POLITECNICO DI MILANO

PhD in INGEGNERIA DELL'INFORMAZIONE / INFORMATION TECHNOLOGY - 40th cycle

Research Area n. 1 - Computer Science and Engineering

PNRR 630 Research Field: MULTIMODAL DATA INTEGRATION AND COMPUTATIONAL APPROACHES FOR PRECISION MEDICINE OF AMYOTROPHIC LATERAL SCLEROSIS AND FRONTOTEMPORAL DEMENTIA

Monthly net income of PhDscholarship (max 36 months)
€ 1500.0
In case of a change of the welfare rates during the three-year period, the amount could be modified.

Context of the research activity	
Motivation and objectives of the research in this field	Amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD) are considered to be two manifestations of the same disease continuum. They are clinically heterogeneous, and approximately 50% of ALS patients developcognitive/behavioral changes in the FTD spectrum, while 5-10% of FTD patients develop ALS. Most ALS/FTD brains show aggregates of pathological TDP-43, which represent a unifying hallmark for these diseases. The exact mechanisms influencing the onset of ALS rather than FTD are still unknown. Therefore, it is crucial to develop reliable disease biomarkers useful to improve ALS/FTD clinical diagnostic accuracy, recognize disease subtypes and predictALS patients at risk of developing FTD and vice versa. To this end, we will analyze cerebrospinal fluid (CSF), serum,tears, skin and olfactory mucosa (OM) samples from patients with bulbar (bALS) or spinal ALS (sALS), FTD, and othernon-neurodegenerative neurological conditions (NNC). In particular, we will perform Next Generation Sequencing(NGS), Simoa, microfluidic, Bioplex, Seed Amplification Assay (SAA), metagenomics, Nuclear Magnetic Resonancespectroscopy of proteins (protein-NMR), and cell studies with the aim of creating specific disease biosignatures.

	Objectives: - To reveal distinct biomarkers useful to distinguish among bALS, sALS, and FTD phenotypes. - To generate robust biological fingerprints for ALS/FTD patients using an innovative biological approach that focuseson the analysis of CSF and other easily collectible tissues. - To computationally stratify patients and monitor the disease progression, and to evaluate the therapeutic efficacy inclinical trials, thus overcoming the limits of clinical interpretation. - To develop a predictive computational model based on the variables reported in the primary objective and thoseobtained from the analysis of the different biological samples by NGS, Simoa, Microfluid analysis, Bioplex, SAA,protein-NMR.
Methods and techniques that will be developed and used to carry out the research	Samples collected from 230 patients, divided as detailed below, will be analyzed. Retrospective data (RS): - Amyotrophic lateral sclerosis (ALS): sALS (n=45), bALS (n=12) - Frontotemporal dementia (FTD): n=30 - Other non-neurodegenerative neurological conditions (NNC): n=12 Prospective data (PS): - Amyotrophic lateral sclerosis (ALS): sALS (n=60), bALS (n=20) - Frontotemporal dementia (FTD): n=36 - Other non-neurodegenerative neurological conditions (NNC): n=15 The collected samples (CSF, serum, tears, skin and OM) will be subjected to the following analyses: Next GenerationSequencing (NGS), Simoa (to quantify NfL, tau, phospho-tau, and beta-amyloid proteins), Microfluidics (to determinemiRNA and long non-coding RNA profiles), Bioplex (to evaluate the innate-adaptive immunity pathway), Seedamplification assay (SAA, to detect peripheral pathological TDP-43), protein-NMR (structural characterization of theTDP-43 aggregates), and MiSeq Illumina (to analyze microbiota composition). The data will be processed and then integrated and

	analyzed through machine learning (ML) approaches, in collaboration with the Besta's Data ScienceCenter. Multiple ML classification algorithms will be trained and tested based on demographic, clinical, andinstrumental data (e.g. sex, age, comorbidities, disease duration and severity, cognitive status, MRI, DAT-SPECT, MIBG,FDG-PET).
Educational objectives	We are aimed at developing specific competence, autonomy, research methodology and skills, in an interdisciplinary environment. The strong connection with the Fondazione IRCCS Istituto Neurologico Carlo Besta (https://www.istituto-besta.it/english-version) makes one of the strength of our PhD. In fact, this PhD is fully developed within the JointResearch Platform NEUROTECH between Politecnico di Milano and Fondazione IRCCS Istituto Neurologico Carlo Besta, in support to the activities of the Computational Multi-omIcs of Neurological Disorders (MIND) joint lab.
Job opportunities	Career development is possible both in research, academic and private institutions, and in production, in Italy and abroad. Start-ups from research results are also encouraged. Employment in this area provides several opportunities.
Composition of the research group	0 Full Professors 2 Associated Professors 4 Assistant Professors 6 PhD Students
Name of the research directors	Marco Masseroli (PoliMi), Erika Salvi (Besta)

Contacts
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Additional support - Financial aid per PhD student per year (gross amount)	
Housing - Foreign Students	--
Housing - Out-of-town residents (more than 80Km out of Milano)	--

Scholarship Increase for a period abroad	
Amount monthly	750.0 €
By number of months	6

National Operational Program for Research and Innovation	
Company where the candidate will attend the stage (name and brief description)	Fondazione IRCCS Istituto Neurologico Carlo Besta
By number of months at the company	12
Institution or company where the candidate will spend the period abroad (name and brief description)	Department of Mathematics and Computer Science, ConsolidatedResearch Group "Artificial Intelligence and Biomedical Applications" (AIBA), Universitat de Barcelona
By number of months abroad	6

Additional information: educational activity, teaching assistantship, computer availability, desk availability, any other information
EDUCATIONAL ACTIVITIES (purchase of study books and material, including computers, funding for participation in courses, summer schools, workshops and conferences): financial aid per PhD student. TEACHING ASSISTANTSHIP: availability of funding in recognition of supporting teaching activities by the PhD student. There are various forms of financial aid for activities of support to the teaching practice. The PhD student is encouraged to take part in these activities, within the limits allowed by the regulations. COMPUTER AVAILABILITY: 1st year: Yes 2nd year: Yes 3rd year: Yes