

Department of Experimental Oncology

Pier Giuseppe PELICCI, M.D., Ph.D.

Chairman

STAFF **Chairman Advisor:** Claudio Basilico: M.D., Ph.D.
Group Leaders: Myriam Alcalay, M.D., Ph.D., Bruno Amati, Ph.D., Susanna Chiocca, Ph.D., Francesca Ciccarelli, Ph.D., Peter De Wulf, Ph.D., Pier Paolo Di Fiore, M.D., Ph.D., Gabriela Grigorean, Ph.D., Kristian Helin, Ph.D., Luisa Lanfrancone, Ph.D., Saverio Minucci, M.D., Heiko Muller, Ph.D., Andrea Musacchio, Ph.D., Gioacchino Natoli, M.D., Ph.D., Giuliana Pelicci, M.D., Ph.D., Pier Giuseppe Pelicci, M.D., Ph.D., Maria Rescigno, Ph.D., Giuseppe Testa, Ph.D., Rosella Visintin, Ph.D.

DEPARTMENTAL STAFF **Technologists:** Liliana Areces, Ph.D., Loris Bernard, Ph.D.
Technicians: Sara Barozzi, Rossana Bettolini, Maria Bono, Linda Cairns, Matteo Dal Molin, Lucia Massimiliano, Giada Matera, Tiziana Melis, Claudia Miccolo, Erika Mileti, Manuela Moia, Silvia Monzani, Ivan Muratore, Daniela Osti, Isabella Pallavicini, Alfonso Passafaro, Elena Prosperini, Francesca Refaldi, Simona Ronzoni, Carlo Alberto Russo, Domenico Sardella, Mirco Scanarini, Cristina Spinelli, Alessandro Verrecchia, Andrea Zanardi, Marika Zanotti
Veterinary Surgeons: Manuela Capillo, Alberto Gobbi
Laboratory Managers: Francesco Contegno, Brona Matoskova
Logistic support: Fabio Viridis
IT Service Manager: Alessandro Della Vedova
IT Service: Mauro Donadello, Ivan Lago, Stefano Leva, Serena Zanfini
Executive Director: Domenico Triarico
Management Control: Giovanni D'Angelo, Laura Massardi
Administrative Services Manager: Annalisa Ariesi
Administrative Assistants: Cristina Bonvicini, Paola Durin, Alessandra Parolini, Giovanna Rognoni, Monica Salvatore, Cristina Signoroni
Auxiliaries: Giuseppina Fiorenza, Giovanna Masarà, Filomena Minafra
Maintenance Responsible: Andrea Vignati

Activities 2007. The Department of Experimental Oncology (DEO) is composed of **eighteen independent research groups**, whose scientific endeavours are described under the pages dedicated to the individual Divisions and Units. The research groups are headed by Myriam Alcalay, Bruno Amati, Susanna Chiocca, Francesca Ciccarelli, Peter De Wulf, Pier Paolo Di Fiore, Gabriela Grigorean, Kristian Helin, Luisa Lanfrancone, Saverio Minucci, Heiko Muller, Andrea Musacchio, Gioacchino Natoli, Giuliana Pelicci, Pier Giuseppe Pelicci, Maria Rescigno, Giuseppe Testa, and Rosella Visintin. Piergiuseppe Pelicci has been acting as the Chairman of the DEO since its foundation in 1996. The scientific interests of the research groups in the DEO range from the molecular bases of regulation of the cell division cycle in normal and cancer cells, to the generation of animal models of tumors, to the development of bioinformatics tools to characterize the complexity of the unbalances of gene expression in cancer cells.

The Department of Experimental Oncology adopts an **open structure** model that inspires communication and collaboration between research groups. Its success relies on competitiveness in fundraising, at both the national and international level. Success in **fundraising** has been the key that supported the steady expansion faced by the DEO in the course of the last several years, which has brought the DEO from its original size of 5-6 research groups to the current organization with 18 groups and a variety of associated core facilities. Hiring of new group leaders has been possible thanks to competitive start-up packages including provisions to hire students and postdoctoral fellows and the possibility to use the many state-of-the-art core facilities of the DEO.

The members of the staff working in the **core facilities** deserve a special mention. These people represent the pulsing heart of the DEO and they provide researchers in the DEO with an array of centralized high-quality departmental services to perform common or more complex



tasks required in the everyday life of any laboratory. A permanent Staff Committee working under the constant supervision of the DEO laboratory manager, Francesco Contegno, controls the organization and management of the common activities of the DEO. The Staff Committee coordinates the work of specific Service Units. For each area of interest in the DEO, the various Units provide for the rationalization and monitoring of expenditures, and for the monitoring and improvement of the general organization of the DEO.

