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POSTERS

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mice show a reduction in lymphomagenesis. These data indicate that cells need to tightly regulate eIF6 gene dosage. The eif6 gene is highly conserved from yeast to human. The well characterized development of *D. melanogaster* and the easy manipulation of its genetics led us to the fly model to study the effects of eIF6 altered gene dosage. Ubiquitous overexpression of eIF6 is lethal. We then focused on the eye, which is dispensable for life. We found that eIF6 overexpression in all eye's cells results in a rough eye phenotype. In addition, eIF6 overexpression only in cone or pigment cells is sufficient to alter the eye morphology. It is well established that the crosstalk between these two cell types during the pupal stage is responsible for the programmed cell death (PCD) of extra-numerary pigment cells to determine the correct structure of the adult eye. We indeed found that eIF6 is critical at this stage, because its overexpression is associated to a delayed and increased PCD, resulting in an aberrant adult eye. Moreover, we found an alteration of translation efficiency with a two-fold increase of general translation upon DeIF6 overexpression. We then analyzed the gene expression by RNASeq analysis, which revealed alterations in genes specific for eye development and, surprisingly, a tremendous decrease in ecdysone pathway related genes. In addition, administration of 20-HydroxyEcdysone (20HE) partially rescued the rough eye phenotype. This is the first evidence of PCD regulation by a translation initiation factor such as eIF6 via the ecdysone metabolism.

P.5.4-044
Role of ceramide synthase 5 as transcription factor identified by ChIP and LC-MS/MS

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Over the last few decades, sphingolipids and their metabolizing enzymes, like ceramide synthases (CerS), have been realized to be important in diseases for example cancer development and progression. In women, breast cancer is the most frequently diagnosed form of cancer with over 1.5 million new cases worldwide diagnosed each year. It is the second leading cause of cancer death in women. Therefore, identifying the exact signaling pathway is important for an efficient and individual breast cancer therapy. CerS-2, -4, -5 and -6 contain a homeobox (Hox)-like domain. The function of this domain in CerS isoforms is mostly unclear but its presence suggests a potential role as transcription factor. First results received by Chromatin-immunoprecipitation (ChIP) support this hypothesis. We established a screening method for proteins and their role as transcription factors based on CerS-5. Formaldehyd was used to cross-link the proteins to DNA, crosslinked lysate was sonicated and CerS-5 was precipitated with an anti-CerS-5 antibody. CerS-5 protein and anti-CerS-5 antibody were captured with beads and the crosslink was reversed. The DNA was degraded to nucleosides and was quantified by liquid chromatography tandem mass spectrometry (LC-MS/MS). The nucleosides were separated with reversed phase chromatography on an Atlantis T3 column. The target DNA sequence was determined. This is a new innovative procedure, which can be assigned to any other protein and provides new insights into the role of CerS-5 in the regulation of cellular mechanism and enhance our understanding of CerS signaling.

P.5.4-045
Distinguishing of pea aminoaldehyde dehydrogenase isoenzymes in plant extracts using a synthetic coenzyme analog

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Aldehyde dehydrogenases (ALDHs) are widespread in living nature. Their role resides in $NAD(P)^+$-dependent oxidation of aldehyde substrates to carboxylic acids, which provides important metabolites or represents a way to remove toxic compounds. Members of the ALDH10 family in plants are aminoaldehyde dehydrogenases (AMADHs) as they readily oxidize omega-aminoaldehydes. Due to their broad substrate specificity, the enzymes used to be named 4-aminobutyraldehyde dehydrogenases (EC 1.2.1.19), 4-guanidinobutyraldehyde dehydrogenases (EC 1.2.1.54) or betaine aldehyde dehydrogenases (EC 1.2.1.8). Plant AMADHs exist as homodimers with a typical ALDH subunit fold comprising a catalytic domain, a coenzyme-binding domain and an oligomerization domain. The active site contains three strictly conserved and essential residues (Cys, Glu and Asn). Usually, there are two isoforms, which differ in their molecular properties and substrate specificity, but the biological significance of this fact has not satisfactorily been addressed. In this work, pea isoenzymes PsAMADH1 and PsAMADH2 were assayed in roots and shoots of germinating seedlings by spectrophotometry and native gel electrophoresis or isoelectric focusing followed by activity-based staining. The assays exploited a different activity of the isoenzymes with NAD^+ and its synthetic analog thio-NAD^+. The latter coenzyme form is accepted efficiently by PsAMADH2 but not PsAMADH1. We demonstrated that the specific activity of AMADH with thio-NAD^+ increased during the germination period in contrast to that with NAD^+ and since the day 5 it was even higher in absolute numbers. This observation indicates a gradual increase in the representation of PsAMADH2 towards PsAMADH1 during germination in both roots and shoots. The same trend was observed by activity staining of gels. The isoenzymes 1 and 2 were identified and distinguished in neighbor bands displaying a different staining intensity using nanoLC-ESI-MS/MS after a tryptic digestion.

