### National Research, development and Innovation Office





## HCEMM TEAMING NATIONAL LABORATORY

#### TRANSLATIONAL MEDICINE

The main activity of the HCEMM Teaming National Laboratory is research into the causes, treatment, diagnosis and prevention of diseases. Its objective is to establish a centre with a strong focus on translational medicine for healthy ageing, to promote the clinical application of basic research results and to ensure scientific excellence based on an international peer review system. A translational medicine centre will be built to train highly qualified researchers and to carry out cutting-edge research in molecular medicine for chronic and infectious diseases.



#### **MAIN RESEARCH AREAS**

- Translational medicine
- Healthy ageing
- Immuno-inflammatory diseases
- Metabolic and cardiovascular diseases
- Genomic instability and cancers
- Communicable diseases, co-morbidities
- Scientific computing



#### **IMPLEMENTER:**

HCEMM Nonprofit Kft.

#### **PLACES OF IMPLEMENTATION: Szeged**



#### BENEFITS TO BE EXPECTED FROM LABORATORY RESEARCH

- Commercialise and exploit intellectual property.
- Position Hungary on the map of international life sciences research.
- Strengthen Hungarian knowledge regions in Hungary and Central and Eastern Europe.
- Involve members of society in research on age-related diseases.
- Strengthen the link between academia and industry.

#### THE PROFESSIONAL TEAM

The current research topics at HCEMM are related to healthy ageing, with special focus on Immuno-Inflammatory Diseases, Metabolic- and Cardiovascular Diseases, Genomic Instability and Cancer, as well as Infectious Diseases, which compound the aforementioned non-infectious chronic diseases. These disease complexes affect the majority of the Hungarian population in old age, with over 75% of the mortality being caused by cancers or cardiac diseases alone.

At the moment, HCEMM includes three Advanced Core Facilities at the host institutions and 16 double affiliated research groups. More than 100 articles in scientific journals (~70% Q1, ~19% D1), 1 chapter in a book and 1 thesis were published by researchers with HCEMM affiliation until now, all articles available in Open Access.

HCEMM currently has established the following groups:

**HCEMM-USZ Skin Research Group**: The Research Group has expertise in skin biology, focusing on skin immunology and translational medicine.

**HCEMM-USZ** Molecular Gastroenterology **Research Group:** The Research Group capitalizes on the advantages of patient-derived pancreatic organoid cultures and works on improving the culture system by establishing disease-relevant co-cultures of stromal and epithelial cells. These co-cultures will be used to study disease mechanisms, intercellular communication and therapeutic possibilities in inflammatory and malignant pancreatic diseases.

Blood Flow **HCEMM-USZ** Cerebral and **Metabolism Research Group:** The evolution of cerebral edema is a life-threatening condition, yet the concept of the research group is that how brain edema develops is incomplete, and treatment options remain limited. The current project addresses two challenges: (i) The development of a new strategy for timely, accurate diagnosis to predict cerebral edema formation; and (ii) to offer novel, targeted, noninvasive and personalized therapy for the effective alleviation of brain edema formation.

**HCEMM-USZ Stem Cell Research Group:** The Research Group focuses on the investigation of human-induced pluripotent stem-cell derived microglia cells and their role in the development neuroinflammatory diseases, mainly Alzheimer's disease.

Fungal **HCEMM-USZ** Pathogens Research **Group:** In their HCEMM project (entitled as 'The link between fungal colonization and cancer progression'), the research group aims to reveal mechanisms activated during fungi-driven oral carcinoma) cancer (oral squamous cell progression in vitro and in vivo. The group's main research interest involves the exploration of the oral mycobiome's role in health and disease.

**HCEMM-BRC Mutagenesis and Carcinogenesis Research Group:** The Research Group is currently carrying out research on UBZ-domain-containing proteins to identify Ub-PCNA-interacting (Ubiquitination of Proliferating cell nuclear antigen) proteins and the key enzymatic activities affected by the interaction. The research will shed light on the regulatory aspects and downstream mechanisms of Ub-PCNA-mediated DNA damage bypass pathways.

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**HCEMM-USZ** Magnetotherapeutics Research **Group:** The research group is developing biophysical technologies based on electrical, ultrasonic and magnetic modalities. These are planned to be serving as high-precision non-pharmaceutical interventions, while also improving drug delivery solutions. The group pays particular attention on the treatment of disorders of the brain.

**HCEMM-BRC Metabolic Systems Research Group:** The Research Group combines systems biology and phylogenetic approaches to understand how metabolic differences impact health and how pathogenic microbes evolve. They have extensive know-how on generating and analyzing omics data, including metabolome profiles.

**HCEMM-BRC** Translational Microbiology Research Group: This Research Group is aiding the Development of Precision Anti-virulence Therapy in Inflammatory Bowel Disease. They test antibiotic resistance evolution at an early stage of drug development. This could have a pivotal role in the identification of promising antibiotic candidates which could remain effective longer in clinical practice. The groups aims at providing a functional metagenomic platform that can be used to investigate horizontal gene transfermediated resistance evolution.

**HCEMM-SU** Extracellular Vesicles Research **Group:** This Research Group focuses on the development of new gene therapeutic tools. The primary goals of the project include development of novel gene therapeutic modalities and testing them both in vitro and in vivo, in genetic murine models of cardiovascular diseases.

**Research Group:** The research group investigates the molecular pathogenesis of various hematological malignancies with a special focus on B-cell lymphomas. The main aim is to identify (epi)genetic biomarkers associated with therapy response and resistance. The goal of this translational research is to develop clinically applicable tools using advanced genomic technologies to support the individualization of therapies and molecular monitoring of patients with B-celllymphomas.

