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| Progetto di ricerca | “Modello di analisi del posizionamento strategico del settore manifatturiero italiano nelle tecnologie chiave per la decarbonizzazione”  
| | “Analysis model of the strategic positioning of the Italian manufacturing sector in key technologies for decarbonization” |
| Tipo/Type | Borsa PNRR cofinanziata ex D.M. 117/2023  
| | Scholarship PNRR co-funded ex D.M. 117/2023 |
| Borse/Scholarships | 1 |
| Abstract | Con le recenti proposte legislative in materia di sostenibilità, tra i quali emergono il Green Deal e Pacchetto Fit for 55%, la Commissione Europea intende assumere la leadership globale nella lotta ai cambiamenti climatici partendo dalla decarbonizzazione dell’economia. Secondo le stime delle valutazioni di impatto il raggiungimento degli obiettivi comporterà oltre quattromila miliardi di euro di investimenti nell’arco dei prossimi dieci anni a livello europeo e l’adozione di nuove tecnologie ancora sperimentali e particolarmente costose. Si tratta di un flusso di investimenti diretti senza precedenti in Europa che potrebbe rappresentare una significativa opportunità di sviluppo. Per questa ragione la Commissione europea ha formulato una proposta di Regolamento - Net Zero Industry Act (NZIA) - con l’obiettivo di implementare la capacità produttiva nelle otto tecnologie chiave per raggiungere gli obiettivi di sostenibilità. Si tratta di un nuovo indirizzo importante, che integra le attività di analisi di scenario energetico funzionali allo sviluppo dei Piani Energia e Clima introducendo accanto al trilemma – sostenibilità, sicurezza, efficienza – un quarto obiettivo rappresentato dallo sviluppo industriale. Questa nuova dimensione richiede di pianificare uno scenario di politica industriale per catturare le interazioni tra il sistema energetico e quello delle politiche di sviluppo. L’obiettivo del progetto di ricerca, in collaborazione con RSE Spa (ricerca del Sistema Energetico), è sviluppare all’interno di una Borsa di Ricerca del Dottorato di ricerca Business for Society e in stretta collaborazione con le competenze scientifiche del Di.SEA.DE un modello di analisi del posizionamento strategico del settore manifatturiero italiano nelle tecnologie chiave per la decarbonizzazione. Il modello è funzionale alla definizione dello scenario energetico del PNIEC e, al tempo stesso, in grado di comprendere le opportunità delle industrie coinvolte. Lo sviluppo di uno scenario di politica industriale presuppongne una mappatura delle principali filiere tecnologiche accanto alla valutazione del fabbisogno di investimenti diretti identificati dalle analisi di scenario energetico indicate dai modelli energetici previsionali, funzionali alle politiche di decarbonizzazione. Lo sviluppo di una mappatura delle filiere è funzionale a comprendere il posizionamento competitivo dell’industria italiana nei settori chiave indicati dalla politica comunitaria. Nello specifico assume particolare rilevanza il posizionamento dell’industria italiana all’interno della catena del valore nelle tecnologie chiave del NZIA. All’interno di questo approfondimento di ricerca dovranno essere identificati anche i nessi e le interdipendenze settoriali nazionali all’interno di un quadro di opportunità funzionale a garantire una effettiva riduzione della dipendenza strategica nello sviluppo della capacità produttiva di queste tecnologie. Questa analisi è funzionale |
a sviluppare la dimensione di politica industriale che dovrà integrare la predisposizione del PNEC con una politica incentivante e per colmare il deficit di capacità produttiva nelle tecnologie chiave con un modello specifico per la politica industriale italiana. Un modello di analisi industriale ha un ruolo fondamentale per la comprensione del funzionamento dei sistemi di politica industriale connessi alla costruzione di uno scenario base energetico. Infatti uno degli obiettivi delle analisi del sistema energetico sta nella valutazione delle relazioni che legano il settore energetico allo sviluppo industriale, per analizzare l’effetto sulla struttura produttiva dei cambiamenti nel sistema energetico, dovuti sia ad interventi esogeni da parte dei policy-makers sia all’innovazione tecnologica. Pertanto, il percorso di ricerca ha come obiettivo atteso il design e l’implementazione di un modello di politica industriale per le tecnologie chiave attraverso una mappatura delle filiere e delle interdipendenze del sistema produttivo italiano, per una maggiore integrazione con le politiche di innovazione tecnologica ed il relativo impatto socioeconomico. Le stime ottenibili rapprendono uno strumento integrabile con i modelli tecnici/energetici nella stesura dello scenario di decarbonizzazione, con la possibilità di analizzare l’impatto dello stesso sul sistema economico.

ENG

With the recent legislative proposals on sustainability, among which the Green Deal and the Fit for 55% package emerge, the European Commission intends to assume global leadership in the fight against climate change starting from the decarbonisation of the economy. According to the estimates of the impact assessments, the achievement of the objectives will involve over four trillion euros of investments over the next ten years at European level and the adoption of new technologies that are still experimental and particularly expensive. This is an unprecedented flow of direct investment in Europe which could represent a significant development opportunity. For this reason, the European Commission has formulated a proposal for a Regulation - the Net Zero Industry Act (NZIA) - with the aim of implementing production capacity in the eight key technologies to achieve sustainability objectives. This is an important new direction, which integrates the energy scenario analysis activities functional to the development of the Energy and Climate Plans by introducing a fourth objective represented by industrial development alongside the trilemma – sustainability, safety, efficiency. This new dimension requires planning an industrial policy scenario to capture the interactions between the energy system and that of development policies. The purpose of the research project, in collaboration with RSE Spa (research of the Energy System), is to develop within a Research Scholarship of the Business for Society research doctorate and in close collaboration with the scientific expertise of Di.SEA. DE an analysis model of the strategic positioning of the Italian manufacturing sector in key technologies for decarbonisation. The model is functional to the definition of the energy scenario of the PNIEC and, at the same time, able to understand the opportunities of the industries involved. The development of an industrial policy scenario presupposes a mapping of the main technological supply chains alongside the assessment of the need for direct investments identified by the energy scenario analyzes indicated by the forecast energy models, functional to decarbonisation policies. The development of a mapping of the supply chains is functional to understanding the competitive positioning of the Italian industry in the key sectors indicated by the Community policy. Specifically, the positioning of Italian industry within the value chain in the key technologies of the NZIA assumes particular importance. Within this in-depth research, the national sectoral links and interdependencies must also be identified within a framework of functional opportunities to ensure an effective reduction of strategic dependence in the development of the production capacity of these technologies. This analysis is functional to develop the industrial policy dimension that will have to integrate the preparation of the PNEC with an incentive policy and to fill the production capacity deficit in key
technologies with a specific model for Italian industrial policy. An industrial analysis model plays a fundamental role in understanding the functioning of the industrial policy systems connected to the construction of a basic energy scenario. In fact, one of the objectives of energy system analyzes is to evaluate the relationships that link the energy sector to industrial development, to analyze the effect on the production structure of changes in the energy system, due both to exogenous interventions by policy-makers and to 'technological innovation. Therefore, the research path has as its expected objective the design and implementation of an industrial policy model for key technologies through a mapping of the supply chains and interdependencies of the Italian production system, for greater integration with the policies of technological innovation and its socio-economic impact. The obtainable estimates represent a tool that can be integrated with the technical/energy models in drafting the decarbonisation scenario, with the possibility of analyzing its impact on the economic system.

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<th>Prof. Massimo Beccarello</th>
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**Specific IPR rules:** Intellectual property clauses agreed with the Company apply to this scholarship
Educazione nella Società Contemporanea

Education in Contemporary Society

| Progetto di ricerca | “Metodologie e modelli di blended learning nella formazione aziendale in materia di buona governance”
|                     | “Blended learning methodologies and models in corporate training on good governance themes”

| Tipo/Type           | Dottorato in Alto Apprendistato
|                     | High level training apprenticeship contract
|                     | OPERARI srl S.B.

| Borse/Scholarships  | 1

| Abstract            | ITA
|                     | Il progetto di ricerca avrà l’obiettivo di verificare l’efficacia di nuovi metodi di formazione per le aziende (prevalentemente e-learning e blended learning), incentrati sulle tematiche della buona governance. In linea con le previsioni dell’ISO 37000:2021 (Governance of organizations) “La buona governance pone le basi per il raggiungimento dello scopo di una impresa in modo etico, efficace e responsabile, in linea con le aspettative dei portatori di interesse”. I metodi formativi oggetto del progetto di ricerca vogliono discostarsi dalle modalità consuete di formazione, sia dal punto di vista della strutturazione dei corsi, che per il linguaggio utilizzato. La ricerca, attraverso un’analisi della letteratura e lo studio empirico condotto direttamente su un campione di aziende e di destinatari, mira a valutare la validità (in termini di efficacia formativa) dei diversi approcci innovativi alla formazione aziendale; tra questi, l’apprendimento basato sui giochi e la gamification e l’utilizzo di tecnologie digitali come la realtà virtuale e aumentata. Obiettivo del progetto è la raccolta di risultati che consentano di verificare come il cambiamento del metodo formativo adottato dalle aziende sia capace di condurre a un aumento della motivazione dei dipendenti e a una maggiore ritenzione delle informazioni apprese, che consenta quindi il consolidarsi di comportamenti virtuosi da parte delle aziende.

