

throughput gene co-expression data to obtain new elements and interactions with the direct neighboring targets of CCN. Interestingly, among our top candidates is a group of genes directly or indirectly associated with the regulation of both cancer and immune system: Elavl1, APOH (Apolipoprotein H), IFNAR1 (Interferon Alpha, Beta, Omega Receptor), SP1 (Sp1 Transcription Factor) and NCL (Nuclein). We are now analyzing the circadian phenotype of these genes in cancer cell lines and our preliminary data indicates differences in the oscillatory profiles pointing to their circadian regulation. Taken together, our findings bring us one step forward in the identification of new potential circadian regulated genes highlighting the influence of circadian deregulation in cancer and the emerging evidences indicating the “circadian” immune functions in cancer development and progression.

P27-008-SP

SJL mice immunized with epstein-barr virus antigen LMP1 develop autoantibodies towards myelin basic protein

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Multiple Sclerosis (MS) is an autoimmune chronic inflammatory disease of central nervous system (CNS). At the present time it is evident that activation of B cells is necessary for pathology development. Despite numerous studies on autoreactive B cells and particularly characterization of autoantibodies still there is no actual description of pathologic autoimmune antibodies. One of the possible mechanisms of MS triggering is crossreactivity. It was shown earlier in our laboratory that myelin basic protein (MBP)-specific IgGs are cross-reactive with epstein-barr virus (EBV) protein LMP-1. Here using deep sequencing technique we characterized the common features of cross-reactive antibodies from human MS scFv phage-display library. Utilizing *in vivo* SJL mice model we showed that antibodies initially derived against viral protein LMP1 are able to recognize autoantigen MBP and thus might be the potential MS triggers or enhance its development. We further state that discovered cross-reactivity is rising mainly due to the production of autoantibodies recognizing both antigens simultaneously rather than consequent bystander activation.

P27-009

Taxonomic profile of type II NADH:quinone oxidoreductases and evolutionary implications

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Type-II NADH:quinone oxidoreductases (NDH-II) are membrane proteins involved in respiratory chains and recognized as suitable targets for novel antimicrobial therapies as well as potential therapeutic agents for human neurodegenerative diseases, including Parkinson's disease and aging, caused by complex I failures. This is because 1) NDH-II are the only enzymes with NADH:quinone oxidoreductase activity in many pathogenic organisms, both bacteria and protozoa and 2) its expression restores the mitochondrial activity in animals with complex I deficiency. Thus, in addition to understand their role in the bioenergetic metabolism, the investigation of NDH-II may have social repercussions, namely in health and quality of life. Using a thor-

ough sequence analyses we aimed at recognizing strictly or highly conserved structural elements (amino acid residues or motifs). We consider if a structural element is conserved and thus retained through evolution it has to be determinant for function. We also aimed to observe the enzyme distribution through the different taxonomic groups. We obtained a working data set with 2004 sequences. We observed that from 1804 species present at KEGG's database, 1033 (57%), distributed among the three domains of life (Eukaryotes 62%, Bacteria 60% and Archaea 25%), contain at least one gene encoding NDH-II. We further performed comparative studies using a range of bioinformatics approaches (amino acid sequence alignment, phylogenetic trees and weighted network), where different NDH-II features (number of copies *per* organism, clustering, quinone type) were analyzed. Our data provided the base to discuss the structural determinates for catalysis and substrate selectivity as well as to hypothesize an evolutionary scenario for NDHs-II.

P27-010

Alternative splicing of U2af26 and its role in circadian rhythm – a conserved function across the mammalian class

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Alternative splicing of the penultimate exon can increase the genomes coding capacity by generating a frameshift allowing translation into supposed 3'UTR. Within the mouse U2af26 gene, circadian exon skipping allows the generation of a novel extended C-terminus with homology to the drosophila clock regulator TIMELESS. This C-terminus destabilizes U2AF26 itself and the interacting core clock component PERIOD1 via proteasomal degradation. As a consequence, U2af26 knockout mice show defects in circadian gene expression and adaption to experimental jet-lag. Splicing of U2af26 is rhythmic in mouse and rat but a conserved circadian function across other mammalian species remained enigmatic. A comprehensive analysis of the last U2af26 exon revealed at least one ORF extending into the 3'UTR in each mammalian species with an annotated U2af26 gene. This includes two alternative C-termini for the human U2af26 gene; one accessible by usage of a conserved alternative 3' splice-site. Despite no or low sequence conservation, extended frames from elephant, rat, mouse and human dramatically decreased the half-life of GFP to below 3 hours. In addition, all analyzed instable C-termini – including human – destabilized the interacting PERIOD1 protein. Together these data suggest a conserved function of U2af26 in regulation of PERIOD1 stability and thereby the molecular clock across the mammalian class. We are currently investigating mechanistic principles that mediate the proteasomal degradation of the diverse C-termini. Strikingly all 61 analyzed prolonged C-termini contain exceptionally high amounts of proline, which might function as a novel signal for proteasomal degradation.

P27-011

Effects of hypoxia/anoxia on amylases activity, carbohydrate metabolism, and survival in saffron (*Crocus sativus* L.) corms

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Plants response to abiotic stresses is complex, involving regulatory network and circadian clock, and designed for the type of stress. Effects of hypoxia/anoxia by flooding were investigated in saffron corms with emphasis on α - and β -amylase activity, carbo-