Two million dollars for science from the Armenise-Harvard Foundation

The return of two young researchers to IFOM and the University of Pavia

Boston-Florence, April 2013. The team of researchers funded by the Armenise-Harvard Foundation through the **Career Development Award** program is growing and now has 18 precious members. In fact, two more scientists are establishing their laboratories in Italy, **Vincenzo Costanzo**, who will relocate from London Research Institute to IFOM IFOM (Istituto FIRC di Oncologia Molecolare) in Milan, and **Federico Forneris** from the University of Utrecht who will come to the University of Pavia.

Vincenzo Costanzo will establish the DNA Metabolism research program at **IFOM, the FIRC Institute of Molecular Oncology** dedicated to studying the formation and development of tumors at the molecular level, with the goal of rapidly transferring results from the laboratory to diagnostic and therapeutic practice. Costanzo's laboratory will addresses one of the greatest challenges in contemporary biomedical research: investigating the role of essential proteins involved in genome stability and in DNA metabolism.
Cells respond to DNA damage by activating a biological process known as the DNA damage response. Defects in this process can lead to genomic instability, namely the inability to maintain the correct DNA structure, a characteristic typical of cancer cells.
The vast majority of proteins involved in the DNA damage response is implicated also in genetic syndromes with exceedingly diverse symptoms but all are united by a single characteristic: high susceptibility to cancer.
Costanzo's research aims to discover the roles of molecular factors of the DNA damage response in the DNA metabolism of vertebrates during DNA replication and repair, and as cells progress through the cell cycle. Costanzo will use a multidisciplinary approach, taking advantage of *in vitro* systems using cell-free extracts, mass spectrometry for analysis of protein-protein interaction circuits, antibody-based techniques, and advanced *imaging* techniques such as electron microscopy and *atomic force microscopy* for analyzing genome structure.
Costanzo's research will be conducted in light of comparative studies with human cells and will integrate analyses of metabolism and development in order to understand the role of DNA metabolism genes in broader aspects of cellular physiology. These studies will help determine the biological function and biochemistry of genes involved in essential processes that, when they do not work properly, can lead to the development of cancer.
At IFOM Vincenzo Costanzo will join Stefano Casola who set up his Molecular Immunology and Biology of Lymphoma laboratory here in 2006. For Costanzo it will be a return to Italy *sui generis*: at IFOM he will find a stimulating scientific community with one quarter of the researchers coming from 27 different countries, worldwide.

Federico Forneris, a structural biologist, will set up the **Armenise-Harvard laboratory of Structural Neurobiology** at the **Department of Biology and Biotechnology "Lazzaro Spallanzani" at the University of Pavia** to study important molecular mechanisms of intercellular communication.

"*For the second time, thanks to the Armenise-Harvard Foundation* - said **Angiolino Stella,** rector of the University of Pavia - *a brilliant young scientist engaged in molecular biology projects is returning to Pavia*. *The Armenise-Harvard Foundation is an example of extraordinary foresight and,*

for all of us, is an injection of confidence both in the ability of young people and in the research potential of Italian Universities, in this case of the University of Pavia and its interdisciplinary research."

"*The return to Italy of young researchers with proven capabilities, such as those who have won the Armenise-Harvard Career Development Award, is like a breath of fresh air for Italian Universities - said* ***Antonio Torroni****, vice-rector of research at the University of Pavia - not only because of the skills, enthusiasm and international financing they bring or attract, but also, and perhaps above all, for the positive signal and hope for the future that it sends to our young (and not so young) researchers or those who simply love scientific research*."

Forneris integrates diverse experimental techniques in his research (molecular and structural biology, biochemistry and biophysics) for the molecular characterization of multiprotein complexes and interpretation of their biological roles. Fascinated by the intricate mechanism of the formation of synapses, Forneris has planned his future research in the field of molecular biology of synapses, in particular the neuromuscular junctions.
Our ability to move and breathe depends on synaptic connections that transmit electrical and chemical impulses between nerve cells and muscles: the neuromuscular junctions. In the last thirty years, these junctions have been the subject of numerous studies that have identified many of the protein molecules responsible for the formation of these particular synapses. Malfunction of these synapses leads to a variety of diseases known as myasthenic syndromes. Myasthenia gravis is an important chronic autoimmune disease associated with neuromuscular junctions that causes severe disability and affects about 15-20 per 100,000 people. Unfortunately, today we still know very little about the processes that determine the formation of a functional neuromuscular synapse and how it transfers messages from neurons to muscles. Some of the proteins essential for these processes have only been identified in recent years, and have not yet undergone detailed molecular characterization.
Forneris will use diverse experimental techniques to investigate the structure-function relationships between various ligands and synaptic receptors at the molecular level, and will study their roles in the processes leading to the formation and stabilization of the neuromuscular junction. The data generated from this project will contribute substantially to future research programs that aim to identify molecules capable of counteracting the effects of neuromuscular diseases (including myasthenia gravis), with important consequences for the quality of life of patients with these pathologies.

At the University of Pavia, Federico Forneris will join Rosangela Sozzani, who established her Plant Physiology laboratory in the Department of Biology and Biotechnology "Lazzaro Spallanzani" in 2012 with support from Giovanni Armenise-Harvard Foundation.