| Abstract            | ENG
|                     | The research project will aim to verify the effectiveness of new training methods for companies (mainly e-learning and blended learning), which focus on the topics of good governance. In line with the provisions of ISO 37000:2021 (Governance of organisations) ‘Good governance establishes the basis for the achievement of a company’s purpose in an ethical, effective and responsible manner, in line with the expectations of stakeholders’. The training methods covered by the research project are intended to break away from the usual training methods, both in terms of the way the courses are structured and in terms of the language used. Through a literature analysis and empirical study conducted directly on a sample of companies and target groups, the research aims to assess the validity (in terms of training effectiveness) of various innovative approaches to corporate training; these include game-based learning and gamification and the use of digital technologies such as virtual and augmented reality. The aim of the project is to collect results that will make it possible to verify how the change in the training method adopted by companies is capable of leading to an increase in employee
engagement and greater learning retention, thus enabling the consolidation of virtuous behaviour by the companies.

Inquadramento professionale di partenza: settore terziario livello 4
Inquadramento professionale d’arrivo: settore terziario livello 2
Numero ore settimanali: 40
Retribuzione lorda annuale: € 23.000
Retribuzione lorda mensile: € 1.642,86

Starting occupational classification: tertiary sector level 4
Target occupational classification: tertiary sector level 3
Number of hours per week: 40
Full annual salary: € 23.000,00
Full monthly salary: € 1.642,86

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| Fisica e Astronomia  
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| **Progetto di ricerca**  
| **Research project** |
| “Simulazioni di edge 3D tramite EMC3-EIRENE di DTT per lo studio dell’interazione tra il plasma ed i componenti affacciati in assenza di simmetria toroidale: antenne ICRH, parete interna conlimiter, gas-puffing, RMP sul divertore”  
| “Edge 3D simulations with EMC3-EIRENE of DTT to study interactions between the plasma and components in absence of toroidal symmetry”  
| DTT S.c. a r.l.  
|  
| **Tipo/Type**  
| *Borsa PNRR cofinanziata ex D.M. 117/2023*  
| Scholarship PNRR co-funded ex D.M. 117/2023  
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| **Borse/Scholarships**  
| *1*  
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| **Abstract**  
| ITA  
| I codici che analizzano il rilascio di potenza e l'interazione plasma-parete possono tipicamente utilizzare una rappresentazione 2D del plasma, sfruttando la simmetria toroidale insita nelle configurazioni magnetiche dei dispositivi Tokamak. Tuttavia, anche nei dispositivi con simmetria toroidale, ci sono situazioni in cui non è possibile descrivere il plasma in 2D a causa di componenti localizzati come limitatori, antenne di riscaldamento, iniettori di gas o il numero limitato di bobine. In questi casi, è necessario utilizzare codici limite 3D. EMC3 è attualmente il codice più utilizzato per gli studi 3D, grazie alla sua integrazione con il codice EIRENE, che descrive i neutroni emessi dalla parete o dal gas puffing. L’obiettivo del progetto di dottorato è imparare a utilizzare il codice EMC3 per studiare il rilascio di energia e l’interazione plasma-parete nei casi in cui la geometria 3D è importante. Una volta appreso e convalidato l’uso del codice negli esperimenti esistenti, si prevede di applicarlo principalmente per studiare l’interazione tra il plasma e componenti quali le antenne di riscaldamento e la parete interna con i rispettivi limitatori nel dispositivo DTT.  
| ENG  
| Codes that analyze power release and plasma-wall interaction can typically use a 2D representation of the plasma, exploiting the toroidal symmetry inherent in the magnetic configurations of Tokamak devices. However, even in devices with toroidal symmetry, there are situations where it is not possible to describe the plasma in 2D due to localized components such as limiters, heating antennas, gas injectors, or the limited number of coils. In these cases, it is necessary to use 3D boundary codes. EMC3 is currently the most widely used code for 3D studies, thanks to its integration with the EIRENE code, which describes neutrals emitted by the wall or gas puffing.  
| The objective of the doctoral project is to learn how to use the EMC3 code to study power release and plasma-wall interaction in cases where 3D geometry is important. Once the use of the code has been learned and validated in existing experiments, it is expected to be mainly applied to study the interaction between the plasma and components such as heating antennas and the inner wall with their respective limiters in the DTT device.  
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| **Tutor**  
| Prof. Giuseppe Gorini  
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**Specific IPR rules:** standard
### Fisica e Astronomia

**Physics and Astronomy**

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<td>“Data analysis with advanced machine learning techniques at the boundary between particle physics and medicine”</td>
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<th>Abstract</th>
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<td>Il dottorando sarà coinvolto in un progetto interdisciplinare che mira allo spin-off delle tecniche avanzate di analisi dei dati utilizzate nell'analisi dei dati della fisica delle particelle ad alta energia (HEP), principalmente basata sull'apprendimento automatico, nell'ambiente medico nel campo della prognosi di neoplasie basata su informazioni quantitative, come le caratteristiche radiomiche estratte da imaging. Il campo HEP offre set di dati molto grandi e perfettamente formatti, con una conoscenza dettagliata delle basi teoriche sottostanti, che consentono una chiara comprensione del loro flusso di dati lungo tutto il processo di analisi. Facendo leva su queste proprietà, lo studente applicherà in campo medico procedure di explainable artificial intelligence solitamente utilizzate per l'optimizzazione e la comprensione dell'apprendimento automatico e sfrutterà i campioni HEP per la convalida incrociata dei modelli di analisi dei dati sviluppati. I risultati della ricerca verranno poi anche valutati nella loro possibili applicazioni pratiche in ambito di ricerca clinica, ed anche degli aspetti specifici dei modelli di ricerca collaborativa pubblico-privato dell'industria farmaceutica. Il dottorando sarà inserito nel dominio delle applicazioni mediche attraverso i collegamenti esistenti del Politecnico di Milano, e nel dominio HEP attraverso quelli dell'Università Milano - Bicocca e dell'INFN, inclusa la possibilità di lavorare in stretta collaborazione con scienziati ed esperti di analisi dei dati presso i laboratori del CERN di Ginevra.</td>
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<td>The PhD student will be involved in an interdisciplinary project that aims at the spinoff of advanced data analysis techniques used in high-energy particle physics (HEP) data analysis, mostly based on machine learning, to the medical environment in the field of cancer prognosis based on quantitative information, such as radiomics features.</td>
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<td>The HEP field offers very large, perfectly formatted datasets, with a detailed knowledge of the underlying theory foundations, that allow for a clear understanding of the data flow all along the data analysis process. Leveraging on these properties, the student will apply explainable artificial intelligence procedures usually employed for machine learning optimisation and understanding to the medical field, and will exploit the HEP samples for cross-validation of data analysis models developed. The PhD student will be embedded in the domain of the medical applications through the existing connections of the Politecnico di Milano, and in the HEP domain through those of the Milano - Bicocca University and INFN, including the possibility to work in</td>
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close collaboration with scientists and data analysis experts at the CERN laboratories in Geneva.

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<th>Tutor</th>
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**Specific IPR rules:** standard
## Progetto di ricerca
### Research project

“Modeling cell-cell communication patterns applying machine learning techniques and spin glasses models to spatial transcriptomic data”

Ospedale San Raffaele S.r.l.

