IBEC-VHIR INTERNATIONAL PhD PROGRAMME

Position

1. Project Title/ Job Position title:
   NRF2 Agonist Nanomedicine for Multiple Sclerosis Therapy

2. Research project/ Research Group description (max. 2.000 characters)

This collaborative PhD project will unite the expertise of **Prof. Giuseppe Battaglia (IBEC)** in molecular bionics and nanomedicine with the translational experience of **Dr. Carmen Espejo** from Vall d'Hebron Research Institute **(VHIR)** in the field of multiple sclerosis (MS). The project focuses on developing novel nanomedicines that target both myeloid cells and the blood-brain barrier (BBB) to deliver nuclear factor erythroid 2–related factor 2 (NRF2) agonists as a therapeutic strategy for neuroinflammation in MS.

The **NRF2** is a critical transcription factor that regulates cellular defense mechanisms against oxidative stress and inflammation. In MS, NRF2 activation promotes anti-inflammatory pathways and protects against oxidative damage, which are key to mitigating the chronic inflammation and neurodegeneration characteristic of the disease. The research will leverage advanced polymer chemistry to design and synthesise polyesters incorporating **Krebs cycle intermediates (KCIs)**, forming the core of amphiphilic block copolymers capable of self-assembling into micelles and vesicles. These nanostructures will be tailored for two targeting strategies: one for selective interaction with myeloid cells to modulate inflammatory phenotypes and another to cross the BBB via receptor-mediated transcytosis. By exploiting phenotypic targeting principles, the nanomedicines will achieve high specificity and minimal off-target effects, addressing the dual challenges of inflammation and neuroprotection in MS. The project will involve extensive ***in vitro* screening** of the nanomedicines to evaluate their cellular uptake, macrophage polarisation toward anti-inflammatory states, and NRF2 activation. These studies will guide the optimisation of nanocarrier composition, size, and surface functionality. The efficacy of the optimised nanomedicines will be tested using ***in vivo* models**, particularly experimental autoimmune encephalomyelitis (EAE) mice, a widely used preclinical model of MS. This translational approach is designed to produce robust data supporting the therapeutic potential of these nanomedicines while laying the groundwork for future clinical applications.

3. Job position description (max. 2.000 characters)

The PhD candidate will lead an interdisciplinary initiative aimed at developing and validating NRF2 agonist nanomedicines for MS treatment. They will take charge of designing and synthesizing polyesters derived from KCIs, employing sophisticated polymer chemistry techniques to create amphiphilic block copolymers. A thorough characterization of these polymers will be conducted, assessing molecular weight, composition, and self-assembly traits through methods like NMR spectroscopy, gel permeation chromatography (GPC), dynamic light scattering (DLS), and transmission electron microscopy (TEM). Additionally, the candidate will perform *in vitro* analyses to evaluate how nanomedicines interact with myeloid cells, particularly their role in promoting anti-inflammatory responses via NRF2 activation. Cellular assays will focus on uptake efficiency, polarization states, and downstream impacts on inflammation-related gene expressions. The project also necessitates *in vivo* validation via EAE mouse models, where the candidate will investigate biodistribution, BBB penetration, and therapeutic effectiveness. This role presents a distinctive chance to merge cutting-edge polymer chemistry, advanced materials characterization, and translational biomedical research. Ideal applicants should possess a background in polymer science, biomaterials, or nanomedicine, as well as expertise in chemical synthesis, molecular characterization, and cell biology. Strong skills in experimental design, data analysis, and a keen interest in interdisciplinary research are crucial. The collaborative nature of this project allows the candidate to engage in impactful translational work that could yield high-impact publications and significant advancements in the treatment of neuroinflammatory conditions such as MS.

Group Leader at IBEC

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Group Leader at VHIR

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