**HCEMM-SU** Cardiometabolic Immunology Research Group: The group focuses on translational cardiovascular research on the interdisciplinary fields of molecular medicine-cardiology-immunology-oncology-pharmacology. During the last 3 years, they have been working on to explore the molecular mechanisms of heart failure.

Neurobiology and Neurobegeneration Research Group: The major interest of this Group is studying healthy ageing and the pathophysiology of age-related, chronic neurodegenerative disorders such as Huntington's disease, Parkinson's disease and Alzheimer's disease. The group is using a unique, direct neuronal reprogramming model system, which was completely absent up to date in Hungary.

**HCEMM-SU Inflammatory Signaling Research Group:** Under the original HCEMM proposal on "Mechanisms of Tissue Damage Induced Inflammation" this group is conducting projects and experiments with the aim of better understanding the fundamental mechanisms that drive leukocytes to wounds.

**HCEMM-SU Molecular Channelopathies Research Group:** The translational relevance of cystic fibrosis transmembrane conductance regulator (CFTR) research is given by the devastating inherited disease cystic fibrosis (CF), which affects ~100 000 people worldwide, and is caused by a multitude of CFTR mutations. Thus, understanding the structural and functional consequences of CF causing mutations, as well as the pharmacological sensitivities of various CFTR mutants, is urgently needed for the development of personalized medicine approaches to combat the disease.

**HCEMM-SU** Thrombosis and Hemostasis Research Group: The research focuses on translational medicine in the field of thrombosis and hemostasis. In their studies they use in vitro, ex vivo and in vivo methods combined with advanced microscopic technics to uncover the pathophysiology of hemostatic processes. They concentrate on the role of neutrophil extracellular traps, von Willebrand factor and the interaction thereof.

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#### THE PROFESSIONAL TEAM

#### **Advanced Core Facilities at HCEMM**

The Advanced Core facilities (ACF) system and services of HCEMM aims at providing a research infrastructure coordination system, which assures that the infrastructure supporting the research projects of HCEMM is utilized efficiently, jointly with the owners. This includes the creation of the HCEMM core facility system and the related coordination and management activities. The Advanced Core Facilities (ACF) are specialized laboratories, which are equipped with cutting-edge technology and state-of-the-art machines. The services offered by each ACF are each focused in particular areas of research and development (e.g. imaging or MassSpec), in support of the activities of the HCEMM Research Groups and work with industrial partners.

The ACFs are also connected to EMBL via the EU Teaming Grant, which allows HCEMM scientists to use the unique offerings of the EMBL advanced core facilities under the same conditions of EMBL employees. So far, three HCEMM Advanced Core Facilities (ACF) have already been established in Hungary, and a fourth one is about to be established (ACF4: Scientific Computing, at the HCEMM headquarters in Szeged):

#### **In Vivo Imaging ACF**

The ACF provides services in a broad range of in vivo imaging applications using an already existing infrastructure, which is continuously being expanded. For the usually needed small animal imaging studies presumably in the forefront of possible users, the ACF has an immediate access to multiple animal models (optimized at conventional and SPF animal facilities). Tumour xenografts including a variety of cell lines are also available based on user-borne cost and maintenance models.

With the complexity of the available technological platform, the ACF offers an unprecedented and highly flexible solution to image all organ systems of the given organism statically, dynamically, and functionally. Moreover, it also provides an excellent technological arsenal for applications in multiple scientific fields of e.g. pharmacology, molecular oncology, histology, inflammation research, biomarker identification and detection – in parallel with assessing physiological and pathophysiological phenomena.

#### **Singe-cell Omics ACF**

The main goal of the ACF is to provide high-sensitivity molecular analyses of limited sample amounts, including lipidomic, proteomic, genomic and transcriptomic analyses and to develop or adopt methods suitable to study a few hundred cells and below.

The ACF offers specific services, such as proteomics, lipidomics, genomics, transcriptomics, phenomics. Mass spectrometers used for proteomics and lipidomics analyses are operated in alternating 2-3 weeks intervals for the respective measurement types. Only trained personnel can operate the instruments, customers do not have direct access to the mass spectrometers. Data evaluation is usually performed by the ACF personnel, therefore raw data are typically given out solely for publication purposes.

The genomics and transcriptomics workflows are performed by the personnel of the NGS Platform of the BRC. The users provide the starting material (DNA, RNA, miRNA, ChIPped DNA, cDNA etc.), preparation of the sequencing libraries and the sequencing is performed by experts working at the NGS Platform. The resulting raw sequence reads are handed over to the users either by downloading from ftp/cloud or deposited on external hard disks.

#### Functional Cell Biology and Immunology ACF

The main goal of this ACF is to provide high-throughput and high-resolution imaging, cell surface and intracellular marker detection as well as the possibility for sorting cells based on their expressed protein markers for cellular and immunology studies.

The ACF offers static and dynamic imaging applications and high-performance cell sorting and marker identification applications. The major available techniques at the Functional Cell Biology and Immunology Advanced Core Facility (FCBI ACF) include conventional (wide-field, confocal) and advanced (super resolution) light microscopy, scanning electron microscopy optimized for biological samples (including array tomography and correlative light and electron microscopy), an advanced cell sorter facility and a molecular biology facility.



#### **TARGET GROUP**

Target groups of the HCEMM Teaming National Laboratory are researchers from national as well as international research institutes (academic and government), the private sector, especially potential industrial partners with outreach to the general society.

#### **POSSIBLE PARTNERSHIPS**

The HCEMM focuses on establishing partnerships for Joint Grants under Horizon Europe and other grant opportunities, i.e. Teaming Opportunities with European research organizations, student exchanges, scientific cooperation. The HCEMM is also looking for potential industrial partners, either for joint work and service provision, or for licensing of HCEMMs Intellectual Property.



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