### Tipo/Type

Borsa PNRR cofinanziata ex D.M. 117/2023
Scholarship PNRR co-funded ex D.M. 117/2023

### Borse/Scholarships

1

## Abstract

ENG

Spatial transcriptomics techniques have the potential to rewrite the way we intend histology and pathological anatomy [1,2]. In fact, they can profile the cellular transcriptomes while retaining the spatial location within tissue with unprecedented throughput, possibly uncovering novel cell to cell molecular interactions, and their role in health and disease. The number of techniques and platforms to profile those data is continuously increasing, but specific software to analyze these datasets are still limited. To date, spatial data are analyzed using software created for single-cell analyses, with small adaptations. Moreover, considering that available techniques are limited either in terms of spatial resolution or genomic throughput, there is the need of integrating results from different platforms to retrieve a more complete view of a tissue [3]. To understand how cells patterning and gene-expression self-organize in space and time, we aim at developing a modeling strategy based on Ising spin glass models that, coupled with machine learning, will be able to encompass the hidden rules behind cellular organization in healthy and diseased tissues. Ising models have been developed during the last century to describe how atomic spins couple and generate extended and systemic-like behaviors like ferromagnetism and antiferromagnetism from simple local interactions [4]. Those models have been then extended to describe materials and systems with complex internal structures that are able to exhibit metastable states, and not only the lowest-energy configuration (spin glass models). Notably, the glass-like phases share with biological systems at least two fundamental features: historical memory and the resulting contingency and complexity [5]. For this reason, spin glass models have been applied to different fields of theoretical biology [6], from modeling of biological evolution to brain states. The aim of this project is to apply Ising spin glasses models to highlight the couplings between genes expressed in contact related cells and understand how they shape the spatial organization of tissues. Consequently, it would be possible to hypothesize how the disruption of specific interactions might determine diseased states and reflect into their tissue organization. Moreover, cell-cell and gene-gene communication patterns can help disentangle the common rule of tissue organization and might be used to integrate information from different spatial omics platforms, different patients, and different conditions, with the final aim of generating meta-representation of mammalian and human tissues.

In conclusion, spatial transcriptomics techniques allow scientists to indagate single cells transcriptomes in their native tissue context, allowing the discovery of new rule of organization of in healthy and diseased conditions.

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<th>Tutor</th>
<th>Prof. Alex Graudenzi</th>
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**Specific IPR rules:** Intellectual property clauses agreed with the Company apply to this scholarship.
| Progetto di ricerca | “Sviluppo di un nuovo approccio di gene editing per la cura della sindrome WHIM”  
“Development of novel gene editing strategy to cure WHIM syndrome” |
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| Tipo/Type          | Borsa finanziata da Ente esterno  
Scholarship funded by external Body |
| Borse/Scholarships | 1                                                                                                                                  |
| Abstract | ITA  
La sindrome WHIM è un'immunodeficienza autosomica dominante ereditaria causata da mutazioni nella sequenza codificante del recettore C-X-C 4 (CXCR4)1, con conseguente troncamento del recettore C-terminale e alterata internalizzazione. L’effetto di questa mutazione causa un mancato rilascio dei leucociti dal midollo dei pazienti con conseguente aumentata suscettibilità allo sviluppo di infezioni severe che possono portare a morte. La terapia risolutiva è il trapianto allogenico di HSC che rimane l'unico trattamento curativo2, sebbene limitato dalla disponibilità dei donatori. La terapia genica rimane una valida alternativa tuttavia essendo questa una malattia causata da un’aumentata attività della proteina, la terapia genica convenzionale non è adatta a questa malattia per ora. L’avvento del gene editing e in particolare la possibilità di correggere la base mutata nelle cellule staminali ematopoietiche (CSE) apre un nuovo scenario terapeutico. I “correttori a singola base” (base editors, BE) sono tecnologie emergenti che consentono la correzione delle mutazioni patogene riconvertendo il nucleotide mutante2,3. Diversamente dalle nucleasi, i BE permettono di correggere senza rotture del doppio filamento del DNA (double strand break, DSB), diminuendo così la tossicità sul DNA dovuta ad imprecisioni della modificazione genetica mirata. In WHIM, la mutazione più comune è l'R334X suscettibile di correzione genica mirata a singola base. In questo progetto, utilizzeremo un modello murino di malattia con tale mutazione nel gene CXCR4, recentemente sviluppato in un altro istituto da nostri collaboratori4, per ottenere la prova di principio in modelli animali di correzione della malattia.  
Obiettivi del progetto di ricerca: Al fine di valutare l’efficacia del nostro approccio di terapia genica ci proponiamo:  
1) valutare la soglia di cellule “sane” richiesta per correggere il difetto genico nel modello murino Cxcr4WHIM/+ mediante trapianti di cellule autologhe e percentuali crescenti di cellule wild type provenienti da topi missmatched per allele CD45.1.  
2) valutare l’efficacia di correzione della mutazione R334X nelle CSE murine mediante Base editing (ex vivo base editing). Verrà quindi valutata la ricostituzione immunologica dei topi.  
3) valutare l’efficacia di correzione della mutazione R334X nelle CSE murine mediante in vivo Base editing in topi Cxcr4WHIM/+  
4) valutare l’efficacia dei processi di mobilizzazione di CSE nel modello murino Cxcr4WHIM/+.  
References  

ENG

WHIM syndrome is an autosomal dominant primary immunodeficiency caused by gain-of-function mutations in the CXCR4 gene. WHIM mutations often truncate the intracellular C-tail of the CXCR4 protein, which results in desensitization to ligand-mediated internalization. WHIM hematopoietic cells show altered migration properties, which leads to neutropenia, hypogammaglobulinemia and myelokathexis due to leukocyte retention in the bone marrow and limited egression into the bloodstream. Therefore, patients suffer from recurrent infections, warts and are predisposed to cancers. Treatment options are aimed to improve leukocyte counts and decrease infection rates, while no definitive cure is currently available. In this project, we aim to establish a long-lasting therapeutic option for WHIM patients by leveraging on autologous transplantation of hematopoietic stem/progenitor cells (HSPCs) gene-corrected by means of innovative base editing strategies. To reach this goal, we will exploit the mouse model of WHIM syndrome recently generated by our collaborator Pereira to assess the ex vivo and in vivo efficacy of base editing strategy. To this goal in this PhD project we plan three following aims:

1) We will identify the minimal dose of wild type Lineage negative cells able to rescue the functional defects in the Cxcr4WHIM/+ mouse model
2) We will apply base editing strategy to murine Lineage negative cells and asses the efficacy of ex vivo gene therapy in the Cxcr4WHIM/+ mouse model
3) We will apply base editing strategy as in vivo gene therapy in the Cxcr4WHIM/+ mouse model and asses its efficacy in the Cxcr4WHIM/+ mouse model
4) We will test novel conditioning regimen based on the use of niche mobilization coupled to ex vivo or in vivo base editing strategies.

This project will provide preclinical proof-of-concept of feasible and efficient targeted base editing for gene correction of WHIM syndrome and will allow to develop novel clinically relevant editing strategies rapidly translatable to the treatment of other hematological diseases.

**Tutor**
Prof. Marta Serafini

**Mesi previsti in azienda/ Expected months at the company**
Da definire/To be defined

**Mesi previsti all’estero/ Expected months abroad**
Max 12

**Specific IPR rules:** Intellectual property clauses agreed with the Company apply to this scholarship
Medicina Traslazionale e Molecolare – DIMET
Molecular and Translational Medicine – DIMET

| Progetto di ricerca | "Terapia avanzata basata su cellule dendritiche antigene-specifiche per ristabilire la tolleranza nelle malattie immuno-mediate"
| Research project | “Advanced Antigen-Specific Dendritic Cell-Based Therapy to Re-establish Tolerance in Immune-Mediated Diseases” |
| Fondazione Telethon ETS |

| Tipo/Type | Borsa finanziata da Ente esterno |
| Scholarship funded by external Body |

