specific conditions and there are compounds repressing the nitrogenase expression.

The aim of the project is to exploit the nitrogenase based hydrogen evolution, to overcome the disadvantages of the process: to reduce the energy requirement and to enhance the hydrogen productivity of the nitrogen fixation process. Additionally, the signaling routes restricting the applicability of the nitrogenase based hydrogen evolving systems are to be eliminated.

Supervisor: Gábor Rákhely, Institute of Biophysics
E-mail address: rakhely@brc.hu

41. Morphological characterization of disease specific hallmarks in a model of motor neuron disease

Amyotrophic lateral sclerosis is a lethal disease, which primarily affects the motor system and results in a complete paralysis and death in patients generally in 3-5 years from the diagnosis. The cause of the disease leading to the degeneration of motor neurons is not completely understood, however, different animal models, including transgenic animals became available to study the underlying mechanisms. The current research is aimed to understand the cause of the specificity (why the motor neurons are the cells which are primarily affected?) and the selectivity of the disease mechanism (why certain groups of motor neurons are preserved?). For such studies, mainly morphological (light- and electron microscopic) methods will be used, and disease specific alterations in differently affected regions of the central and peripheral nervous system of the animals (SOD1 transgenic mice, modeling the disease) will be characterized as the disease develops.

The candidate will learn the basics of light- and electron microscopic specimen preparation methods as well as immunocytochemical techniques, he/she should develop elementary skills in electron microscopic operation and will be introduced to basic procedures for recording, interpretation and analysis of digital images. The candidate is expected to work, occasionally, with experimental animals.

Supervisor: László Siklós, Institute of Biophysics
E-mail address: siklos@brc.hu
42. Relevance of the misfolded Cu/Zn superoxide dismutase in the pathomechanism of amyotrophic lateral sclerosis

There are certain neurodegenerative diseases (e.g. Alzheimer’s-, Hunntington’s-, Parkinson’s disease, amyotrophic lateral sclerosis (ALS), etc.) which are commonly considered as conformational diseases, as well. The general characteristic of these disorders is that there are well defined, specific proteins which have fundamental role in the pathomechanism through misfolding or aggregation. One of the central aim of our research project is the understanding the structural origins of the misfolding or aggregation processes. The current research is focused on the mechanisms of misfolding of the Cu/Zn superoxide dismutase (SOD1), since several point mutated forms of this enzyme are associated with the disease mechanisms in ALS patients. Moreover, the design of new, neuroprotective compounds based on the structural information characterizing the aggregated or misfolded proteins is also feasible. Our investigation method is a molecular level computational simulation which is based on a recently available good hardware and software background in a very dynamically increasing research area. Regarding the applicant’s background (informatics or biology or chemistry or physics) we would like to modeling and investigating the ALS disease by computational simulation, where the effect of point-mutation in the structure of the SOD1 peptide would be examined. The simulations are mainly performed at molecular mechanical level (molecular dynamics, homology building, docking, etc.), but in certain cases quantum-chemical calculations are also possible.

The candidate, who should have firm background in bioinformatics and computer simulation methods, will be expected to work in close collaboration with researcher at the Regional Knowledge Center at the University of Szeged who have developed significant expertise in computer based molecular dynamical-, homology building-, etc. methods in applications aiming at understanding mechanisms of ALS and other neurodegenerative diseases.

Supervisor: László Siklós, Institute of Biophysics
E-mail address: siklos@brc.hu

43. Characterization of regulatory genes controlling abiotic stress responses in higher plants

Program: cDNA library transformation have been developed in our group to identify regulatory genes which control responses of higher plants to environmental stress such as drought, and high salinity. We have identified a number of Arabidopsis genes which can enhance salt tolerance, modify sensitivity to abscisic acid, or control the expression of stress-induced genes. The ITC program will include the genetic and molecular characterization of some of the identified genes. The successful candidate will join the ongoing program and contribute in the characterization of one or two genes. The work will include genetic and physiological characterization of the identified lines, cloning and molecular characterization of the identified genes, gene expression studies by Northern
hybridization, RT-PCR analysis or microarray transcript profiling, etc.

**Methods used:** We use molecular and genetic techniques to characterize genes and gene function. The genome sequence of *Arabidopsis* is available and insertion mutants can be identified to practically all genes in this species, facilitating genetic analysis. Gene cloning, genetic analysis, different physiological assays and biochemical methods for protein analysis will be used.

