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MUR

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Amendments or updates are in red

ALLEGATO 1 / ANNEX 1

Corso di Dottorato in
COMPLEX SYSTEMS FOR QUANTITATIVE BIOMEDICINE

PhD Programme in
COMPLEX SYSTEMS FOR QUANTITATIVE BIOMEDICINE

Coordinatore / Coordinator	Prof. Enzo MEDICO
Email Coordinatore/*Coordinator's email*	enzo.medico@unito.it
Dipartimento / *Department*	Oncologia / *Oncology*
Durata Corso di Dottorato / *Programme Length*	3 anni / 3 *years*
Sito web Corso di Dottorato / Programme website	https://phd-csqb.campusnet.unito.it/do/home.pl
Data inizio attività / *Programme start date*	1° novembre 2023 / 1st November 2023
Strutture / *Departments*	Dipartimento di Fisica, Dipartimento di Oncologia, Dipartimento di Scienze della Vita e Biologia dei Sistemi, Dipartimento di Scienze Cliniche e Biologiche, Dipartimento di Informatica, Dipartimento di Biotecnologie Molecolari e Scienze per la Salute, Dipartimento di Scienza e Tecnologia del Farmaco, Dipartimento di Scienze Mediche, Dipartimento di Neuroscienze "Rita Levi Montalcini", Dipartimento di Matematica "Giuseppe Peano", Politecnico di Torino. / *Department of Physics, Department of Oncology, Department of Life Science and Systems Biology, Department of Clinical and Biological Science, Department of Computer Science, Department of Molecular Biotechnology*

	and Health Science, Department of Pharmaceutical Science and Technology, Department of Clinical Science, Department of Neuroscience "Rita Levi Montalcini", Department of Mathematics "Giuseppe Peano", Polytechnic of Turin

Totali posti disponibili: n. 11, di cui n. 1 posto con borsa riservato ai/lle laureati/e all'estero / *Total number of available positions: no. 11, of which no. 1 with scholarship reserved to candidates holding a foreign degree*	
BORSE D.M. 117/2023 **DOTTORATI INNOVATIVI CHE RISPONDANO AI BISOGNI DI INNOVAZIONE DELLE IMPRESE (M4C2 I. 3.3)** ***PhD IN COOPERATION WITH INDUSTRIAL PARTNERS (M4C2 I. 3.3)***	
N. **2** posti con borsa **DM 117/2023** / *No. **2** positions with **D.M. 117/2023** scholarships*[1]	Di cui / *Of which*: n. 2 borse **M4C2 I. 3.3** (vincolate a progetto n. 1 e 18) / *no. 2* **M4C2 I. 3.3** scholarship *(bound to project no. 1 and 18)*;
BORSE ORDINARIE (FINANZIATE DALL'ATENEO O DA TERZI) ***STANDARD SCHOLARSHIPS (FUNDED BY THE UNIVERSITY OR THIRD PARTIES)***	
N. 8 posti con borsa di studio / *No. 8 PhD scholarships*[2]	Di cui / *Of which*: - n. 8 borse di Ateneo / *No. 8 PhD scholarships funded by the University of Torino;*
BORSE PNRR	
N. 1 borse PNRR Missione 4, componente 2	- n. **1** borsa Ecosistemi dell'Innovazione - EI (vincolata a progetto n. 19) / *no. 1 Innovation ecosystems scholarship - IEs 1 (bound to projects no. 19)*;

[1] Si noti che le borse D.M. 117/2023 sono vincolate alla presentazione di progetti specifici, i cui titoli sono elencati al fondo del documento / Please, note that D.M. 117/2023 scholarships are bound to specific projects listed at the end of the sheet.

[2] Eventuali borse aggiuntive e contratti di Apprendistato di Alta Formazione e Ricerca (Art. 45 D.lgs 81/2015), finanziati in tempi successivi alla pubblicazione del presente bando, saranno resi noti mediante pubblicazione sul sito della Scuola di Dottorato, entro la data di scadenza del bando/*Any additional scholarships and apprenticeship contracts (Legislative Decree no. 81/2015 art.45), which may become available after the publication of this Call, will be announced on the Doctoral School website until the Call's deadline*.