| Borse/Scholarships | 1 |

| Abstract | ITA |
| Abstract | |

Le malattie autoimmuni sono attualmente trattate con terapie immunosoppressive e di supporto, che modulano l'infiammazione, ma non fermano la causa della malattia. Tali trattamenti sono necessari per tutta la vita. Pertanto, rimane importante identificare nuove terapie sicure ed efficaci per queste malattie, che siano ben tollerate e che targhettino le cause della malattia. Le terapie cellulare a base di dendritiche tollerogeniche (tolDC) offrono la possibilità di ripristinare la regolazione immunitaria portando ad effetti di lunga durata. Studi preclinici hanno dimostrato che le tolDC modifiche con VitD3 (VitD3DC) pulsate con peptidi derivati dalla mielina generate sia da pazienti affetti da sclerosi multipla (SM) che da donatori sani (HD) promuovono l'iporeattività delle cellule T specifiche per Ag e stimolazioni ripetute in vitro delle cellule T da parte di Ag-pulsed VitD3DC promuovono l'induzione di cellule Treg Ag-specifiche che sopprimono indirettamente le risposte delle cellule T effettrici attraverso la modulazione di cellule DC. Tuttavia, non è stato dimostrato un effetto potente e diretto delle Ag-pulsed VitD3DC per promuovere il differenziamento diretto di cellule Treg Ag-specifiche. Ag-pulsed VitD3DC sono state utilizzate in studi clinici di fase I in pazienti con forme attive di SM e i risultati preliminari hanno mostrato che il trattamento con VitD3DC è sicuro e ben tollerato, senza effetti avversi gravi riportati; tuttavia, il trattamento non ha fermato la malattia. La manipolazione genetica di VitD3DC rappresenta un approccio innovativo per generare cellule con una capacità più potente ed efficace di promuovere Treg Ag-specifiche, migliorando nel complesso il loro potenziale e efficacia tollerogenica. Tra le diverse strategie applicate per generare efficaci tolDC umane con la capacità di promuovere Tregs, il condizionamento IL-10 è stato identificato come l’approccio più adatto. Recentemente, sono state generate tolDC ingegnerizzate con IL-10 che modulano le risposte delle cellule T specifiche per allog, promuovono le cellule Tr1 specifiche per allog, sono stabili all’attivazione (Comi et al. Frontiers in Immunology 2020). Pertanto, ipotizziamo che esista il potenziale per aumentare le proprietà tollerogeniche di VitD3DC tramite il trasferimento del gene IL-10 migliorando la loro capacità di promuovere le cellule Tregs di tipo 1 (Tr1) Ag-specifiche. Lo scopo del progetto è lo sviluppo e la validazione di un nuovo prodotto cellulare tolDC basato su VitD3DC geneticamente ingegnerizzate. Genereremo VitD3DC ingegnerizzate e le caratterizzeremo fenotipicamente e funzionalmente mediante citometria a flusso valutando l'espressione di marcatori associati alle DC che producono VitD3DC e IL-10 (e.g., CD14, CD16, CD141, CD163, HLA-G, ILT4, CD86, PDL1 ) e mediante MLR (test di proliferazione, espressione di marcatori di attivazione e produzione di citochine). Inoltre, per valutare la capacità della VitD3DC ingegnerizzata di indurre il differenziamento delle cellule Tr1, faremo co-cultura di VitD3DC ingegnerizzate con IL-10 e cellule T CD4 allogene valutando, dopo 10 giorni, la presenza di CD49b+LAG-3+.
Autoimmune diseases are currently treated with immunosuppressive and supportive therapies, which dampen inflammation, but do not stop the cause of the disease and are required life-long. Thus, there is an unmet need for safe and effective therapies for these diseases, which are well-tolerated and targeting the cause of disease. Tolerogenic dendritic (tolDC) cell-based therapies, offer the possibility of restoring immune regulation leading to long-lasting effects. Preclinical studies showed that VitD3-modified tolDC (VitD3DC) pulsed with myelin-derived peptides from both Multiple Sclerosis (MS) patients and healthy donors (HD) promote Ag-specific T cell hypo-responsiveness, and in vitro repetitive stimulation of T cells by Ag-pulsed VitD3DC promote Ag-specific Tregs that indirectly suppress T cell responses through DC modulation. However, thus far a powerful and direct effect of Ag-pulsed VitD3DC to promote Ag-specific Tregs is so far not realized. VitD3DC pulsed with myelin-derived peptides has been tested in Phase I clinical trials in patients with active forms of MS, and preliminary results showed that VitD3DC treatment is feasible, safe, and well-tolerated, with no severe adverse effects reported; however, the treatment did not stop the disease. Genetic manipulation of VitD3DC represent an innovate approach to generate cells with a more potent and effective ability to promote Ag-specific Tregs, overall improve their tolerogenic potential and efficacy. Among the different strategies applied to generate effective human tolDC with the ability to promote Tregs, IL-10 conditioning has been identified as the best-suited approach. Recently, IL-10-engineered tolDC that modulate alloAg-specific T cell responses, promote alloAg-specific Tr1 cells, are stable upon activation have been generated (Comi et al. Frontiers in Immunology 2020). Thus, we hypothesize that there is potential to boost VitD3DC tolerogenic properties via IL-10 gene transfer improving their ability to promote Ag-specific Tr1 cells and the balance between tolerance and (auto)immunity to restore immune homeostasis in MS patients. The aim of the project is the development and validation of a new tolDC based on gene engineered VitD3DC for immunotherapy approaches. We will generate engineered VitD3DC and we will characterize them phenotypically and functionally by flow cytometry assessing the expression of VitD3DC and IL-10-producing DC associated markers (e.g., CD14, CD16, CD141, CD163, HLA-G, ILT4, CD86, PDL1) and by MLR (testing proliferation, expression of activation markers, and cytokine production). Furthermore, to assess the ability of IL-10-engineered VitD3DC to drive Tr1 cell differentiation we will perform the co-culturing of IL-10-engineered VitD3DC and allogeneic CD4 T cells evaluating, after 10 days, the presence of CD49b+LAG-3+ Tr1 cells, cytokine profile (e.g., IL-10, IL-4, IFN-g), and ability to suppress T cell responses. Results will lead to define whether upon IL-10 gene transfer VitD3DC will acquired the ability to promote Ag-specific Tr1 cells.

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<th>Tutor</th>
<th>Prof. Marta Serafini</th>
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<td>Mesi previsti all’estero/Expected months abroad</td>
<td>Max 12</td>
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**Specific IPR rules:** Intellectual property clauses agreed with the Company apply to this scholarship
### Abstract

Gene therapy aims to produce a therapeutic effect through the manipulation of gene expression or through altering the biological properties of living cells, through the delivery of exogenous genetic material (e.g., DNA, mRNA and siRNA). This concept is explored for several multifactorial diseases such as cancer, cardiovascular, blood, neurological and immune disorders. In particular, the recent advent of COVID-19 vaccines by Pfizer and Moderna boost significantly the interest around mRNA-based therapies. This approach, in fact, has numerous advantages over the use of DNA, including reversibility, specificity, activity in both dividing and non-dividing cells, lack of integration, greater efficacy and easier design and synthesis of "interfering" or "antisense" molecules. However, it is crucial to consider that to be effective after in vivo administration, mRNA require to overcome various extracellular barriers (e.g.: rapid degradation, presence of biological barriers to be overcome, i.e. endothelia) and gain the cellular entry. RNA-based therapy, has delivered numerous progress to the treatment of diseases thanks to the development of lipid nanoparticles (LNPs) as a delivery vehicle and their modifications aimed at improving complex stability during systemic delivery, implementing targeted delivery, and increasing transfection efficacy. Although several LNPs formulations have been approved for this purpose, there are several tricky barriers for complexes with a therapeutic genetic construct, represented by the cell membrane, endosome, and nuclear membrane (in the case of delivery of therapeutic genes). Therefore, an improvement of RNA delivery systems is needed. Given these premises, the aim of this project is to develop alternative platforms for mRNA delivery opening up new treatment possibilities. In particular, the activity of the candidate aims to design delivery systems with a specific targeting, which can be synthesized with scalable processes, taking advantage of biocompatible materials. Specifically, an improvement in the design of liposomes, niosomes and hybrid polymer-lipid nanoparticles for siRNA and mRNA delivery will be required.
**Psicologia, Linguistica e Neuroscienze Cognitive**  
**curriculum Mente, Cervello e Comportamento**  

**Psychology, Linguistics and Cognitive Neurosciences**  
**curriculum Mind, Brain and Behaviour**

<table>
<thead>
<tr>
<th>Progetto di ricerca</th>
<th>“Effects of virtual reality-based Behavioral Rehabilitation and Activation with Innovative Neurostimulation techniques on DRIVING skills in older adults and MCI patients”</th>
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| Tipo/Type            | Borsa PNRR cofinanziata ex D.M. 117/2023  
Scholarship PNRR co-funded ex D.M. 117/2023  
Casa di Cura Igea S.p.A. |
| Borse/Scholarships   | 1 |
| Abstract            | ENG  
Due to the multitasking nature of driving, drivers are physiologically distracted by both relevant and irrelevant environmental stimuli. Visual selective attention, namely the ability to select relevant stimuli and suppress irrelevant distractors, is anatomically mediated by the (right) dorsal fronto-parietal attentional network, with the frontal eye field (FEF) having a crucial role. Furthermore, non-invasive brain stimulation techniques (NIBS) have proven effective in fostering attentional abilities, by decreasing the negative effects of task-irrelevant distractors. A recent study recruiting young healthy participants demonstrated an effect of one-session high-definition tDCS (HD-tDCS) delivered over FEF, compared to conventional tDCS and sham stimulation, in attentional response during an ecological Virtual Reality (VR) driving simulator task (Lega et al., under revision). In particular, participants improved their performance in two different tasks, responding faster after HD-tDCS: i) to brake light events of a preceding car in front of them while driving; ii) in case of distractors (road signs of countries and cities) that appeared together with braking lights or alone. Even stronger results were obtained with the same paradigm on healthy older adults (Lega et al., in preparation). The aims of the present Ph.D. project are to extend these findings to a population of Mild Cognitive Impairment (MCI). Age-related cognitive decline is often associated with unsafe driving behaviour and increasing crash risks, being more significant in case of MCI. A second phase of the project will include the implementation of a rehabilitation program with multiple, repeated tDCS sessions, using the methodology that has proven most effective in reducing interference from irrelevant distractors, thereby improving driving skills assessed through an ecological VR driving simulator for older adults and MCI patients. |
| Tutor               | Prof. Roberta Daini |
| Mesi previsti in azienda/Expected months at the company | 18 |
| Mesi previsti all’estero/Expected months abroad          | 6 – 12 |
| Specific IPR rules: | standard |
### Progetto di ricerca

