8th SIBBM Seminar

Frontiers in Molecular Biology

# Epigenetics in Development and Disease

*Programme & Abstracts*

Palermo, 24-26 May 2012

# Sponsors


BIO-RAD


ITALIA s.r.l.
DBA
OTC AND SELF TESTING
ALLERGOLOGY
LAB PRODUCTS
PROFESSIONAL DEVICES
VETERINARY
MEDICAL SUPPLIES
SCIENTIFIC PRODUCTS


EuroClone
serving science through innovation


MERCK MILLIPORE


PerkinElmer
For the Better


QIAGEN


Roche


ACTIVE MOTIF
Tools to Analyze Nuclear Function
Vinci-Biochem

# Thursday, 24 May

14:00-14:15 **Welcome Address**
*Giovanni Spinelli (Director of STEMBIO, Palermo)*
*Valerio Orlando (SIBBM President)*
*Pier Paolo Di Fiore (ABCD President)*

## Session I » Environment, Stress & Epigenetics – *Chair: Davide Corona (Palermo)*

14:15-14:55 **Keynote Lecture:** *Sergio Pimpinelli* (*Rome*) Environmental stress, transposons and evolution

14:55-15:20 **EMBO YIP Lecture:** *Fabrizio D'Adda di Fagagna* (*Milan*) Molecular mechanisms of cellular senescence

15:20-15:45 *Stefan Schoeftner* (*Rome*) ncRNAs tune the function of mammalian telomeres

15:45-16:00 *Fabio Ciccarone (Rome)* Poly(ADP-ribosyl)ation acts in DNA demethylation of mouse primordial germ cells through DNA-damage independent roles

16:00-16:15 *Angelo Rosa (Trieste)* Structure and dynamics of interphase chromosomes

16:15-17:45 **Coffee break and Poster Session I**

17:45-18:00 *Dupriez Vincent* (*Perkin Elmer*) Homogeneous microplate format assays to monitor histone modifications in biochemical and cell-based assays

18:00-18:15 *(Merck presentation)*

18:15-18:45 **Science & Society Talk:** *Giuseppe Testa (Milan)* Reprogramming genomes and reframing rights

18:45-19:15 **Science & Society Talk:** *Enzo De Simone (Naplese)* How (and why) to expose high school students to the emerging concepts at the frontiers of molecular biology: five years experience with the "Eureka" project

# Friday, 25 May

## Session II » Chromatin Modifications & ncRNA – *Chair: Marco Bianchi (Milan)*

9:00-9:40 **Keynote Lecture:** *Marco Bianchi (Milan)* HMGB1 and the control of nucleosome number

9:40-10:05 **Armenise-Harvard Talk:** *Tiziana Bonaldi (Milan)* Mass Spectrometry approach dissects the proteomic landscape of chromatin functional domains

10:05-10:20 *Maria Cristina Onorati (Palermo)* An RNA memory mechanism to inherit epigenetic marks

10:20-10:35 *Elena Magnani (Busto Arsizio,VA)* CDH1 epigenetic regulation: a role for UHRF1 modulation via promoter associated non-coding RNAs?

10:35-11:00 Coffee break

11:00-11:25 *Davide Gabellini (Milan)* A long non-coding RNA links copy number variation to a Polycomb/Trithorax epigenetic switch in FSHD muscular dystrophy

11:25-11:40 *Francesca Munari (Göttingen, Germany)* Molecular basis of hHP1β/nucleosome interaction in dependence of histone 3 methylation

11:40-11:55 *Marco Di Stefano (Trieste)* Gene co-regulation and co-localization in human chromosome 19: a knowledge-based computational approach

11:55-12:15 **Progetto Bandiera - Coordinator talk:** *Giuseppe Macino (Rome)* The Italian Epigen Project

12:30-14:00 Lunch break

## Session III » Epigenetic Signaling in Development, Differentiation & Reprogramming – *Chair: Giovanni Spinelli (Palermo)*

14:00-14:40 **EMBO ABCD Lecture:** *Maria Pia Cosma (Barcelona, Spain)* Wnt signalling and the reprogramming of cell fate to pluripotency

14:40-15:05 *Michelangelo Cordenonsi (Padua)* The Hippo transducer TAZ confers cancer stem cell traits on breast cancer cells downstream of epithelial-to-mesenchymal transition and the deregulation of the cell polarity determinant Scribble

15:05-15:30 *Valerio Orlando (Rome)* Epigenetic control of Repetitive Elements mobilization contributes to cell differentiation and disease

15:30-15:45 *Cecilia Battistelli (Rome)* MyoD regulates p57kip2 expression by interacting with a distant cis-element and modifying a higher-order chromatin structure