P.5.4-046
Siderophores produced by *Serratia marcescens* SM6

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Iron is an essential micronutrient for nearly all forms of life. Its availability is tightly controlled by the mammalian host during infection. To overcome iron deficiency bacteria produce small molecules – siderophores which exhibit high binding affinity to Fe (III) ions and make iron available for bacterial cells. In addition to well-known role in iron acquisition siderophores also contribute to cell to cell signaling and oxidative stress defense. Here we report identification of siderophores in opportunistic pathogen *Serratia marcescens*. Genome of *S. marcescens* SM6 encodes two gene clusters involved in siderophore production. The gene that encodes the key enzyme for siderophore synthesis in cluster 1 shares 63% identity with gene *cbsF* of *Dickeya chrysanthemi* EC16. In *D. chrysanthemi cbsF* is involved in production of siderophore chrysobactin. LC-MS analysis of secondary metabolites

present in the conditioned media used for growth of *S. marcescens* SM6 under iron-limiting conditions showed the presence of the compound with mass-to-charge ratio (m/z) 370.16 and chemical formula $C_{16}H_{23}N_3O_7$ that matches the expected size of chrysobactin along with three additional compounds with m/z 721.32, 1072.45 and 1054.44 (dichrysobactin, trichrysobactin and cyclic trichrysobactin, respectively). Genomic organization of siderophore cluster 2 *S. marcescens* SM6 is similar to serratiochelin biosynthetic cluster of *Serratia plymuthica* V4. LC-MS analysis of metabolites in the siderophore extract of *S. marcescens* SM6 identified the compound with m/z 430.16 and a chemical formula $C_{21}H_{24}N_3O_7$. ^{1}H-NMR analysis confirmed that this compound is Serratiochelin A. We are currently working on characterization of phenotypes associated with the loss of individual genes in both siderophore biosynthetic clusters.

P.5.4-047
Loss of ELOVL3 reduces lipogenesis in skeletal muscle

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The fatty acid elongase ELOVL3 is involved in the synthesis of C20–C24 very long chain fatty acids. It was shown that ablation of ELOVL3 leads to reduced levels of adiponectin and leptin, constrained expansion of adipose tissue, and resistance against diet-induced obesity. Moreover, in cold-acclimated ELOVL3-/- mice, there is an increased heat loss due to impaired skin barrier, and lack of hyperrecruitment of brown adipose tissue. Instead, the muscle shivering in order to maintain body temperature was observed. This fact suggests a possible involvement of ELOVL3 in the regulation of skeletal muscle metabolism. Therefore, the aim of the present study was to investigate the effect of ELOVL3 ablation on the lipid metabolism in skeletal muscle. First, we measured level of sterol regulatory element-binding protein 1 (SREBP1), a transcription factor involved in regulation of lipogenesis. Our study showed decreased protein levels of both premature SREBP1 and mature SREBP1 in white gastrocnemius (WG) muscle of ELOVL3-/- mice. Also the protein levels of targets of SREBP1, i.e. fatty acid synthase, acetyl-CoA carboxylase, and stearoyl-CoA desaturase 1 were decreased in WG of ELOVL3-/- mice. These results suggest decreased fatty acid *de novo* synthesis and reduced lipogenesis in WG of ELOVL3-/- mice. Next, we analyzed protein level of adipose triglyceride lipase (ATGL), the rate-limiting enzyme in TG hydrolysis. ATGL protein level was decreased in muscle of ELOVL3-/- mice indicating reduction of lipolysis. Summarizing, presented results show important role of ELOVL3 in the regulation of skeletal muscle energy metabolism.

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P.5.4-048
The role of urokinase-type plasminogen activator system in regeneration properties of resident stem cells

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Mesenchymal stem cells (MSC) supposed to take a part in regeneration especially when it became activated by injury and inflammation. Restoration of tissue function is accompanied by angiogenesis, progenitor cell activation/migration and extracellular matrix reorganization. These effects are associated with two major fibrinolytic factors: urokinase plasminogen activator (uPA; urokinase) and uPA receptor (uPAR). It was shown that uPAR is expressed on the surface of MSC and in addition that the proteolytic activity of urokinase may regulate MSC behavior during regeneration. The aim of this work was to investigate the effects on MSC developed in our laboratory recombinant uPA and its forms (proteolytically inactive uPA with His204Gln mutation (uPA-H/Q), uPA lacking the growth factor-like domain (ΔGFD), kringle domain (KD), and aminoterminal fragment (ATF)). We studied human adipose tissue-derived mesenchymal stromal cell (ADSC) migration, proliferation and matrix metalloproteinases secretion induced by uPA. We found that uPA and its recombinant forms had no effect on ADSC proliferation assessed by MTT test. Directed ADSC migration was slightly induced by uPA, with no effect of other uPA forms. Full urokinase and kringle domain enhanced spontaneous migration of ADSC. Chemotaxis induced by platelet-derived growth factor (PDGF) was attenuated by proteolytically inactive uPA, KD and by blocking antibody to urokinase receptor. Urokinase and all of its recombinant forms induced secretion of matrix metalloproteinase-9 by ADSC, this effect was absent in PDGF. These findings suggest that uPA system is involved in the regulation of migration and secretion of MMP9 by MSCs. Modulation of uPA-system activity may be considered as a possible tool for induction of regeneration potential of MSC.

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P.5.4-049
Metabolic changes in the *Opisthorchis felineus* infected liver

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Opisthorchiasis caused by *Opisthorchis felineus* is a fish-borne parasitic worm infection spread in Russia and some European countries. This fluke inhabits the bile duct of the host liver, causing local tissue damage and chronic inflammation. The aim of the study was to investigate the local metabolic changes provoked by *O. felineus* in infected liver an experimental animal model. 5-week-old hamster *Mesocricetus auratus* were infected intragastrically with 50 metacercariae per hamster and divided in 3 groups; age-matched intact hamsters were used as controls for each group. After 5 weeks of infection hamsters were euthanized; blood and liver samples were collected for examination. Serum and blood analyses were performed using routine procedures. Liver samples were analyzed by histological (to determine the fibrosis stage) and biochemical analyses (to estimate cholesterol, triacylglycerols (TAG), phospholipids, proteins, glycogen and ATP concentration in tissue). Western blot analysis was applied