

WE ARE SEEKING FOR MOTIVATED AND TALENTED CANDIDATES FOR 5 FELLOWSHIPS AVAILABLE IN THE PHD DOCTORATE PROGRAM IN BIOTECHNOLOGY (SCUOLA DI DOTTORATO IN BIOLOGIA E MEDICINA SPERIMENTALE, MOLECOLARE E CLINICA) OF THE UNIVERSITY OF GENOVA

YEARS 2010-2012.

All information will be soon available at <http://www.studenti.unige.it/postlaurea/dottorati/> and <http://www.sdobem.unige.it/>. For any further info refer to the e-mail indicated in each specific project below.

3 fellowship will be awarded by the Regione Liguria (indicated by an *), and will have an higher salary compared to the minimum indicated by MIUR.

The PhD students will be enrolled in one of the following projects:

*** Studies of biomineralisation process in marine invertebrates and achievement of new biomaterials for medicine and nanotechnology. Group leader: Marco Giovine**

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Advanced Biotechnology Center, Genova, Italy

The research activity will be focused on the study of the molecular pathways leading to the building of biosilica in marine sponges and of biocarbonates in corals. Laboratory models from marine invertebrates will be established for the "in vitro" production of biosilica and biocarbonates suitable for the production of new scaffolds for cell culture and for the production of new composite materials for optical applications.

Development and validation of a modular molecular platform for in vivo imaging and targeting. Group leader: Rodolfo Quarto

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Advanced Biotechnology Center, Genova, Italy

Aim of the project is the development and validation a platform of multifunctional fusion proteins for "in vivo" imaging and targeting. We plan to produce different polyspecific recombinant proteins to be used in tissue engineering and stem cells biology. The fusion protein design will have to consider the targeting of specific antigens expressed on the cell surface or deposited in the extracellular matrix. The protein fusion will have to carry molecules for imaging and or bioactive molecules to influence stem cell status governing their final fate.

Expertise in biochemistry, molecular and cell biology is necessary to carry on the project.

Role of microRNAs in the control of glycosylation processes and in the glycan function. Group leader: Michela Tonetti

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Dept. Experimental Medicine, University of Genova, Italy

This project will analyze the effects of microRNAs on expression and activity of key enzymes involved in the synthesis and processing of glycoconjugates. Particular interest

will be devoted to understand the effects of microRNA on the aberrant glycosylation observed in cancer cells.

***Development of immunoliposome based breast cancer therapy. Group leader Carlo Tacchetti**

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MicroSCoBiO Research Center, University of Genova and IFOM-IEO Campus, Genova

The receptor tyrosine kinase family (ErbB) of the EGFR is formed by 3 additional members, ErbB2 (HER2), ErbB3 (HER3), e ErbB4 (HER4). Activation of these receptors is followed by homo- or hetero-dimerization and a signal transduction whose amplitude, type and output is dependent on the composition of the dimer and the type of stimulus. Lack of regulation of the downstream ErbB signaling network correlated with the onset and progression of human carcinomas. Among these, the ErbB2 over-expressing breast cancer (*Breast-Ca_ErbB2⁺*) represents about 30% of breast cancers and is characterized by a fast progression, bad prognosis, high rate of metastasis and recurrence, and resistance to hormone- and chemo-therapy. In the recent years several molecular target therapy strategies have been developed to counteract the activity of ErbB family members.

In this project we propose to set up a *target-driven drug delivery* carriers based immuno-functionalized sterically stabilized liposomes (CCL). Liposomes, encapsulating doxorubicin (an effective but toxic anti-cancer agent), will be functionalized with single chain antibodies (VHH) directed to ErbB2. These antibodies are formed by a single heavy chain holding the specific antigen recognition site, without the need for coupling with the light chain, lack the CH1 region and consequently they are not recognized by the Fc receptor present on reticulo-endothelial cells.

We will test the possibility to deliver a conventional chemotherapeutic agent (i.e. doxorubicin) to cancer cells, evaluating the possibility to use this highly toxic, but anti-cancer effective antracyclins in a smart targeted manner.

This study requires interest and curiosity towards basic cell biology; the methodological approaches will consist of canonical cell biology technique, biochemistry, bioimaging, and use of both cell and animal model systems.

OA1 signalling pathway: role in melanosome biogenesis and melanoma progression. Group leader: Caterina Valetti

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OA1 is the gene responsible of Ocular albinism: albinisms are characterized by defects in production, organization and deposition of melanin pigment. Ocular albinism type I (OA1) patients do not show a rough alteration in the amount of melanin production, but rather a reduction in the total number and an increase in size of melanosomes. The enlarged melanosomes, i.e. macromelanosomes, do not form by fusion of several normal-sized melanosomes, but represent the overgrowth and uncontrolled melanin deposition inside a single organelle.

The protein product of the human OA1 gene has been characterized and our group has participated to its characterization. OA1 is an integral membrane glycoprotein of 404aa, with seven transmembrane domains and homologies with members of the GPCR superfamily. Unique among GPCRs, OA1 is primarily localized to the intracellular compartments of the endo-lysosomal and melanosomal system.

OA1 is activated by MITF, the master gene of pigmented cells, but new data obtained in our laboratory suggest a further hierarchy: we have evidence that OA1 protein can regulate MITF expression, mainly at the transcriptional level, and we are characterizing the molecular mechanisms through which it exerts its function.

Aim of this study is to define the physiological role for OA1: to define how OA1 controls the melanosome biogenesis and through which signaling pathway it exerts its function.

This study requires interest and curiosity towards basic cell biology; the methodological approaches will consist of canonical cell biology techniques such as primary cell culture, immunofluorescence, electron microscopy, biochemical analysis and DNA, mRNA manipulation and, above all things, the attempt to acquire a valid experimental approach.

***Integrative genomics of uveal melanoma. Group leader: Ulrich Pfeffer**

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Uveal melanoma is a rare malignancy that is molecularly distinct from cutaneous melanoma. Aim of the project is to develop a molecular classification of uveal melanoma through analyses of genomic alterations (array CGH) and mRNA and miRNA expression profiling, to explore its prognostic power and to identify targets of existing biological therapies. The project will be carried out in close collaboration with other groups who use genomic data to study the metastatic tropism and the immunophenotype of uveal melanomas.

Array CGH and mRNA expression profiling will be performed using our Affymetrix platform, miRNA studies will be carried out using in house spotting of microarrays. Bioinformatic analyses are based on R/Bioconductor.

The ideal candidate has a background in bioinformatics, genomics and/or molecular biology. He/she will work in the laboratories of our partners in Munich and Liverpool for a period of at least three months each.