The Service Units include:

- **Cell Culture** (Giardina G., Cairns L., Dal Molin M., Melis T., Moia M., Spinelli C., Zanotti M.): It provides: maintenance and control of all Departmental cell lines, user-provided cell line and primary cell cultures; mass cultures of specific cell lines; set-up of new cell culture protocols; maintenance of cell culture room, aliquot preparation; rules implementation and orders.

- **Laboratory Supplies** (Verrecchia A., Miccolo C., Pallavicini I., Passafaro A., Prosperini E.): It provides chemicals, general supplies and radioactive reagents for general use of the Department.
- **Molecular Biology** (Bettolini R., Osti D., Sardella D., Zanardi A.): It provides enzymes, kits and other items related to molecular biology.
- **Biochemistry** (Massimiliano L., Matera G., Mileti E., Monzani S.): It distributes antibodies and reagents related to protein biochemistry of general usage.
- **Information Technology** (Dellavedova A., Donadello M., Lago I., Leva S., Zanfini S.): It maintains network and servers infrastructure, computers software, Help Desk, informatic counseling and courses.
- **Kitchen** (Fiorenza G., Masarà G., Minafra F.): It takes care of the glassware washing, ordering, storage and distribution of common plasticware and personal starter kit, production of solutions and reagents of general usage for the Dpt.
- **Technical Services** (Vignati A.): It provides maintenance and usage procedures of departmental instruments.
- **Chairman Office** (Ariesi A., Bonvicini C., Durin P., Parolini A., Rognoni G., Salvatore M., Signoroni C.): It provides scientific secretariat, general services and administrative procedures.

The IFOM-IEO Campus and the Molecular Medicine Program. During 2006, DEO has finalized the organizational and scientific plans for two strategic events that will occur within the first months of 2007 and that will profoundly change its structure: i) the moving of the Dpt laboratories to a new site, in proximity of IFOM, and the creation of the IFOM-IEO Campus; ii) the launching of the Molecular Medicine Program.

The IFOM-IEO Campus. Born from the vision of the Italian Foundation for Cancer Research, the FIRC Institute of Molecular Oncology (IFOM) brings together research teams from the best research institutions in the Milan area, including the IEO, the Università degli Studi di

IEO Administration Team at Campus IFOM—IEO



Milano, the DiBit-Ospedale San Raffaele, the Istituto Nazionale Tumori and the Mario Negri Institute. IFOM and the DEO are undergoing an integration of their scientific activities whose final act was the acquisition, by IEO, of a new research facility physically located in proximity of IFOM (in Milan, at the corner of Via Adamello and Via Serio, at 10' distance from the IEO hospital building).

Together, the IFOM and IEO research facilities consist of about 24,000 m² and will host about 400 researchers. The DEO laboratories will move to its new location at the beginning of 2007, creating, together with IFOM, one of the largest European research centers for

cancer research (IFOM-IEO Campus; <http://www.ifom-ieo-campus.it>). The campus hosts also the three PhD programs of the European School of Molecular Medicine (SEMM, <http://www.semm.it>) Foundation, focusing on: i) Molecular Medicine, ii) Medical Nanotechnology and iii) Foundations Of the Life Sciences, enrolling over 100 PhD students from around the world.

The Molecular Medicine Program: The recent development of Genomic Sciences has provided new conceptual frameworks and technological tools for the genetic classification of cancer and the discovery of novel approaches to the prevention, diagnosis and treatment of cancer. IEO has



launched a Molecular Medicine Program, hosted within the DEO, whose primary goals are the development of translational research and the creation of an active interface between the basic research programs of the IFOM-IEO Campus and the IEO clinical activities. Main goals of the Molecular Medicine Programs are: potentiation of the Tumor Bank and Tumor Registry, promotion of Phase 0 clinical trials for the rapid screening of new drugs, patient stratification and treatment personalization through the usage of genomic screens, stem cell research, cell therapy.

Technological Platforms and Facilities: DEO and IFOM have developed together a number of technological platforms, including genomic technologies. These activities have been placed within a Consortium (Cogentech) between IFOM and IEO, which is based at the IFOM-IEO campus. Cogentech has developed the following technological platforms:

DNA Services (Coordinator: Bernard L., Head Technician: Volorio S., Technicians: Riboni M., Tizzoni L., Sardella D., Capra F. Dall'Olio V., Ficarazzi F., Fortuzzi S., Mariette F., Pensotti V.): This facility masters DNA sequencing, human cDNA Library Colony Picking and Real Time PCR technologies. The Real Time PCR Service uses the very sensitive, accurate and reproducible quantitative PCR technique to measure the levels of gene expression by a relative quantification approach. The typical application is in validation of data coming from microarray experiments or in comparison of the RNA levels between two or more different systems.