WHAT IS THE GIOVANNI ARMENISE-HARVARD FOUNDATION?
The Giovanni Armenise-Harvard Foundation supports young scientists with special skills, contributing to the creation of new areas of life sciences research in Italy, by encouraging international mobility to promote a multidisciplinary culture and fostering deep collaboration between Italian scientists and Harvard Medical School (HMS) in Boston.
To date, the Armenise-Harvard Foundation has invested about $22 million in Italy, creating 18 laboratories for Career Development Award recipients, financing 3 PhD students at Harvard Medical School and presenting awards to 25 young science journalists.
The **Armenise-Harvard Career Development Award** currently consists of $200,000 per year for a period of three to five years, and includes remuneration commensurate with the position occupied at the host institution, salaries for other members involved in the research program and annual funding for equipment/infrastructure.

Important program dates:
Armenise-Harvard Career Development Award, apply by July 15, 2013
Armenise-Harvard PhD Program, December 2013
Armenise-Harvard Summer Fellowship for Italian University Students, apply before December 20, 2013
Armenise-Harvard Science Writer Fellowships, apply by March 15, 2014

For more information, please visit "http://www.armeniseharvard.org/grants/"
or contact Alexa Mason, Director of Italian Affairs, "mailto:amason@harvard.edu", tel. +39 055 603251.

WHO IS VINCENZO COSTANZO?

Born in Naples in '73, he graduated in Medicine and Surgery from the University of Naples Federico II in 1998. And it was there that Costanzo began his career as a researcher, conducting experiments in the cell biology of *Xenopus laevis*, a frog used as a model organism since the 60s.
After completing his PhD in Cellular and Molecular Biology and Pathology in 2002 at the University of Naples Federico II, Costanzo continued his career at Columbia University in the laboratory of Jean Gautier, an *Xenopus* expert who had helped set up this model for cell cycle research. There, Costanzo made an extraordinary discovery: a complete cellular DNA damage response can be reproduced by adding fragments of DNA to extracts of fertilized oocytes in a test tube. This was the first *in vitro* system for studying the biochemical functions of the proteins needed to replicate and repair DNA lesions. The discovery received wide coverage in the scientific community, such that in the 3 years between 2003 and 2006, Costanzo published six scientific articles in the most authoritative specialist journals.
In 2004, he moved to Cancer Research UK's Clare Hall Laboratories, considered to be among the world's most important institutions in for DNA research. There he was asked to establish a laboratory to study genome stability in vertebrates. By combining in vitro biochemistry with imaging techniques like electron microscopy, Costanzo was able to understand the mechanism of action of molecules fundamental for the life of the cell, such as Rad51, which is directly controlled by the BRCA-2 protein. Mutations in the BRCA-2 gene are associated with Hereditary Breast–Ovarian Cancer Syndrome. In London, he worked closely with Tim Hunt, Nobel Prize recipient in 2002 for cell cycle research, with whom he published important studies on the control of DNA replication. Costanzo's laboratory, has collaborated recently with the group of John Gurdon, Nobel Prize recipient in 2012 for discoveries on cellular reprogramming in Xenopus, which have recently led to the identification of molecules involved in the formation of embryonic stem cells. In his biography, Gurdon writes: "The best time to leave an institution is when you are at the peak of your career." - "This sentence particularly struck me, and in a sense it led me to leave Clare Hall, where I had a solid established group, and to start out on a new adventure."
In 2013, thanks also to the contribution of the Foundation Armenise-Harvard, he returned to Italy and started the DNA Metabolism research program at IFOM. "Here you breathe technology and research at the highest-level – comments Costanzo - The international environment and the network of collaboration established recently with leading Asian institutions are an added benefit: this connection gives us the opportunity to access powerful technologies and interact with brilliant minds from all over the world."

WHO IS FEDERICO FORNERIS?

Born in Cuneo in 1978, he graduated in 2002 from the University of Turin in Physical Chemistry after completing a one-year internship in Structural Biology with Professors L. Randaccio and S. Jeremiah at the CEB, the "Centro di Eccellenza di Biocristallografia" at the University of Trieste. He conducted his PhD studies in basic and applied biomolecular sciences at the University of Pavia "Istituto Universitario Di Studi Superiori", under the supervision of Professor A. Mattevi. During his PhD, he contributed to the discovery of histone lysine-specific demethylase LSD1, describing for the first time at the molecular level the enzymatic mechanism of histone demethylation and defining a new paradigm in chromatin molecular biology by showing that histone methylation is a dynamic process and not irreversible as had been thought for over 30 years. This discovery opened the way to numerous studies on the biological role of LSD1, which in the ensuing years would lead to the discovery that this enzyme has key roles in cell differentiation, with important implications in oncogenic processes. Subsequent attention on structure-function relationships between LSD1 and its interactors led to publication of the three-dimensional structure of LSD1 complexed with the co-repressor CoREST and the LSD1 substrate - the N-terminal region of histone H3. This important structure is still the basis of numerous efforts to develop compounds capable of inhibiting the enzymatic activity of LSD1 and possibly preventing or limiting the development of tumors.
Since 2009, Forneris has been working at the Bijvoet Center for Biomolecular Research at Utrecht University studying enzymatic mechanisms that activate the complement component of the immune system, in the group of Prof. P. Gros, winner of the prestigious Spinoza prize in 2010 for his studies on complement. Combining biophysics, biochemistry and structural biology, Forneris has determined the three-dimensional structures of important macromolecular complexes responsible for the activation and amplification of the complement immune response, providing a molecular explanation for the mechanisms that activate this complex immune defense system. Thanks to this structural characterization, studies are now underway to develop drugs in the fields of autoimmune, renal and cardiovascular diseases.
In 2013, he will return to Pavia, where he will establish the Armenise-Harvard laboratory of Structural Neurobiology in the Department of Biology and Biotechnology "Lazzaro Spallanzani" at the University of Pavia to pursue the ambitious goal of characterizing the mechanisms of synapse formation, an area of scientific research still almost completely unexplored at the molecular level.

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