**Research project**

"Valutazione dell'impatto dell'inquinamento atmosferico sull'incidenza di malattie cardiovascolari e loro complicanze in regione Lombardia”

“Evaluation of the impact of air pollution on the incidence of cardiovascular diseases and their complications in the Lombardy region”

**Istituto di Ricerche Farmacologiche Mario Negri IRCCS**

### Tipo/Type

Borsa PNRR cofinanziata ex D.M. 117/2023

Scholarship PNRR co-funded ex D.M. 117/2023

### Borse/Scholarships

1

### Abstract

**ITA**

L'inquinamento atmosferico è considerata una delle più grandi minacce ambientali per la salute dell'uomo. Infatti è nota la correlazione tra gli agenti inquinanti (ad es. PM10, PM2.5, NO2, O3) e l'insorgenza di diverse malattie quali, in particolare, le malattie respiratorie ed i tumori, ma anche le patologie cardiovascolari. In particolare una correlazione con l'insorgenza di queste ultime, che rappresentano la principale causa di mortalità e morbilità a livello globale, ha un impatto rilevante sia direttamente sui soggetti interessati che sul sistema sanitario in termini di costi dovuti ad ospedalizzazioni, consumo di farmaci e prestazioni ambulatoriali. Il contesto geografico della regione Lombardia è di particolare interesse a causa di una circolazione dell'aria estremamente ridotta. L'attività del dottorando sarà finalizzata a valutare la correlazione tra l'esposizione agli inquinanti atmosferici e l'incidenza di malattie cardiovascolari e di loro complicanze in regione Lombardia mediante l'utilizzo di diversi disegni epidemiologici tradizionali e innovativi. Le fonti di dati utilizzate per la stima delle associazioni saranno da una parte i dati contenuti nei database sanitari regionali, ovvero dati anagrafici, prescrizioni farmaceutiche, ricoveri, interventi, esami e visite ambULATORIALI, e dall'altra i dati estratti da sistemi di monitoraggio territoriali degli inquinanti atmosferici, come ARPA, ISPRA, Copernicus, Air Quality Index. Utilizzando questi dati il dottorando dovrà studiare come i periodi di esposizione agli agenti inquinanti e le caratteristiche del soggetto possano essere sfruttati per sviluppare algoritmi di previsione del rischio di incidenza di malattie croniche. L'analisi di questi dati richiederà l'uso di pacchetti informatici dedicati all'analisi di grandi moli di dati e la conoscenza di modelli bio-statistici avanzati. La specificità dei dati imporrà l'utilizzo di tecniche di analisi, eventualmente bayesiane, che considerino l'associazione fra inquinante e incidenza di malattia tenendo in considerazione la variabilità spazio-temporale, ovvero alla luce della presenza di clustering spaziale composto con la contemporanea presenza di variabilità temporale, sia a breve termine a seguito di eventi meteorici, che a lungo termine determinata da variazioni stagionali ricorrenti.

**ENG**

Air pollution is considered one of the greatest environmental threats to human health. In fact, there is a known correlation between pollutants (e.g. PM10, PM2.5, NO2, O3) and the onset of various diseases such as, in particular, respiratory diseases and tumors, but also cardiovascular diseases. In particular, a correlation with the onset of the latter, which represent the main cause of mortality and morbidity globally, has a significant impact both directly on the subjects involved and on the health system in terms of costs due to hospitalizations, drug consumption and outpatient services. The geographical context of the Lombardy region is of particular interest due to an extremely reduced air circulation. The PhD student’s activity will be aimed at evaluating the correlation...
between exposure to air pollutants and the incidence of cardiovascular diseases and their complications in the Lombardy region through the use of different traditional and innovative epidemiological designs. The data sources used for the estimation of the associations will be, on the one hand, the data contained in the regional health databases, i.e. demographic data, pharmaceutical prescriptions, hospitalizations, surgical operations, laboratory examinations and outpatient visits, and on the other hand, the data extracted from territorial monitoring systems of air pollutants, such as ARPA, ISPRA, Copernicus, Air Quality Index. Using these data, the PhD student will have to study how the periods of exposure to pollutants and the characteristics of the subject can be exploited to develop algorithms for predicting the risk of incidence of chronic diseases. The analysis of these data will require the use of IT packages dedicated to the analysis of large amounts of data and the knowledge of advanced biostatistical models. The specificity of the data will impose the use of analysis techniques, possibly Bayesian, which consider the association between pollutant and disease incidence taking into account the space-time variability, i.e. in the light of the presence of composite spatial clustering with the simultaneous presence of temporal variability, both in the short term following meteoric events, and in the long term determined by recurring seasonal variations.

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<th>Tutor</th>
<th>Prof. Antonella Zambon</th>
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<td>15</td>
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Specific IPR rules: standard
### Public Health Epidemiology, Statistics and Economics

<table>
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<tr>
<th>Progetto di ricerca Research project</th>
<th>“The prediction of short and long-term outcomes in critically ill patients”</th>
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<td>Istituto di Ricerche Farmacologiche Mario Negri IRCCS</td>
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<th>Tipo/Type</th>
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<td>Scholarship PNRR co-funded ex D.M. 117/2023</td>
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| Borse/Scholarships                   | 1                                                                             |

#### Abstract

**ENG**  
Septic shock is a devastating condition often observed in ICU. It is characterized by pro-inflammatory and immune responses, organ failures, high incidence of AKI and lethality. Fluid resuscitation is pivotal as supportive therapy. At present, there are no effective therapies to improve survival of such clinical condition, often characterized by a mortality as high as 40% during the first 90 days from diagnosis. The department of Cardiovascular medicine has concluded a multicenter, randomized trial, the ALBIOS trial, in which, in a post-hoc analysis, albumin, in addition to crystalloids, reduced 90-day mortality in patients with septic shock, as compared to crystalloids alone (Caironi P et al, 2014). Crystalloids with supra-physiological chloride content may deteriorate renal perfusion, increasing the risk of acute kidney injury (AKI) and mortality. Therefore, ALBIOSS-BALANCED trial is currently ongoing. This trial is a large 2-by-2 factorial randomized clinical trial testing the efficacy of albumin and the low-chloride balanced crystalloid solutions in septic shock.

The PhD track will consist of the following points:

1. To assess combinations of circulating biomarkers in the ALBIOS trial to predict the onset of septic shock in patients with sepsis by means of bio-statistical models. The ALBIOS trial on patients with sepsis has been concluded and post-hoc analyses on single biomarkers have been published. Thusfar single biomarkers have been assessed to predict the onset of septic shock. The PhD-candidate will perform an analysis to assess combinations of biomarkers to predict the onset of this devastating phase of sepsis.

2. Assess the results of the ALBIOSS-BALANCED trial in patients with septic shock. The ALBIOSS-BALANCED trial on patients with septic shock will conclude in 2024 and the principal analyses will be performed. The PhD-candidate will participate in the conclusion and analyses of one of the largest trials in intensive care units in Italy.

3. Long term neurological outcomes of patients with septic shock in ALBIOSS-BALANCED trial. No information is known on the long-term functional outcome of patients who survive septic shock. Therefore, the PhD-candidate will collect data, insert this in the database and perform analyses. The scope for the PhD-candidate is to understand how to systematically collect data by means of the RedCap database platform and analyse these data.

4. Biomarker assessment in septic shock ALBIOSS-BALANCED The ALBIOS-BALANCED trial will collect biological samples of septic shock patients. These samples may be used to validate findings of the analyses performed in section (1). The PhD-candidate will get insights on the management of biobanks, logistics of biological sample collection, selection of candidate circulating biomarkers and the statistical analyses of the circulating biomarkers.