15:45-16:00 *Paola Tognini (Pisa)* Experience-dependent expression of miR132 regulates ocular dominance plasticity

16:00-16:20 **Editor Talk:** *David del Alamo (The EMBO Journal, Heidelberg, Germany)* Behind the scenes of scientific publication

16:20-17:45 Coffee break and Poster Session II

## Session IV » Functional Epigenomics – *Chair: Valerio Orlando (Rome)*

17:45-18:25 **EMBO Lecture:** *Amos Tanay (Rehovot, Israel)* Hi-C and the hierarchical domain chromosomal topology

18:25-18:40 *Raffaele Giancarlo (Palermo)* The chromatin organization of an eukaryotic genome: sequence specific + statistical=combinatorial

18:40-20:00 General SIBBM Society & Board Meeting (SIBBM members only)

20:30 Social dinner (tickets available at SIBBM registration desk)

# Saturday, 26 May

## Session V » Epigenetics, Disease & Regenerative Medicine

*Chair: Irene Bozzoni (Rome)*

9:00-9:40 **Keynote Lecture:** *Irene Bozzoni (Rome)* The increase in complexity of the RNA landscape: new functions of non coding RNAs

9:40-9:55 *Anna Garbelli (Pavia)* A new paradigm for HIV-1 chemotherapy: targeting the host cell viral cofactor DDX3

9:55-10:10 *Federica Lo Sardo (Rome)* PcG-mediated higher order chromatin structures modulate replication programs at the *Drosophila* BX-C

10:10-10:25 *Anna Comel (Trieste)* Dissecting the tumor suppression activity of the bromodomain containing protein BRD7

10:25-10:40 *Italia Anna Asteriti (Rome)* A high-throughput imaging approach to study Aurora-A inhibition in human cell

10:40-11:00 Coffee break

11:00-11:25 *Gabriella Minchiotti (Naples)* Molecular control of satellite cell lineage progression and muscle regeneration through a novel Cripto -dependent mechanism

11:25-11:50 *Vania Broccoli (Milan)* Reprogramming cellular identity for *in vitro* modeling and replacement therapy of Parkinson's disease

12:00-12:30 Chiara D'Onofrio "Giovani" Award (prize to be awarded to the best Selected Talk) - Final Remarks & Departure

# Poster Abstracts

(presenting authors are shown underlined)

**P26**

## Cytotoxic effects induced by JA47, a novel histone deacetylase inhibitor (HDACi), on MDA-MB231 breast cancer cells

M. Librizzi[1], A. Longo[1], M. Agnello[1], J. Amin[2], J. Spencer[3], C. Luparello[1]
[1]Dipartimento STEMBIO, Univ. di Palermo, Italy
[2]School of Science at Medway, Univ. of Greenwich, United Kingdom
[3]Dept of Chemistry, Univ. of Sussex, United Kingdom

It is acknowledged that epigenetic alterations are involved in the repression of tumor suppressor genes and the promotion of tumorigenesis in cancers; for this reason, novel compounds endowed with HDAC inhibitory activity are considered as an attractive anti-cancer therapeutic approach. Here, we describe the biological effects induced by the novel HDACi JA47, an organo-metallic SAHA analogue [1] on viability/proliferation, cell cycle progression, apoptosis/autophagy induction and mitochondrial activity/ROS accumulation of a triple-negative highly-tumorigenic breast cancer cell line, MDA-MB231, taken as an in vitro model system of "aggressive" breast carcinoma. Viability and growth rate were determined using an MTT assay, and the results obtained strongly suggest that JA47 exerted a cytotoxic effect with an IC50 = 8.45 μM at 72 h. Different sets of experiments performed at 24 and 48 h of exposure to JA47 indicate that it induced a non-apoptotic cell death, as evaluated by an annexin assay, characterized by the accumulation of cells in the G1 and subG0 phases of the cycle. Moreover, we observed a prominent reduction of acidic vesicular organelles (AVO), hallmarks of autophagy, in JA47-treated cells, which may be related to a deprivation of energy supply indispensable for tumor cell survival. In addition, we also demonstrated that JA47 affected mitochondrial activity, as shown by a JC-1 assay, and triggered generation of reactive oxygen species; noteworthy, cytotoxicity was reversed in a dose-dependent manner by co-incubation with the anti-oxidant butylated hydroxytoluene. We conclude that JA47 plays a potential anti-tumoral role towards triple-negative breast carcinoma cells via autophagy down-regulation and oxidative injury.

1. Spencer et al. Synthesis and biological evaluation of JAHAs: ferrocene-based class I histone deacetylase inhibitors. ACS Med Chem Lett 2011; 2: 358-62