**Preference:** Candidates with experience in biochemistry, molecular biology and genetics, working with DNA and proteins will have preference. Strong interaction with other group members is required. Upon mutual agreement the ITC fellowship can be extended to get Ph.D. degree in the University of Szeged.

**Supervisor:** László Szabados, Institute of Plant Biology  
**E-mail address:** szabados@brc.hu

**Selected publications:**


### 44. Proline metabolism as model for stress responses in plants

**Program:** Proline is considered as compatible osmolyte, which is accumulated to high concentration when plants are subjected to drought or salt stress. In previous years our group has characterized the proline metabolism in *Arabidopsis thaliana*, the model organism for molecular and genetic studies. We have isolated and characterized the genes that control proline biosynthesis and degradation and identified regulatory genes that influence proline accumulation. We are looking for candidates to participate in the further analysis of this metabolic pathway. Effect of other environmental factors such as light will be studied. Function of recently identified regulatory genes will be characterized with special emphasis on proline metabolism. Physiological role of proline during dehydration or salt stress on photosynthesis, mitochondrial respiration, redox balance, etc. will be studied using *Arabidopsis* mutants and transgenic plants with altered proline accumulation.

**Methods used:** We use molecular and genetic techniques to characterize genes and gene function. The genome sequence of *Arabidopsis* is available and insertion mutants can be identified to practically all genes in this species, facilitating genetic analysis.

**Preference:** Candidates with experience in biochemistry, molecular biology and genetics, working with DNA and proteins will have preference. Strong interaction with
other group members is required. Upon mutual agreement the ITC fellowship can be extended to get Ph.D. degree in the University of Szeged.

**Supervisor:** László Szabados, Institute of Plant Biology  
**E-mail address:** szabados@brc.hu

**Selected publications:**


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**45. Comparative analysis of stress responses in stress adapted and non-adapted plant species**

**Program:** *Arabidopsis thaliana* has emerged as the main model organism in higher plants, leading to the complete sequencing of its genome. Important information has been accumulated on this species about the regulation of stress responses and numerous *Arabidopsis* genes have been identified that are important in stress perception and adaptation. However, *Arabidopsis* is not adapted to extreme environments such as drought or high salinity. The close relative of *Arabidopsis*, *Thellungiella halophyla* is known to withstand high salt concentrations in the soil and is better suited to study long-term stress adaptation. In order to identify those factors which can contribute to the better stress adaptation of this species, several *Thellungiella* genes have been cloned which are orthologs of known *Arabidopsis* stress factors. The isolated genes will be characterized to reveal important molecular differences that may lead to enhanced salt tolerance. *Thellungiella* genes will be introduced into *Arabidopsis* to study their effect on salt tolerance. RNAi technique will be employed to reduce or eliminate transcription of selected genes in *Thellungiella* and study the salt tolerance in the silenced plants. Expression of stress-responsive genes in *Thellungiella*, *Arabidopsis* and the transgenic plants will be characterized and compared. The successful candidate will be responsible for the characterization of one such gene or small gene family.

**Methods used:** We use molecular and genetic techniques to characterize genes and gene function. Gene cloning, genetic analysis, different physiological assays and biochemical methods for protein analysis will be used.

**Preference:** Candidates with experience in biochemistry, molecular biology and genetics, working with DNA and proteins will have preference. Strong interaction with
other group members is required. Upon mutual agreement the ITC fellowship can be extended to get Ph.D. degree in the University of Szeged.

**Supervisor:** László Szabados, Institute of Plant Biology  
**E-mail address:** szabados@brc.hu

**Selected publications:**


### 46. Structure and dynamics of biological membranes, lipids, proteins, lipid-protein interaction

Membranes are essential in the maintenance of living state, besides providing structural bases for basic bioenergetic and biochemical processes, they form barriers and communication surfaces at the same time between either the interior and the exterior, or between different compartments of the living systems. In performing of its multifunctional role, the interplay between the lipidic and proteinic components of the membranes is extremely important, and the cells have sophisticated mechanisms to maintain the optimal membrane structure and dynamics, even under stress conditions. Fourier transform infrared spectroscopy is a non-invasive experimental approach, by which the structure and the dynamics of the different membrane components can be simultaneously studied *in situ*. The concrete aim of the studies will be to understand the structural basis of thylakoid stability in thermophilic cyanobacteria, the role of phosphatidyl-glycerol in the organisation of thylakoid membranes.