**Tutor**  
Prof. Antonella Zambon
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<th>Mes previsti in azienda/Expected months at the company</th>
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**Specific IPR rules:** standard
### Research Project

“Sviluppo di tecnologie termoelettriche rivolte ad applicazioni sensoristiche”  
“Development of thermoelectric technologies for sensing”

**ISC S.r.l.**

### Type

Borsa PNRR cofinanziata ex D.M. 117/2023  
Scholarship PNRR co-funded ex D.M. 117/2023

### Scholarships

1

### Abstract

**ITA**

ISC s.r.l. ha maturato nel corso degli anni una ampia esperienza nelle applicazioni delle tecnologie termoelettriche in vari contesti industriali, ed è interessata all’impiego della termoelettricità per lo sviluppo di sensori fisici in due ambiti applicativi distinti ma convergenti, relativi alla misurazione di temperatura e di flussi di calore. Tale interesse converge con le competenze di UNIMIB nel campo dei materiali termoelettrici e delle applicazioni della termoelettricità, con particolare riferimento all’impiego di silicio nella forma di film sottili nanocristallini e di nanopillar monocristallini come materiale termoelettrico. Il progetto di dottorato prevede la realizzazione di sensori di temperatura aptici per l’automa umanoide ‘Robie’ che sarà impiegato a sostegno della missione lunare ‘Artemis’ (NASA/ESA/CSA) nella gestione dello shelter lunare e la realizzazione di sistemi calorimetrici con profilazione spaziale per la caratterizzazione di fasci ionici, a supporto delle attività di ricerca di INFN.

**ENG**

ISC s.r.l. has gained extensive experience over the years in the application of thermoelectric technologies in various industrial contexts and is interested in employing thermoelectricity for the development of physical sensors in two distinct yet converging application areas, related to temperature and heat flow measurements. This interest aligns with the expertise of UNIMIB in the field of thermoelectric materials and thermoelectric applications, with particular reference to the use of silicon in the form of nanocrystalline thin films and single-crystal nanopillars as thermoelectric materials. The doctoral project involves the development of haptic temperature sensors for the humanoid robot ‘Robie,’ which will be used in support of the ‘Artemis’ lunar mission (NASA/ESA/CSA) in the management of the lunar shelter; and the development of calorimetric systems with spatial profiling for the characterization of ion beams, supporting the research activities of INFN.

### Tutor

Prof. Dario Narducci

### Expected months at the company

6

### Expected months abroad

Min 6

### Specific IPR rules: standard
| Progetto di ricerca | “Sviluppo di tecniche analitiche e modelli per molecole odorigene di natura industriale”  
“Development of analytic techniques and models related to odour molecules emitted from industrial sources” |
|---------------------|-------------------------------------------------------------------------------------------------------------------------------------|
| Tipo/Type           | Borsa finanziata da ente esterno D.M. 117/2023  
Scholarship funded by external body D.M. 117/2023  
**Ricerca sul Sistema Energetico – RSE- S.p.A.** |
| Borse/Scholarships  | 1                                                                                                                                  |
| Abstract            | **ENG**  
Odour pollutions generated by industrial activities arise many serious technical, economical and legal problems, and are one of the major causes of citizens’ complaints to local authorities. For this reason, odours are now subject to control and regulation in many countries, thus making it necessary to have reliable and accurate methods for the assessment of odour impacts.  
Indeed, dynamic olfactometry, which is the reference method for the measurement of odour concentration, is intrinsically discontinuous, and applies to the quantification of emission sources, as stated in the scope of the reference standard for dynamic olfactometry; the standard EN13752:2022 is not able to define the hedonic nature of odour, and so the possible original source.  
The interest of scientific community is then directed to electronic noses, that are turning from being only scientific and research objects to air quality monitoring tools. Nowadays there are some situations in which e-noses are prescribed on a regulatory level. When odour monitoring data produced by electronic noses start having a legal value, the need arises to have standards and quality programs allowing to ensure the quality of the whole monitoring process. Standards play an important role for developing functional and reliable products for the global marketplace: they typically provide performance criteria that can be used to optimize the reliability and safety of new products. According to this, standardized quality protocols are particularly needed for the instruments’ performance verification. Such standards have the aim to guarantee the main characteristics of the instrument for both the final user and the local authorities, let the user establish a suitable maintenance procedure and give information on measurement uncertainty. This project will be conducted in strict relations with the activities of CEN standardisation group CEN TC 264 WG 41 “Emissions- Electronic Sensors for Odorant Monitoring” and of the UNI National Group GL4 “Emissioni e Qualità dell’aria” and has the aim to analyse and develop innovative experimental approaches in the area of odour monitoring, with particular focus on annoyances from industrial plants.  
This project is part of the RdS 2022-2024 research program “Efficienza energetica dei prodotti e dei processi industriali” and aims to support decarbonisation of industrial productions by the means of increasing of accuracies of emission measurements. |
<p>| Tutor               | Prof. Ezio Bolzacchini                                                      |</p>
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**Specific IPR rules:** rules intellectual property clauses agreed with the Company apply to this scholarship
### Abstract

Decarbonisation of industrial energetic sources is one of the hard challenges of research community and dependence on combustion technologies is still very strong and need time to be replaced. It's still necessary to pay high level of attention on the management of polluting emissions which, if they cannot be eliminated for now, much can be done to limit their effects, limiting them, and using fuels of a biogenic nature or with low environmental impact. In particular, the interest in emission control from volatile compounds emitted from biofuels is becoming more and more of interest as:

- Emissions measuring methods are not normally applied to such components and require specific implementations
- Standardisation in this field is still very weak and applied, normally, only to ambient air monitoring.

Scope of this project is to investigate the new methods in the field of volatile compounds emissions implementing such techniques using a metrological approach.

This project will be conducted in strict relations with the activities of CEN standardisation groups CEN TC 264 WG 45 “Emissions- Proficiency Testing Schemes”, CEN TC 264 WG 9 “Emissions- Quality assurance of Automated Measuring Systems” and of the UNI National Group GL4 “Emissioni e Qualità dell'aria” and has the aim to analyse and develop innovative experimental approaches in the area of proficiency testing, with particular focus on organic pollutants like CH2O and CH3CHO, aldehydes that have a great importance in the field of decarbonisation, like other compounds as mercury and metal traces.

This project is part of the RdS 2022-2024 research program “Efficienza energetica dei prodotti e dei processi industriali” and aims to support decarbonisation of industrial productions by the means of increasing of accuracies of emission measurements.
This PhD research project aims to investigate the activity and nature of microorganisms in underground geological formations impacted by the presence of H2, CO2 and CH4. on indigenous microbial communities and explore the potential of bioelectrochemical conversion via microbial electrosynthesis to transform gas vents from natural environments into valuable products. As concerns about the increasing levels of carbon dioxide (CO2) in the atmosphere escalate, innovative approaches for CO2 and CH4 capture, utilization, and storage are of paramount importance. The first objective of this study is to assess the impact of autochthonous microbial communities on H2 storage in geological formations. Geological storage of H2 in deep saline aquifers or depleted oil and gas reservoirs is a considered strategy for long-term energy storage. However, the potential effects of this process on the indigenous microbial communities inhabiting these storage sites remain poorly understood. This research will employ advanced molecular techniques, such as metagenomics and metatranscriptomics, to investigate changes in microbial community structure, diversity, and metabolic potential after H2 injection, in different condition of nutrients and temperature and other elements. Furthermore, microbial activity and potential shifts in functional pathways will be evaluated to determine the resilience and adaptability of these communities to altered environmental conditions.

The second objective of this study focuses on the bioelectrochemical conversion of H2 and CO2 into added value products through microbial electrosynthesis. Microbial electrosynthesis harnesses the capability of electroactive microorganisms to utilize electrical energy for the conversion of CO2 into value-added chemicals. Examples of potential added value products include but are not limited to:

- methane
- Organic acids, such as acetic acid, formic acid, or butyric acid
- Biofuels, such as ethanol, butanol, or even long-chain hydrocarbons, providing sustainable alternatives to fossil fuels.
- Polymers, such as polyhydroxyalkanoates (PHA)

By investigating the impact H2 on microbial communities and exploring the potential of microbial electrosynthesis for CO2 conversion, this research aims to advance our understanding of the intricate relationship between geological rocks, microbial ecology, and sustainable resource utilization. The findings of this study will contribute valuable insights to the development of effective strategies for energy storage and the
bioelectrochemical production of value-added products through microbial electrosynthesis. Ultimately, this research has the potential to pave the way for a more sustainable and circular carbon economy, making possible a more effective use of renewable, unprogrammable sources.

