FISV - Federazione Italiana Scienze della Vita

Program and Abstracts of the XIV FISV CONGRESS

Sapienza University of Rome, Italy

September 20 - 23, 2016

PSI.2 (Giacomini Hall)

14:30 - 16:00 **Genomics, Proteomics and Systems Biology**

Chairs: Lilia Alberghina, Diego Di Bernardo

Emanuele Bosi *(Florence)*
Comparative genome-scale modelling of *Staphylococcus aureus* strains identifies strain-specific metabolic capabilities linked to pathogenicity

Alexey Kolodkin *(Belvaux, Luxembourg)*
Dynamic networks dealing with oxidative stress: from design principles to personalised therapies for Parkinson's disease

Marco Montini *(Florence)*
Using CRISPR/Cas9 to determine the order of specific events in a cellular system

Marco Vanoni *(Milan)*
Multi-level modeling of Metabolism, Growth and Cycle in *Saccharomyces cerevisiae*

Domenico Raimondo *(Rome)*
Computational design of short linear D-tripeptides as binding moieties for protein pockets

16:00 - 17:30 **Transcription Mechanisms and Networks**

Chairs: Paolo Vincenzo Pedone, Giorgio Dieci

Flavia Bernardi *(Rome)*
Inhibition of Hedgehog-dependent tumors and cancer stem cells by a newly identified naturally occurring chemotype

Leonardo Gatticchi *(Perugia)*
Intracellular trafficking of labelled BODIPY-FF-MAS reveals nuclear lipid droplets localization

Ilaria Baglivo *(Caserta)*
A new DNA target site for transciption factors from *M. loti*

Susanna Ambrosio *(Naples)*
LSD1 mediates MYCN control of epithelial-mesenchymal transition through silencing of metastatic suppressor NDRG1 gene

Annapina Russo *(Naples)*
5-FU targets rpL3 to induce mitochondrial apoptosis via cystathionine-b-synthase in colon cancer cells lacking p53

Stefano Amente *(Naples)*
High-resolution genome profiles of 8-oxodeoxyguanine, gH2AX and NBS1 reveals their co-association at transcribed long genes

and identified a new DNA target site for the five transcription factors from *M. loti*. The new target sequence is located at -35 bp from the start codon of the *M. loti* gene called *exoy* encoding a crucial enzyme for exopolysaccharide (EPS) production. Biosynthesis of EPS are strictly connected with biofilm formation. Furthermore, we show, for the first time, the biofilm formation of *M. loti* and the attachment and detachment stages.

O8.4
LSD1 mediates MYCN control of epithelial-mesenchymal transition through silencing of metastatic suppressor NDRG1 gene

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Neuroblastoma (NB) with MYCN amplification is a highly metastatic tumor in children, and unraveling the key players involved in MYCN-induced invasion may identify new targets for therapy. Recently, we reported that Lysine Specific Demethylase 1 LSD1/KDM1A can form a tight complex with MYCN and this complex controls transcription of genes involved in MYCN-driven oncogenesis, proposing LSD1 as candidate therapeutic target in NB. RNA sequencing of NB cells treated with pharmacological LSD1 inhibitor (TCP) or LSD1 knockdown indicates that LSD1 affects Epithelial-mesenchymal transition (EMT) pathway, and we identify the *metastatic suppressor N-myc down regulated gene 1* (NDRG1), a potent metastasis suppressor, as a direct LSD1 target. We found that LSD1 co-localizes with MYCN at the promoter region of the NDRG1 gene and inhibits its expression; LSD1 knock down re-activates NDRG1 gene expression, with concomitant block of motility and invasiveness of NB cells. Our data suggest that LSD1 pharmacological targeting by small molecules could modulate invasiveness of cancer cells and knock down the ability of MYCN-amplified Neuroblastomas to metastasize, through NDRG1 de-repression.

O8.5
5-FU targets rpL3 to induce mitochondrial apoptosis via cystathionine-b-synthase in colon cancer cells lacking p53

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Recent findings revealed in cancer cells novel stress response pathways, which in response to many chemotherapeutic drugs causing nucleolar stress, will function independently from tumor protein p53 (p53) and still lead to cell cycle arrest and/or apoptosis. Since it is known that most cancers lack functional p53, it is of great interest to explore these emerging molecular mechanisms. Here, we demonstrate that nucleolar stress induced by 5-fluorouracil (5-FU) in colon cancer cells devoid of p53 leads to the activation of ribosomal protein L3 (rpL3) as proapoptotic factor. rpL3, as ribosome-free form, is a negative regulator of cystathionine-β-synthase (CBS) expression at transcriptional level through a molecular mechanism involving Sp1. The rpL3-CBS association affects CBS stability and, in addition, can trigger CBS translocation into mitochondria. Consequently apoptosis will be induced through the mitochondrial apoptotic cell death pathway characterized by an increased ratio of Bax to Bcl-2, cytochrome c release and subsequent caspase activation. It is noteworthy that silencing of CBS is associated to a strong increase of 5-FU-mediated inhibition of cell migration and proliferation. These data reveal a novel mechanism to accomplish p53-independent apoptosis and suggest a potential therapeutic approach aimed at upregulating rpL3 for treating cancers lacking p53.

O8.6
High-resolution genome profiles of 8-oxodeoxyguanine, gH2AX and NBS1 reveals their co-association at transcribed long genes

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The 8-oxo-7.8-dihydro-2'-deoxyguanine (8-oxodG) is one of the major oxidative modifications occurring to DNA coming from ROS-producing cell activities. There are constitutively several thousand residues of 8-oxodG in the nuclear genome of human tissues and cultured cells, however the genomic distribution has not yet fully characterized. Here, we applied a novel method named OxyDIP-Seq to analyze the genome-wide distribution of 8-oxodG at a single nucleotide level, using next-generation high-throughput sequencing technology. We mapped 8-oxodG distribution in human non-tumorigenic epithelial breast cell line MFC10A and querying 8-oxodG profiles for multiple genomic features. We found a non-stochastic distribution of DNA oxidation in the genome, rather a peculiar correlation between 8-oxodG residues and Polymerase II (Pol-II) coding genes was observed. We determined that spontaneous residues of 8-oxodG occur preferentially at gene body of Pol-II active genes. Moreover, ChIP-Seq analysis of gH2AX and *NBS1* showed a peculiar overlapping between 8-oxodG, gH2AX and *NBS*1. Indeed, we found accumulation of 8-oxodG, gH2AX and *NBS*1 expecially in long, transcribed and late-replicating genes. Our characterization of genome distribution of 8-oxodG reveals a rationale of gene fragility and suggests a potential mechanism linking transcription and DNA breaks.