Microarray (Coordinator: Minardi S., Technicians: Venturini E., Lassandro L., Rotta L.): This state-of-the-art facility routinely performs complete genomic microarray analysis for internal and external users using proprietary platforms such as Affymetrix and Nimblegen. The service includes the synthesis and labeling of targets, quality controls, hybridization, image acquisition, data analysis and elaboration using both commercial and proprietary software.

Model Organisms: Under the banner of "model organisms" are included several facilities, which provide researchers with the possibility to carry out certain experiments in animal model systems that are particularly suited to ask specific scientific questions. Among the more widely used animal facilities are i) the Mouse Genetics facility (Director: Gobbi A., Assistants: Giulini B., Capillo M., Natale G., Airaghi C., Cattaneo G., Mottura., Perrazza M., 5 Handy-workers), which is occupied with mice housing and caring, colony maintenance and expansion; ii) the Yeast Genetics facilities

(Director: Foiani M., 2 technicians), providing yeast models and libraries for synthetic lethality and other screening programs; iii) the *C. elegans* facility (Responsible: Kloess P., 2 technicians), providing researchers with the possibility to carry out screenings for mutants in the genetically friendly worm *C. Elegans*; and iv) the newly established Zebra Fish facility (Director: Mione M., 2 technicians).

Molecular Pathology Unit (Coordinator: Nuciforo P., Technicians: Luise C., Bianchi M., Capra M., Quarto M., Jodice G.): The goal of this facility is to identify novel putative cancer targets for drug discovery, diagnostic and/or prognostic applications. For this purpose, a high throughput screening technology (Tissue Microarrays, TMA) is used together with in situ detection methods (ISH and IHC) to rapidly translate early discoveries into clinical application. TMAs allow i) the validation of basic research findings, based on rapid and simultaneous analysis of thousands of patient's tissues; ii) an assessment of the prevalence of deregulation of target genes, based on comparative expression analysis between the tumor and the normal counterpart; iii) the identification of new diagnostic and prognostic markers, based on correlation of expression results with clinico-pathological and follow-up data; iv) the optimization of the drug discovery process, based on analysis at a cellular resolution level of human tissues samples representing the disease against which a drug is directed.

Mass Spectrometry Unit (Coordinator: Grigorean G., Technician: Soffientini P., Di Fonzo A., Maiolica A.): The Protein Analysis Unit aims to providing expert assistance in the design of experiments and data interpretation as well as scientific and technical knowledge in proteomics that will contribute to the research programs of all of the investigators at IFOM-IEO Campus. This will be accomplished providing tools for protein isolation, identification and characterization using mass spectrometry.

Protein Chemistry Unit (Coordinator: De Marco A., Tech-

nicians: Cinquanta M., Aliprandi M., Bossi S., Ossolengo G., Ami D., Capasso P., Monegal A. Venuto N., Martinelli C., Piccini D.): This Facility offers integrated services for the production and characterization of recombinant proteins. For instance, the facility can assist users wishing to attempt protein production in different microorganisms, such as bacteria, insect cells and yeast cells. It also maintains a collection of vectors, strains, and protocols, and is actively involved in the development of research tools for the optimization of protein production, for instance based on co-expression of molecular chaperones, use of chemical chaperones, optimization of in vivo and in vitro re-folding. This will be combined with biochemical characterization by several methods, including ITC, CD, Fluorimetry, N-terminal sequencing, Surface Plasmon Resonance. The facility will also help users generate monoclonal and polyclonal antibodies, and is developing recombinant antibody technology (panning and characterization of binders in ScFv and Vhh formats).

Imaging Unit (Coordinator: Faretta M., Units Resp.: Ronzoni S., Muradore I., Garrè M., Transidico P., Frittoli E., Barozzi S., Refaldi F.): This facility provides Fluorescence Microscopy, Cell Microinjection, Fluorescence Wide Field, Confocal and Time-Lapse Microscopy, FACS and Sorting technologies for researchers at the IEO-IFOM campus, thus providing access to optical technology for biomedical research. The provided services cover all the main needs of basic and advanced cancer research: flow cytometry and cell sorting, cell microinjection, wide field and confocal fluorescence microscopy, time-lapse microscopy, and digital image analysis basic and advanced applications (deconvolution, 3D rendering). The major objectives of the facility are i) setting up up, maintenance and development of optical technology for basic and advanced research; ii) providing of competent help in sample acquisition and analysis, including training on-site and assistance to advanced imaging applications; iii) performing independent and collaborative research for the development of advanced imaging- based technology.