Novinky v biomedicínském výzkumu/Biomedical Research News

Přednáškové odpoledne s předními světovými odborníky
Lectures of international experts in biomedicine

Úterý 28. listopadu/Tuesday November 28, 2017
Síň Coriových , U Nemocnice 5, Praha 2

1. LÉKAŘSKÁ FAKULTA Univerzita Karlova

Jeffrey A. Medin

Is the Inaugural MACC Fund Endowed Chair in the Departments of Pediatrics and Biochemistry at the Medical College of Wisconsin in Milwaukee, Wisconsin. He is also Vice Chair of Research Innovation for the Department of Pediatrics and Director of the MCW Vector Production Facility.

Dr. Medin is an Academic Founder of AVROBIO Inc of Boston, MA. He is a member of the SAB of Rapa Therapeutics and an editorial board member of the World Journal of Stem Cells, Biomedicines, and Cell and Gene Therapy Insights. Dr. Medin is the PI of an on-going clinical gene therapy trial in Canada targeting correction of autologous CD34+ hematopoietic cells for amelioration of Fabry disease and a co-investigator on another on-going clinical trial that involves IL-12 gene transfer into blasts to treat AML. Dr. Medin has published more than 150 peer-reviewed papers, edited an immunotherapy book, and presented at more than 150 invited conferences and workshops.

14.15 – 15.30 Systemic Consequences of Acid Ceramidase Deficiency

The sphingolipid family includes over 4000 distinct molecules, which together perform numerous essential functions. Ceramides have been called the central hub of the sphingolipid pathway. They are an extensive family of lipid molecules composed of a sphingosine and a fatty acid tail and are precursors for gangliosides and sphingomyelin; key components of cell membranes. Ceramides are also involved in many cellular processes themselves including cell differentiation, apoptosis, growth arrest, and senescence. In contrast, a downstream product of ceramide catabolism, sphingosine-1-phosphate (S1P), has the opposite effect. S1P has been implicated in cell growth and an actual inhibition of ceramide-mediateda poptosis.

Improper control of ceramides, and more generally SL stasis itself, manifests in a variety of debilitating conditions. Our laboratory has studied two of these disorders, Farber disease, and Fabry disease, for over 20 years. Farber disease (aka Farber Lipogranulomatosis or ACDase Deficiency) is an ultra-rare inherited Lysosomal Storage Disorder (LSD) characterized by the accumulation of ceramides in all tissues. Farber disease results from misregulation of ceramide stasis as a result of mutations in the enzyme acid ceramidase (ACDase). ACDase is expressed in every cell and modulates ceramide levels by both breaking down ceramides and catalyzing the ‘reverse reaction’ wherein ceramides are synthesized from sphingosine and free fatty acid precursors. A complete 'knock-out' of ACDase in mice has been shown by another group to be lethal at the 4-cell stage. Subsequent to this, we have made the first viable model of ACDase deficiency by 'knocking-in' a human mutation into the analogous mouse locus (Alayoubi et al 2013). Homozygous Farber mice live about 10 weeks and have impairments in many organs.

Together with our collaborators, including Dr. Jakub Sikora from Charles University, we have been examining the consequences of ceramide dysregulation in the hematopoietic system, the brain, the lung, and the eyes of these Farber mice. Results of published and unpublished studies will be discussed as will new experiments directed towards the development of therapy for this very severe disorder.

Přednáškové odpoledne je součástí kurzu „Novinky v biomedicínském výzkumu“, který je jeden z doporučených povinně volitelných kurzů pro Ph.D. studenty oboru Biochemie a patobiochemie (Oborová rada 04) a Fyziologie a patofyziologie člověka (Oborová rada 05). Účastníci na konci kurzu získají zápočet. Kurz je sestaven z přednášek zahraničních a domácích světově uznávaných odborníků zabývajících se molekulovými mechanismy etiologie, patogeneze a terapie chorob. Vítáni jsou i studenti jiných oborů a zájemci z řad vědeckých pracovníků a lékařů.

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