In the case of mutual interest, this project can evolve into a PhD thesis.

**Requirements:**

background in physics, biophysics or chemistry is favourable.

**Supervisor:** Balázs Szalontai, Institute of Biophysics  
**E-mail address:** balazs@brc.hu

### 47. Expression of ion channels and extracellular matrix molecules in healthy and diseased myocardium

There are marked differences in the electrocardiogram (ECG) waveforms and resting heart rates between healthy and diseased mammalian species, suggesting molecular alteration in the expression and functional roles of individual Na+, Ca2+ and K+ ion channels. The inward rectifier potassium channel family (Kir2.x) has a role in the modulation of cell excitability, repolarization of the action potential and it determines the
cellular resting membrane potential. Kir2.x ion channels are composed of four pore-forming α-subunits assembled as homo- and hetero-tetramers forming K⁺ selective pores and these ion channels are modulated by accessory subunits. Recently it was demonstrated that the Kir2.x isoforms co-localize with dystrophin, syntrophin and dystrobrevin (DAG complex) in cardiac muscle suggesting that the Kir2.x channels interact with protein complexes that may be important to target and traffic channels or are anchored and stabilized into the plasma membrane. In addition, the ion channels are influenced by intracellular scaffolding, trafficking and regulatory proteins. Other ion channels were connected to the DAG complex and this altered function in patients may lead to severe heart diseases, even sudden death.

We aim to study the differences in the amount, organization and activity of calcium and potassium ion channels between healthy and diseased heart muscle. We are interested to examine the expression, interactions and distribution of Kir2.x isoforms and DAG complex. Biological material gained from heart tissue of model animals, failing heart and permanent cell lines will be investigated using high through-put real-time qPCR, immunoblotting, immunoprecipitation, histology and pull down assay. We also aim to investigate the expression and possible function of extracellular molecules such as fibronectin, matrilin-2, and collagens in healthy and diseased heart tissues.

Supervisor: Viktória Szüts, Institute of Biochemistry
Email address: szucsi@brc.hu

Selected references:


48. Preparation of proteins by chemical methods

The continuation of the successful genome projects is the exploration of the special gene products. In this field, the preparation of proteins with covalent modifications is essential. We focus on the preparation of modified protein molecules for structural and functional studies and on the development of proteins geared for specific properties. Chemical synthesis, which extends the ribosomal protein synthesis is applied for the protein production. It promises unlimited variation of the covalent structure of the polypeptide chain, and thus, the ability to systematically tune the properties of a protein molecule.
ITC fellows are welcome to participate in the synthesis and chemical modification of the prion protein and in the development of new strategies to extend the chemical ligation methods. Experience in peptide chemistry, chromatographic methods, MS and NMR spectroscopy is advantageous.

Supervisor: Csaba Tömböly, Institute of Biochemistry
E-mail address: tomboly@brc.hu

49. How mutations arise – the yeast model of mutagenesis

A growing body of evidence supports the idea that the roots of cancers lay in mutations in DNA, the inheriting material of cells. DNA damages, caused by extrinsic or intrinsic agents, are usually removed from DNA and repaired by one of the several DNA repair systems of the cell, preserving the genetic information. However, high exposure to DNA damaging agents can lead to the accumulation of damaged bases. Unrepaired DNA damages block the replication machinery, which can lead to cell death. To ensure survival, cells have evolved mechanisms that can sustain DNA replication on damaged DNA. These so called damage tolerance or DNA damage bypass processes allow replication to continue on damaged DNA without removing the damaged bases. In humans, increased error-prone bypass of DNA lesions causes increased mutagenesis and a rise in the incidence of cancers, whereas error-free replication of damaged DNA contributes to genetic stability.

In yeasts, the Rad6-Rad18 ubiquitin-conjugating complex governs three alternative pathways of replication of damaged DNA: the Rad5-dependent error-free, the DNA polymerase η dependent error-free, and the polymerase ζ dependent error-prone damage bypass. Almost all the elements of these pathways are conserved from yeasts to humans.