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<th>Tutor</th>
<th>Prof. Francesca Pittino</th>
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### Progetto di ricerca

**Scienze Chimiche, Geologiche e Ambientali**  
**curriculum Scienze dell’Ambiente Terrestre e Marino**  
**Chemical, Geological and Environmental Sciences**  
**curriculum Terrestrial and Marine Environmental Science**

| Progetto di ricerca | “Effetto degli effluenti dei depuratori e di eventi di precipitazione meteorica ad alta intensità sul rilascio nell’ambiente e sull’esposizione della popolazione a determinanti di resistenza antimicrobica ed ad agenti biologici potenzialmente patogeni”  
“Effects of wastewater treatment plant effluents and of high intensity precipitation events on the release into the environment and on the exposure of the population to determinants of antimicrobial resistance and to potentially pathogenic biological agents” |
|---------------------|-------------------------------------------------------------------------------------------------|
| Tipo/Type           | Borsa finanziata da Ente esterno  
Scholarship funded by external Body  
BRIANZACQUE srl |
| Borse/Scholarships  | 1 |
| Abstract            | ITA  
La resistenza agli antibiotici è stata considerata una delle maggiori sfide per la salute pubblica e il suo aumento globale è stato riconosciuto come un’imminente crisi di salute pubblica da entità intergovernative. Nonostante i processi di trattamento ne riducano il livello nelle acque, è noto che i sistemi fognari e gli impianti di trattamento delle acque reflue rappresentino un punto di immissione nell’ambiente di batteri antibiotico-resistenti (ARB) e dei geni di resistenza antimicrobica (ARG, definiti nel seguito “resistoma”). Gli studi finora condotti per quantificare questo impatto sono stati generalmente effettuati in condizioni di normale funzionamento dell’impianto. Tuttavia, molti sistemi fognari e impianti subiscono regolarmente eventi di precipitazioni ad alta intensità. È stimato inoltre che la frequenza e l’entità di questi eventi sarà in costante crescita nei prossimi anni in uno scenario di aumento della temperatura media dovuto ai cambiamenti climatici in corso. Recenti studi hanno ipotizzato che il livello di ARG nei corpi idrici aumenti a seguito di eventi di precipitazione ad alta intensità. Questo aumento dei livelli ambientali di ARG è dovuto all’effetto combinato dell’incremento del rilascio da sorgenti non puntiformi quali suoli/sediamenti risospesi e run-off superficiale e dallo scarico di acque non tratteggiate dagli scolmatori di piena. Ad oggi sono pochi gli studi condotti che abbiano sistematicamente esaminato l’effetto di differenti sorgenti sull’abbondanza e la composizione del pool di ARG (resistoma microbico) a seguito di precipitazioni da alta intensità e che abbiano investigato l’effetto di opere ingegneristiche per la gestione di acque di ruscellamento (come vasche volano, vasche/aree di laminazione e sustainable urban drainage systems) sul rilascio in ambiente di agenti biologici potenzialmente patogeni e di determinanti genetici dell’antimicrobico-resistenza (resistoma).  
Gli obiettivi della ricerca sono quindi quelli di:  

1) Determinare l’eventuale effetto di magnificazione della presenza di depuratori sul resistoma microbico  
2) Determinare in modo qualitativo e quantitativo l’effetto di precipitazioni ad alta intensità sulla concentrazione di antibiotici e sul resistoma microbico di un corpo idrico recettore;
3) Individuare e determinare il contributo relativo delle differenti sorgenti che contribuiscono al rilascio di antibiotici nel corpo idrico recettore e all’alterazione del resistoma microbico;

4) Prevedere l’evoluzione dei fenomeni descritti e dei relativi impatti nel corso dei prossimi anni in funzione degli scenari attesi di cambiamento climatico e della possibile implementazione di opere ingegneristiche di gestione delle acque di riuscimento meteorico urbano a in aggiunta alle infrastrutture esistenti;

5) Ipotizzare misure di gestione del rischio e mitigazione dell’impatto per mezzo dell’implementazione di opere ingegneristiche per la gestione delle acque e della pianificazione di pratiche di gestione innovative delle infrastrutture legate al ciclo idrico urbano. Tali misure verranno integrate in un sistema di supporto alle decisioni al servizio delle autorità competenti.

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Specific IPR rules: standard
**Abstract**

The increase in atmospheric CO2 concentrations has three main negative consequences: global warming, sea-level rise and progressive drop in ocean pH (ocean “acidification”) caused by the increased dissolution in sea water. The oceans are mitigating these problems: during the last 50 years the ocean has absorbed 90% of the excess heat produced by man-made emissions and between 20 and 30 percent of human-induced CO2 emissions since the 1980s. Since the beginning of the Anthropocene, the pH of surface ocean waters has decreased by 0.1 pH unit. This change represents an increase of about 30% in acidity. The IPCC established that the strategy of global reduction of greenhouse gas should be accompanied by a global effort of implementing technologies for negative CO2 emissions (NETs) in order to substantially mitigate the ongoing climate change.

In the Limenet technology calcium hydroxide is produced by collecting the CO2 produced during calcination in reactors that mix CO2, seawater and subsequently half of the same calcium hydroxide produced, thus obtaining calcium bicarbonates that buffers CO2. The other half of the calcium hydroxide could thus be considered decarbonized and could be used to remove CO2 from industrial sources.

The calcium bicarbonates are then released into the sea in the form of sea water with controlled, raisen alkalinity and pH. This process results in carbon being stored in seawater in the form of bicarbonates. The results of the life cycle assessment applied to the Limenet process show that the benefits of CO2 capture and storage clearly offset the potential greenhouse gas emissions generated by the entire process. However, there is still some degree of uncertainty about the complete neutrality of the treated water in respect of the marine biota. For this reason, it is necessary to explore the possible impacts of the Limenet-treated waters by mesocosm experiments, in order to assess the chemical dynamics and the biological response of the plankton community after repeated/prolonged release of treated sea-water back into the natural environment.
### Abstract

**ENG**

The increase in atmospheric CO2 concentrations has three main negative consequences: global warming, sea-level rise and progressive drop in ocean pH (ocean “acidification”) caused by the increased dissolution in seawater. The oceans are mitigating these problems: during the last 50 years the ocean has absorbed 90% of the excess heat produced by man-made emissions and between 20 and 30 percent of human-induced CO2 emissions since the 1980s. As a consequence, the pH of surface ocean waters has decreased by 0.1 pH unit, a change representing an increase of about 30% in acidity. The IPCC established that the strategy of global reduction of greenhouse gas should be accompanied by a global effort of implementing technologies for negative CO2 emissions (NETs) in order to substantially mitigate the ongoing climate change.

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The calcium bicarbonates are then released into the sea in the form of seawater with the same pH as seawater but with higher alkalinity. This process results in carbon being stored in seawater in the form of bicarbonates. The results of the life cycle assessment applied to the Limenet process show that the benefits of CO2 capture and storage clearly offset the potential greenhouse gas emissions generated by the entire process. However, there is still some degree of uncertainty about the complete neutrality of the treated water in respect of the marine biota. For this reason, it is necessary to explore the possible impacts of the Limenet-treated waters by mesocosm experiments, in order to assess the chemical kinetics and the biological response of the benthic communities after repeated/prolonged release of treated sea-water back into the natural environment.
**Marine Sciences, Technology and Management**

<table>
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<th>Progetto di ricerca</th>
<th>“Restoration of Native Oyster Beds (Ostrea edulis) in the Gulf of La Spezia”</th>
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<td>Agenzia nazionale per le nuove tecnologie, l’energia e lo sviluppo economico sostenibile (ENEA)</td>
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The Blue Economy (BE) is essentially a subset of the global economy linked to ocean resources while also acting as a strategic framework for ocean sustainability. BE activities including both marine-based and marine related activities are expected to double by 2023 thus their continuous monitoring to prevent or at least adapt to undesirable situations or scenarios is required. On the base of principles of regenerative economics (Faith et al. 2019) Nature Based Solutions (https://www.iucn.org/our-work/region/europe/our-work/european-nature-based-solutions) will contribute to the vitality and health of economic systems by constructing and maintaining regenerative pathways. Within regenerative processes, marine ecosystems play a key role. They can provide Ecosystem Services (Nature’s contribution to people, Costanza 2017) such as regulation (carbon storage), provisioning, support and cultural services. According to 17 Sustainability Goals (https://sdgs.un.org/goals), SDG14 is focusing on the Ocean, including the conservation and restoration of its ecosystems, and aiming at the sustainable use of the resources they provide. However, quantification of the services provided by key marine ecosystems and especially their restoration is at the very beginning, despite the urgent need. This project aims at increase knowledge and restore a native population of a key-stone species - the European native oyster (Ostrea edulis) - in the Gulf of La Spezia (Eastern Ligurian Sea). Present in the Gulf since the end of 1800, direct anthropogenic impacts such as sedimentation and pollution due to the exploitation of the coast (commercial harbor, touristic boating, Navy), diseases, as well as indirect anthropogenic impacts such as climate change, invasive species have contributed to the near functional extinction of the native oyster habitat. Over the past decade, efforts to rebuild native oyster populations and the complex biogenic habitat they create have increased in scale and number across Europe (https://noraeurope.eu), often with the aim of restoring both the biodiversity and ecosystem services these complex habitats support. O. edulis is a calcifying biogenic habitat builder providing a set of Ecosystem Services, including climate regulation, food provisioning, biodiversity support and enhancement of habitat complexity and underwater landscape. Thus, this challenging and innovative project will aim to restore, for the first time, Ostrea edulis natural beds in the Gulf of La Spezia, thus contributing to the regeneration of a highly impacted environment (harbor) and providing a Natura Based Solution for local BE regenerative pathways. Moreover, a morpho-molecular approach will be used at the university of Milano Bicocca to investigate the health and disease conditions of the target species through both the analyses of biomolecular markers of stresses and the use histopathology to assess and characterize unhealthy conditions of the animal found during the project period. This project is cofounded by ENEA within the framework of PNRR RAISE (Ecosystem of Innovation, Regione Liguria) and is part of SMART BAY S. TERESA activities (https://smartbaysteresa.com/en/) developed in collaboration with Cooperativa Mitilicoltori Associati, Mediterranean Association of Aquaculture (AMA) and
International Marine Centre (https://www.fondazioneimc.it). Candidate will spend 18 months at ENEA (at Marine Research Centre Santa Teresa, La Spezia) collaborating with above mentioned subjects and with international and/or national academics involved with Native Oyster Restoration activities within the NORA (Native Oyster Restoration Alliance) Network with whom the Ph.D. student may spend training periods (6 months maximum).