I documenti richiesti possono essere prodotti in inglese o italiano/ The required documents can be provided in English or Italian MODALITÀ' DI AMMISSIONE (titoli incluso progetto di ricerca + colloquio) / ADMISSION PROCEDURE (qualifications, including research project + interview)		
	Punteggio massimo / Score max	***Informazioni/ Documentazione per la candidatura Information/ Application documents***
TITOLI / ***QUALIFICATIONS***	***35***	
CV	10	CV redatto come da modello (allegato 2) / */ CV as per template (annex 2)* Incluse le **pubblicazioni** da caricare su piattaforma domanda (massimo 2) / *Including publications to be uploaded on application platform (max 2)* Incluse eventuali lettere di referenza (massimo 2)*/ Including any reference letters (max. 2)*
Progetto di Ricerca / *Research Project*	25	*Il **Progetto di Ricerca** deve essere scelto tra quelli proposti dal Dottorato nella lista sottostante* *Va allegato documento **in inglese** di massimo 8000 caratteri spazi inclusi, contenente le seguenti sezioni:* *I. (4000 caratteri): Progetto, con stato dell'arte, obiettivi, piano sperimentale, metodi, risultati attesi, bibliografia;* *II. (3000 caratteri): una breve lettera motivazionale;* *III. (1000 caratteri): un breve riassunto della tesi magistrale.* *The research project should refer to one of the listed research topics* *Please provide a document **in English** of maximum 8000 characters including spaces, containing the following sections:* *I. (4000 characters): The project, with: state of the art, objectives, plan, methods, expected results, bibliography;*

		II. *(3000 characters): a short motivational letter;* *(1000 characters): a short summary of the master thesis.*
Soglia minima per l'accesso al colloquio*/ Threshold to be admitted to the interview*	*20*	
COLLOQUIO / *INTERVIEW*	**65**	Il colloquio verterà sugli argomenti del progetto di ricerca / *The interview will focus on the research project*
Soglia minima per il superamento del colloquio */ Threshold to pass the interview*	*40*	

Titoli dei progetti di ricerca abbinati a borse: D.M. 117 (M4C2 I. 3.3)
Dottorato di Ricerca in Complex Systems for Quantitative Biomedicine

Research Topics bound to scholarships: D.M. 117 (M4C2 I. 3.3)
PhD Programme in* Dottorato di Ricerca in *Complex Systems for Quantitative Biomedicine

Per maggiori informazioni, contattare il referente scientifico / *For any further information concerning the research topics, please, contact the scientific director*

Progetto n. 1 / *Project n. 1*	
Titolo Progetto/ *Research Topic*	Molecular basis of the crosstalk between energy-stressed adipocytes and breast cancer cells.
Referente scientifico / *Scientific Director*	Michele De Bortoli
Lingua progetto/ *Project language*	*INGLESE / ENGLISH*
Descrizione sintetica / *Abstract*	Obesity is a well-known risk factor for breast cancer and has been shown to predict poor prognosis. However, the molecular basis of the crosstalk between energy-stressed adipocytes and cancer cells remains poorly understood. This proposal aims to elucidating the molecular mechanisms that control the remodeling of the adipocyte secretome in response to obesity and oxidative stress, and to investigate their role in modulating the crosstalk between adipocytes and cancer cells, with the goal of identifying innovative targets for developing therapeutic strategies aimed at reducing the pro-tumorigenic and metastatic impact of obesity. This project will be performed in partnership between the PhD Program in Complex Systems for Quantitative Biomedicine at UniTO and the Biochemistry and Cell Biology Department at Boston University. This will provide access to a diverse and international research community and provide ample training opportunities in molecular and cell biology techniques, as well as computational approaches for the analysis of omics data.

Progetto n. 18 / *Project n. 18*	
Titolo Progetto/ *Research Topic*	Application of artificial intelligence in the 3D reconstruction of electron microscopy images
Referente scientifico / *Scientific Director*	Ferdinando Di Cunto
Lingua progetto/ *Project language*	INGLESE / ENGLISH
Descrizione sintetica / *Abstract*	Volume electron microscopy (vEM) and tomography allow visualization of cellular structure and ultrastructure at its finest detail. By means of computational tools, the complex three-dimensional architecture of the brain and its cellular processes can be revealed down to its synaptic connections. Large scale mapping, for instance, revealed new connectivity patterns, thanks to connectomics, and 3D observations on organelles highlighted their intracellular strategic distribution, allowing scientists to confirm functional observations and nanolevel scale. This project will be focused on implementing new experimental and computational strategies for applying vEM to 3D reconstruction of data generated from mammalian and genetically tractable experimental models

Titoli dei progetti di ricerca abbinati a borse ordinarie
Dottorato di Ricerca in Dottorato di Ricerca in Complex Systems for Quantitative Biomedicine