Our goal is to understand how the different DNA lesion bypass proteins get access to the replication fork, and how the different mechanisms are controlled.

Supervisor: Ildikó Unk, Institute of Genetics
E-mail address: ilunk@brc.hu

50. Regulation of gene expression in cyanobacteria

The applicant would join a group with active research on the regulation of gene expression in the cyanobacterium Synechocystis 6803. The research covers DNA microarray and RT PCR studies on the effect of various stress factors, like visible and ultraviolet light, reactive oxygen species and heavy metals on the expression profile of stress related genes and aims at the understanding of the complex signal transduction pathways involved in stress-related gene responses. The applicant is expected to have expertise in basic molecular biology techniques (DNA and RNA isolation, PCR, transformation methods) and preferably some knowledge of bioinformatics methods.
51. Plant stress diagnostics

The applicant would join a group with an active program on plant stress diagnostics. Our research aims at the precise characterization of plant growth and physiological state under various stress conditions (currently drought, and leaf rust) by the application of imaging techniques (digital photography, chlorophyll fluorescence, infrared/thermal and near infrared) in combination with controlled plant growth.

The applicant is expected to participate in the application of the stress diagnostic system to study the consequences of infections by fungal pathogens (such as leaf rust) on the photosynthetic activity of wheat leaves. The main objectives of the study are the characterization of various resistant wheat lines against fungal infection, as well as the development of markers for early warning of fungal infections, that could be used for the detection of infection before the appearance of visual symptoms. Knowledge of working with computers is required, and learning basic computer methods for data evaluation (such as image analysis) is expected. Experience in working with plants under greenhouse conditions is preferred. Experience with fungal pathogens attacking plants would be an advantage.

52. Conformational diseases; study of the cellular prion protein

Transmissible Spongiform Encephalopathies (TSE) or prion diseases are fatal neurodegenerative disease caused by the misfolding and consequent accumulation of a cellular protein called prion protein (PrP) in the brain. At present there is no available cure to the disease mostly because neither the exact mechanism of developing the disease, nor the cellular role of the normal form of the protein is known. One of our research interests is to study the function of the normal, non-disease associated form of the cellular prion protein (PrP\textsuperscript{C}). Among our aims is to find possible binding partners of the protein in vivo, in cellular environment. Our approach involves a combination of cell biology and biochemical techniques. These include recombinant protein expression and purification using \textit{E. Coli} expression systems, tissue culturing, microscopy, sub cellular fractionation, protein identification by immunolabeling and gel-electrophoresis, mass spectrometry. The successful candidate will take part in our ongoing projects in this area. Applicants are encouraged to apply from the field of biology, biochemistry. Previous experience in either of the above mentioned techniques will be an advantage for selection of the candidate. Selected candidates will be interviewed by phone (or personally, if visiting our laboratory is possible), proficiency in English language is required.
53. Biophysical characterization of recombinant cytochromes

Cytochromes are heme-containing proteins, whose major function is transferring an electron between electron donor and electron acceptor molecules. The maturation of mitochondrial cytochrome c, which includes the covalent heme attachment to two cysteines and the proper folding of the protein, is catalyzed by the enzyme cytochrome c heme lyase (CCHL). Soluble cytochrome c and members of the transmembrane cytochrome b561 family will be heterologously expressed in *E. coli* and yeast, respectively, and purified. CCHL will also be heterologously expressed and purified. The structural-functional aspects of the interaction of CCHL with its two substrates, heme and apocytochrome c, will be studied *in vitro* by various spectroscopic methods. Site directed mutagenesis of both proteins is planned to better understand cytochrome c maturation. Wild type and site directed mutant cytochromes c will be used as a model to understand the role of the protein matrix in intraprotein electron transfer. The expressed wild type and site directed mutant cytochrome b561 proteins will be characterized by spectroscopic and voltammetric methods (redox potential, secondary structure, etc.). The successful candidate will join the Metalloprotein research group of three senior principal investigators. Available techniques for the characterization of the structure and function of the studied cytochromes are UV-visible static and fast kinetic absorption spectroscopy, CD, EPR and FTIR spectroscopy, voltammetry. Protein purification and characterization are assisted by state-of-the-art FPLC and HPLC. Candidates with strong background in molecular biology and/or protein biochemistry and/or spectroscopy are particularly encouraged to apply.