CENTER FOR TRANSLATIONAL MEDICINE (CTM)

INTERNATIONAL CLINICAL RESEARCH CENTER (ICRC)

ST. ANNE'S UNIVERSITY HOSPITAL, BRNO, CZECH REPUBLIC

The Center for Translational Medicine (CTM) is a highly interdisciplinary research platform in the International Clinical Research Center (FNUSA-ICRC), a European Union-funded project of the St. Anne's University Hospital Brno (Czech Republic). The funds so far collected from EU were mostly used to build its own state-of-the-art translational medical research premises. The research center, currently hosts young promising researchers and students from all over the world (9 nationalities represented) and aims at unveiling the molecular mechanisms involved in the onset and progression of the diseases of aging. For this purpose, CTM adopts original and interdisciplinary approaches based on the use of smart materials, microfluidics systems, bioreactors, mechanically-assisted devices and multi-faceted molecular and cellular biology skills to investigate the molecular basis of complex diseases.

CTM is currently coordinated by 4 Principal Investigators (PI):

1) **Giancarlo Forte, PhD**, serving as CTM Group Leader, coordinates the Cardiovascular System - Mechanobiology Group (CSM). The group is internationally recognized for its studies on cell-matrix interaction, namely the impact of mechanosensor system in controlling cell function and determining the onset and progression of cardiovascular pathologies;

2) **Gorazd Bernard Stokin, MD, PhD**, serving also as FNUSA-ICRC Chair, leads the Translational Neuroscience and Aging Program (TNA), aiming at disclosing the link between the impairment of axonal transport and the occurrence of neurodegenerative pathologies;

3) **Jan Fric, PhD**, head of the Cellular and Molecular Immunoregulation Group (CMI). His group is devoted to investigate how acute and chronic inflammation contributes to tissue remodeling during regeneration and ageing.

4) **Manlio Vinciguerra, PhD,** coordinator of the Epigenetic, Metabolism and Aging Group (EMA). His research activities are mostly focused on highlighting the epigenetic mechanisms of liver cancer progression. Dr. Vinciguerra is also interested in the effectiveness of short term fasting to treat gastrointestinal cancers and aging pathologies.

PREMISES:

CTM features state-of-the-art equipment for biological sample production, manipulation and analysis. The center can be formally divided into 3 parts:

The cell factory is composed of two fully equipped cell culture rooms (one for adult animal and human cells, the other dedicated to pluripotent cells), molecular biology and biochemistry premises, cell separation and bioimaging facilities.

The cell separation/biochemistry facility is equipped with BD FACSCanto II cell analyzer and Beckman Coulter MoFlo Astrios FACS Sorter suited for cell analysis and separation based on the expression of up

to 12 antigens contemporary. The molecular biology premises are equipped with Roche LightCycler 480 II for high throughput analysis of gene expression and the necessary tools for plasmid cloning and manipulation. The biochemistry unit features all the top notch protein analysis apparatuses (BIORAD V3 WB workflow, ChemiDoc MP, 2D electrophoresis, DIONEX UltiMate RSLNano system, capillary electrophoresis, BRUKER microTOF-Q II mass spectrometer). CTM recently acquired MALDI TOF MS instrument.

The bioimaging facility features cutting edge laser scanning microscope equipped for live imaging (ZEISS LSM780, ZEISS LSM 7 live), two-photon microscope (ZEISS LSM 7MP), laser cut microscope mounted on ZEISS AXIO Observer Z.1 and JEOL JCM-6000 plus Neoscope Scanning Electron Microscope. The facility is equipped with brand new and complete workflow for tissue processing, including LEICA Tissue processor, cryostat, fully automated rotary microtome and ZEISS Axio Scan Z.1 automatic slide scanner. Microplate ELISA reader and Microplate Luminometer are also available. Finally, the availability of Maestro multielectrode array (MEA) platform allows for the stimulation and recording of 12,500 data points/second (12.5 kHz) to perform single cell, high throughput electrophysiology studies in electrically active cells and tissues.

SELECTED PUBLICATIONS:

1) Mosqueira D, Pagliari S, Uto K, Ebara M, Romanazzo S, Escobedo-Lucea C, Nakanishi J, Taniguchi A, Franzese O, Di Nardo P, Goumans MJ, Traversa E, Pinto-do-Ó P, Aoyagi T, Forte G. Hippo pathway effectors control cardiac progenitor cell fate by acting as dynamic sensors of substrate mechanics and nanostructure. **ACS Nano**. 2014; 8: 2033-47. doi: 10.1021/nn4058984.

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3) Farra R, Grassi G, Tonon F, Abrami M, Grassi M, Pozzato G, Fiotti N, Forte G, Dapas B. The Role of the Transcription Factor E2F1 in Hepatocellular Carcinoma. **Curr Drug Deliv**. 2016 May 27. In press

4) Barba AA, Lamberti G, Sardo C, Dapas B, Abrami M, Grassi M, Farra R, Tonon F, Forte G, Musiani F, Licciardi M, Pozzato G, Zanconati F, Scaggiante B, Grassi G, Cavallaro G. Novel Lipid and Polymeric Materials as Delivery Systems for Nucleic Acid Based Drugs. **Curr Drug Metab**. 2015; 16: 427-52.

5) García-Romero N, González-Tejedo C, Carrión-Navarro J, Esteban-Rubio S, Rackov G, Rodríguez-Fanjul V, Oliver-De La Cruz J, Prat-Acín R, Peris-Celda M, Blesa D, Ramírez-Jiménez L, Sánchez-Gómez P, Perona R, Escobedo-Lucea C, Belda-Iniesta C, Ayuso-Sacido A. Cancer stem cells from human glioblastoma resemble but do not mimic original tumors after in vitro passaging in serum-free media. **Oncotarget**. 2016 Aug 29. doi: 10.18632/oncotarget.11676.

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7) Zelante T, Wong AY, Mencarelli A, Foo S, Zolezzi F, Lee B, Poidinger M, Ricciardi-Castagnoli P, Fric J. Impaired calcineurin signaling in myeloid cells results in downregulation of pentraxin-3 and increased susceptibility to aspergillosis. **Mucosal Immunol**. 2016. doi: 10.1038/mi.2016.52.

8) Pazienza V, Panebianco C, Rappa F, Memoli D, Borghesan M, Cannito S, Oji A, Mazza G, Tamburrino D, Fusai G, Barone R, Bolasco G, Villarroya F, Villarroya J, Hatsuzawa K, Cappello F, Tarallo R, Nakanishi T, Vinciguerra M. Histone macroH2A1.2 promotes metabolic health and leanness by inhibiting adipogenesis. **Epigenetics Chromatin**. 2016 Oct 25;9:45.

9) Jueliger S, Lyons J, Cannito S, Pata I, Pata P, Shkolnaya M, Lo Re O, Peyrou M, Villarroya F, Pazienza V, Rappa F, Cappello F, Azab M, Taverna P, Vinciguerra M. Efficacy and epigenetic interactions of novel DNA hypomethylating agent guadecitabine (SGI-110) in preclinical models of hepatocellular carcinoma. **Epigenetics**. 2016 Aug 11:1-12. In press

10) Krell-Roesch J, Pink A, Roberts RO, Stokin GB, Mielke MM, Spangehl KA, Bartley MM, Knopman DS, Christianson TJ, Petersen RC, Geda YE. Timing of Physical Activity, Apolipoprotein E ε4 Genotype, and Risk of Incident Mild Cognitive Impairment. **J Am Geriatr Soc**. 2016. doi: 10.1111/jgs.14402.

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