Research Topics bound to standard scholarships
PhD Programme in Dottorato di Ricerca in Complex Systems for Quantitative Biomedicine

Per maggiori informazioni, contattare il referente scientifico / *For any further information concerning examinations, please, contact the scientific director*

Numero Titolo / *Topic number*	**Referente scientifico / *Scientific director***	**Titolo del progetto / *Project Title***	**Abstract del progetto / *Project Abstract***
n. 2	Michele Caselle	The role of gene duplication in shaping the Gene Regulatory Network	The aim of the project is to study the role of gene duplication events, and in particular the two rounds of whole genome duplication at the beginning of the vertebrate lineage, in shaping the human gene regulatory network. Exploiting current knowledge on duplication of protein coding genes, the project will focus on the identification of duplicated long non coding RNAs (lncRNAs) in the human genome and the mapping of their putative targets. We hope in this way to gain a deeper undestanding of the functional role of these lncRNAs.
n. 3	Francesca Cordero	Dissecting the origin of drug tolerance to anti-EGFR therapy in metastatic colorectal cancer.	Single-cell RNA sequencing allows the investigation of cancer cells at different functional states. This opens the opportunity to study the dynamics of functional heterogeneity within a tumor and its contribution to drug tolerance. However, the sensitivity of current state-of-the-art analytical approaches is not sufficient to discriminate between different transcriptional states in the context of a single lineage. The project aims to fill this gap by leveraging scRNA datasets from colorectal cancer organoids before and after therapy. The goal is to develop a new analytical approach for characterizing the different functional states that pre-exist treatment and their temporal evolution under therapy.
n. 4	Michele De Bortoli	System Biology approaches to investigate host-microbial interactions mediated by noncoding RNAs.	Noncoding RNAs are emerging as pivotal molecules in mediating the host-gut microbiota interaction in physiological and disease conditions. However, given the extensive heterogeneity of cellular populations in the gut ecosystem and possible molecular interactions,

			only systems biology methods applied on information from high-throughput experiments can provide insights on the RNA-mediated cross-kingdom communications. This project aims at implementing a systems biology strategy to characterize host-microbiota interactions mediated by noncoding RNAs by the analysis of transcriptomic, metagenomics, and metabolomics data.
n. 5	Piero Fariselli	Multimodal learning on biomedical data.	Adopting a multi-modal machine learning approach can yield substantial benefits in several prediction tasks, like time-to-event predictions and tumor subtypes classification in multifactorial and complex diseases. Using multiple biomedical sources also requires predictive models that clinicians can easily interpret. Therefore new methods are necessary to increase the prediction accuracy and enhance our comprehension of the disease. The project will aim to integrate different data types (e.g. multi-omics, histopathological images, electronic health records) through explainable structure learning (e.g. graph-neural networks) to address this methodological trade-off, testing on different types of diseases.
n. 6	Enrico Giraudo	Gene reprogramming of immune cells and cancer-associated fibroblasts induced by Semaphorin3A and its receptor PlexinA4: new target for immunotherapy in triple negative breast cancer and PDAC	By a multi-omics approach including Single Cell RNAseq and Spatial Transcriptomics the project is aimed to evaluate the molecular changes and cross-talk among the different cell types of tumor microenvironment ecosystem of triple negative breast cancer (TNBC) and PDAC induced by the treatment of Sema3A. We will dissect the differential gene expression and pathways governing the cross-talk among tumor vasculature, CAFs and immune cells and we will design and test novel combinatorial immunotherapy to hamper cancer growth in mouse models of TNBC and PDAC
n. 7	Claudio Isella	Identification of tumor-stroma interaction circuits by integrative analysis of bulk and single-cell RNA sequencing profiles from tumours and patient-derived cancer models	The tumor microenvironment plays a critical role in cancer progression, but understanding the interactions between cancer cells, stromal cells, and cancer-associated fibroblasts (CAFs) in colorectal cancer (CRC) is limited. This project aims to address this by using comprehensive RNA-seq to analyze both CRC cell lines mouse xenografts and patient-derived xenografts (PDX). The goal is to characterize distinct populations of cancer and stromal cells contributing to tumor growth and treatment responses. By integrating transcriptomic profiles from bulk and single-cell