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<tr>
<th>Tutor</th>
<th>Prof. Davide Seveso</th>
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**Specific IPR rules:** Intellectual property clauses agreed with the Company apply to this scholarship
### Tecnologie Convergenti per i Sistemi Biomolecolari (TeCSBi)

**Converging Technologies for Biomolecular Systems (TeCSBi)**

| Progetto di ricerca | “Analisi integrata dei dati di valutazione della salute per la medicina preventiva e la longevità”
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**Il Progetto si pone l’obiettivo di analizzare i dati aggregati raccolti negli ultimi anni dalla divisione Pharma Health Methods di Unifarco.**

Pharma Health Methods è la divisione di Unifarco che sviluppa e commercializza alle farmacie del gruppo metodi di valutazione dello stato di salute e benessere delle persone.

Nello specifico, gli attuali metodi offerti includono:
- analisi genetica del microbiota intestinale (BIOMAPLAN)
- analisi della composizione corporea (BODYPLAN)
- analisi delle sensibilità alimentari (FOODPLAN)
- analisi della pelle (SKINPLAN)

L’offerta di Pharma Health Methods è caratterizzata da una continua evoluzione nel corso del tempo che potrà ampliare il dataset a disposizione per il progetto. Una prima fase del progetto riguarderà l’analisi dei dati aggregati riguardo al metodo BIOMAPLAN, l’analisi genetica del microbiota intestinale sviluppato in collaborazione con il laboratorio BMR Genomics. BMR Genomics è un’azienda biotech nata come Spin-off dell’Università di Padova e che vanta 20 anni di esperienza nel sequenziamento del DNA e nell’analisi genetica.

I dati raccolti con BIOMAPLAN dal 2019 ad oggi riguardano più di 6,600 analisi. Verrà effettuato innanzitutto un lavoro di classificazione dei dati, per indagare eventuali pattern significativi. I dati relativi alle analisi genetiche sono corredati da dati raccolti per mezzo di un questionario anamnestico, che effettua una valutazione delle abitudini e dei fattori esterni che influenzano la composizione del microbiota. Il secondo step vedrà la razionalizzazione degli eventuali pattern individuati per andare a sviluppare migliorie dell’attuale metodologia di analisi e l’algoritmo bioinformatico e interpretativo dei risultati. Il lavoro verrà svolto insieme ai responsabili di laboratorio e di bioinformatica di BMR Genomics.

Una seconda fase del progetto riguarderà invece l’analisi dei dati relativi agli altri metodi di valutazione, seguendo a grandi linee la stessa impostazione di lavoro della prima fase. Verranno analizzati in ordine di priorità BODYPLAN, FOODPLAN e SKINPLAN. BODYPLAN è il metodo di analisi della composizione corporea, che si effettua per mezzo di un innovativo bioimpedenziometro tetrapolare monofrequenza di tipo mano-manò, sviluppato in collaborazione con Akern Srl, azienda italiana con oltre 40 anni di esperienza nelle soluzioni di analisi di bioimpedenza. Il metodo ha permesso di raccogliere dal 2020 più di 20,000 analisi. È in corso un ulteriore lavoro di sviluppo delle attuali formule di stima dei parametri di composizione corporea in collaborazione con Akern e con l’Università Pablo de Olavide di Siviglia.
FOODPLAN è il metodo di analisi delle sensibilità alimentari, che oltre ad indagare la reattività IgG mediata ad un pannello di 92 alimenti, valuta lo stato infiammatorio attraverso l’analisi dell’interleuchina 6 da sangue capillare e la predisposizione genetica all’intolleranza al lattosio da campione salivare. Il metodo FOODPLAN è stato sviluppato in collaborazione con il laboratorio Diagnostica Spire e l’Università di Modena e Reggio Emilia.

SKINPLAN è il metodo di analisi della pelle attraverso uno strumento con un sensore ottico ad ingrandimento per la valutazione dei parametri cutanei visibili e un sensore capacitivo per la valutazione dello stato di idratazione della pelle. Lo strumento e l’algoritmo interpretativo dei dati è stato sviluppato in collaborazione con Aram Huvis, azienda coreana leader nella distribuzione di analizzatori della pelle.

Una terza fase del progetto riguarderà l’analisi dei dati in senso trasversale, con l’obiettivo di identificare eventuali correlazioni tra i vari metodi di analisi.

Questa ultima fase si colloca all’interno di un grosso ed importante progetto di Unifarco legato alla medicina preventiva e alla longevità, con l’obiettivo di sviluppare nuovi metodi di indagine e di consiglio volti a prolungare lo stato di benessere e di salute delle persone in maniera preventiva, evitando di dover agire sul sintomo.

ENG

The project aims to analyze the aggregated data collected in recent years by Unifarco’s Pharma Health Methods division.

Pharma Health Methods is the division of Unifarco that develops and markets health assessment methods for pharmacies within the group.

Specifically, the current offered methods include:
- Genetic analysis of intestinal microbiota (BIOMAPLAN)
- Body composition analysis (BODYPLAN)
- Food sensitivity analysis (FOODPLAN)
- Skin analysis (SKINPLAN)

The offerings of Pharma Health Methods continuously evolve over time, which will expand the available dataset for the project.

The first phase of the project will involve analyzing the aggregated data related to the BIOMAPLAN method, the genetic analysis of intestinal microbiota developed in collaboration with BMR Genomics laboratory. BMR Genomics is a biotech company that originated as a spin-off from the University of Padua and has 20 years of experience in DNA sequencing and genetic analysis.

The collected data with BIOMAPLAN from 2019 until now consists of more than 6,600 analyses. The first step will involve data classification to investigate any significant patterns. The genetic analysis data is accompanied by information collected through a questionnaire that evaluates habits and external factors influencing microbiota composition. The second step will involve rationalizing any identified patterns to develop improvements to the current analysis methodology and the bioinformatic and interpretive algorithm for results. This work will be carried out in collaboration with laboratory and bioinformatics experts from BMR Genomics.

The second phase of the project will focus on analyzing data related to the other evaluation methods, following a similar working approach as the first phase. The priority order for analysis will be BODYPLAN, FOODPLAN, and SKINPLAN.

BODYPLAN is the method for analyzing body composition using an innovative hand-to-hand tetrapolar monofrequency bioimpedance device developed in collaboration with Akern Srl, an Italian company with over 40 years of experience in bioimpedance analysis solutions. The method has enabled the collection of over 20,000 analyses since 2020. Ongoing work involves further development of the current formulas for estimating body
composition parameters in collaboration with Akern and the University Pablo de Olavide in Seville.

FOODPLAN is the method for analyzing food sensitivities, which investigates IgG-mediated reactivity to a panel of 92 foods, evaluates inflammatory status through interleukin 6 analysis from capillary blood, and assesses genetic predisposition to lactose intolerance from salivary samples. FOODPLAN was developed in collaboration with Diagnostica Spire laboratory and the University of Modena and Reggio Emilia.

SKINPLAN is the method for skin analysis using an optical magnification sensor to evaluate visible cutaneous parameters and a capacitive sensor to assess skin hydration. The instrument and the interpretive algorithm for data were developed in collaboration with Aram Huvis, a leading Korean company in the distribution of skin analyzers. The third phase of the project will involve a cross-sectional analysis of the data with the aim of identifying any correlations between the various analysis methods. This final phase is part of a major and important project at Unifarco related to preventive medicine and longevity. The objective is to develop new investigation and advisory methods aimed at prolonging people’s well-being and health preventively, avoiding the need to address symptoms directly.

**Tutor**

Prof. Dario Pescini

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