			analysis, tissue architecture, and in vivo growth fitness, the study aims to shed light on tumor-stroma interactions and identify potential therapeutic strategies.
n. 8	Claudio Isella	Identification of candidate cancer neoantigens generated by aberrant RNA splicing and evaluation of their potential immunogenicity for RNA-mediated cancer vaccination.	Cancer immunotherapy has revolutionized treatment by using the immune system to target cancer cells. RNA vaccines have emerged as potent candidates, and this project focuses on developing them to target cancer neoantigens generated by alternative splicing. By analyzing genomic data, cancer specific alternative splicing events will be identified, leading to unique neoantigens with potential immunogenicity. RNA constructs encoding these targets will be synthesized and optimized for stability and delivery. A diverse experimental platform comprising over 600 cancer models will be used to validate the efficacy of the RNA vaccines. This project aims to uncover novel neoantigens for future clinical development.
n. 9	Enzo Medico	Experimental evaluation of therapeutically relevant tumor-stroma interactions in colorectal cancer	Tumor-stroma interactions play a significant role in cancer development, progression, and treatment resistance. Understanding the paracrine interactions between cancer cells and the tumor microenvironment can lead to the development of effective therapies. Systematic analysis of RNA-seq data of colorectal cancer tumors and patient-derived models will be employed to identify prominent candidates for tumor-stroma interactions, i.e. soluble factors released by cancer cells signaling to stromal cells, and the reverse. Subsequently, the project aims at experimental validation of candidate interactions through in vitro and in vivo experiments. The project will enhance our understanding of epithelial-mesenchymal interactions improving diagnosis, clinical management, and potentially identifying actionable targets.

n. 10	Francesco Neri	Analysis of the transcriptome, DNA methylome and gut microbiome in a novel colon cancer mouse model	Recent data suggest that colon cancer is influenced by aging and changes in the gut microbiome. In our laboratory we have recently developed a new mouse model of colon cancer that develops tumors in late life. The candidate will be involved in the analysis of the transcriptome and DNA methylation profile of tumor and healthy intestinal cells and microbiome of these mice. The project aims to investigate the causal link between the intestinal microbiome and the proliferation/differentiation of somatic and colon cancer stem cells. Moreover, we also want to develop models of epigenetic clocks that are specific for intestinal aging and colon cancer.
n. 11	Salvatore Oliviero	Multi-omics analysis to dissect the epigenetic control of differentiation in human brain organoids.	The objective of this project is to elucidate the specific roles of nuclear factors in modulating the epigenetic landscape and gene expression patterns in the control of cellular differentiation in a model of human brain organoid development. The mutants will be generated by CRISPR/Cas9 technology and the mutant hESC lines will be differentiated into brain organoids. We will perform multi-omics analysis, including genomics, transcriptomics, and epigenomics, on both mutant and control organoids at different time points during differentiation. These analyses will enable us to examine the global changes in gene expression, epigenetic modifications, and chromatin structure. This project will advance our understanding of the molecular mechanisms underlying epigenetic regulation and cellular differentiation in the human brain.
n. 12	Salvatore Oliviero	Role of DNA methylation in colon cancer.	DNA methylation is frequently altered in cancer, However clear understanding which are the regulatory events contributing to the tumorigenic processes of DNA methyltransferases and how they recognize their target sites is still missing. Aim of this project is to Identify the role of DNMT3B in colorectal cancer (CRC) and characterise the molecular interactions of DNMT3B in CRC. The approcah will be to perform loss of function gain of function experiments by CRISPR technology and analyse the resulting phenotype, pattern of expresion coupled with genomic analyses the molecular mechanisms that lead to aberrant DNA methylation in tumours and new molecular targets to fight cancer.

n. 13	Luca Primo	Development of quantitative approaches for studying signal trandsuction dynamics in 3D cultures	Recent studies have demonstrated that temporal activity of cell membrane receptors and downstream signaling nodes might be more informative than genomic-based stratification to predict the responsiveness to targeted therapie in cancer. Fluorescent biosensors can be used to report the activity of several intacellualr signalling components in real-time at the single-cell level, and this variation linked to differential degrees of drugs sensitivity between individual cells. We will apply to 3D cell spheroids and patient-derived organoids a multiplexed biosensor system that allows to image the dynamics of Erk and Akt activity as well as cell cycle entry.
n. 14	Alberto Puliafito	Quantitative approaches based on live imaging and single cell transcriptomics to dissect phenotypic heterogeneity in developing cancer organoids	Recent evidence points at a significant phenotypic heterogeneity in tumors, potentially influencing the response to drug treatments. Single cell transcriptomics represent the elective approaches to investigate such heterogeneity, and the project will encompass data mining and data analysis of single cell sequencing data. In order to dissect inter-tumor hyerarchies dynamics, fluorescent reporters will be used as a tool to follow phenotypic heterogeneity over time and detect underlying differentiation hyerarchies. To this aim quantitative image analysis pipelines based on digital image processing and machine learning will be developed to track single cells in growing cancer organoids.
n. 15	Dario Roccatello	Improving the research and clinical management of undiagnosed rare renal diseases with innovative decentralised data strategies and tools applied to artificial intelligence.	The Project mission is to prove the efficacy of innovative decentralised data strategies and tools in improving the integration of critical, highly-fragmented clinical data collected during standard clinical practice, and to apply them to the development of Artificial Intelligence for Undiagnosed Rare Renal Diseases (URRD) research and clinical management. The vision of project is that by applying innovative architectures, frameworks and governance strategies the linkage of real-world and research data across medical domains, institutions, and regions will be improved to the point where an enormous amount of federated data will be made available for transparent and safe use. This will enable new options for research, training, and for the development of Artificial Intelligence applications for data-based patient management. The project plans to validate the effectiveness of the strategy under study by implementing a demonstrator and focusing on the specific field of

			Undiagnosed Rare Diseases (URDs), pathologies for which no causative genetic variant was identified after an appropriate, highly sensitive test. The demonstrator will be centered on a set of AI-driven use-cases, including the innovative use of digital pathology imaging data. The use-cases will be relevant to the understanding ana management of URDs, with a focus on nephrological and immunological pathologies, and will include a recommendation system providing healthcare professionals with useful information, a decision support system aiding decisions, plus other two or more AI models investigating, more in general, genetic and non-genetic pathogenesis.
n. 16	Dario Roccatello	Immunothrombosis: Molecular Aspects and New Therapeutic Perspectives	Thromboinflammation or immunothrombosis is a concept that explains the existing link between coagulation and inflammatory response present in many situations, such as sepsis, venous thromboembolism, or COVID-19 associated coagulopathy. The purpose of this project is to provide further insghit of the current data regarding the mechanisms involved in immunothrombosis in order to understand the new therapeutic strategies focused in reducing thrombotic risk by controlling the inflammation.
n. 17	Ezio Venturino	Formulation and analysis of models to mitigate the negative effects that some human activities cause on human health	In an industrial environment, workers and populations living near a plant are exposed to adverse factors. The latter, e.g. chemicals or gases, may be potentially dangerous for the human health, posing high risks as after prolongued exposure. Often, a tumor incidence increase has been observed due to releases in the atmosphere by thermoelectric power-production facilities. Studying cures for these diseases is important; it would also be effective finding ways of lessening the problem at its onset, reducing emissions in the open and introducing ecofriendlier processes. The project, coherently with the tematics PNRR 2021-27, Salute bioeconomia, ambiente, and PNR Promozione della salute, prevenzione delle malattie, aims at building models to investigate and control such situations, reducing their impact.
n.20	Caterina Guiot	Iron and neurodegeneration: AI-based data	Iron plays an important role in promoting plaque formation and neuroinflammation in AD and PD. Iron detection from MRI imaging can be correlated with concentration in physiological fluids, istologic, genetic and metabolic

		analysis and modeling	biomarkers and clinical evidences in order to allow early prediction and more effective treatment. International database (e.g. UKBB, ADNI, ..) mining and advanced mathematical modeling are used to produce a predictive model to be challenged against data collected in ASO Molinette- Neuroscience Dept in Torino.

Titoli dei progetti di ricerca abbinati a borse PNRR
Dottorato in COMPLEX SYSTEMS FOR QUANTITATIVE BIOMEDICINE

Research Topics bound to NRPP scholarships
***PhD in* COMPLEX SYSTEMS FOR QUANTITATIVE BIOMEDICINE**

Per maggiori informazioni, contattare il referente scientifico o visitare la seguente pagina web / *For any further information concerning examinations, please, contact the scientific director or visit this webpage*.

Progetto n. 19 / *Project n. 19*	
Titolo Progetto / *Research Topic*	Developing AI-based methods for genomic variability interpretation, variant effect prediction and tumor subtyping. Evaluation and comparison of classical and quantum machine learning models.
Referente scientifico / *Scientific Director*	Piero Fariselli
Descrizione sintetica / *Abstract*	*The project aim is to develop AI-based methods that can be able to predict the impact of variants on protein stability and function. Furthermore, machine learning tools will be designed to identify tumour subtyping starting from different biological sources. Quantum machine learning models will be implemented and tested on specific tasks to evaluate their capability in contrast with classical approaches.*
Lingua progetto/ *Project language*	**INGLESE/ENGLISH**
Codice CUP / *Project Code*	B83C22003930001