IBEC-SJD INTERNATIONAL PhD PROGRAMME

Position

1. Project Title/ Job Position title:
   Placenta inspired mini-oxygenator

2. Research project/ Research Group description:

The main objective of this project is to develop placenta-inspired mini-oxygenator to support the life of neonates born with extreme prematurity. Premature birth carries a high burden of mortality and morbidity mainly due to the poor development of the lungs that are not mature enough for oxygen exchange. Artificial Placenta Systems aims to overcome this biological limitation using an extracorporeal membrane oxygenator (ECMO) that directly oxygenates blood. However, there is no device in the market able to provide the flows conditions, proper gas exchange and that is sufficiently safe (hemocompatibility of the membrane) to support these extremely preterm children.

Our ambition is to engineer a specific mini-oxygenating membrane to work as part of an artificial placenta system to preserve fetal conditions such as circulation. This demands to overcome the 2 unsolved challenges: (i) the need for designs that poses minimal resistance to flow and shear to prevent excessive loads in fetus heart while having the capacity for gas exchange, (ii) and the insufficient blood compatibility of membrane surfaces that activates coagulation and inflammation. This project will tackle these challenges by (a) investigating radically different membrane designs based on 3D printed minimal surfaces (e.g. gyroids) that maintaine the flow with minimal disturbances, and (b) introducing nanoscale coatings capable of modulating and interacting blood, but only at the interfaces causing no effect in global hemostasis, i.e. minimizing risks thrombosis or hemorrhage. Thus, the project will include work in the development of the 3D membranes, including material design, characterization of ultra-structure and gas transport as well as the design of polymer brushes and their functionalization with active biomolecules that interact with blood factors and the in vitro studies of the activity with blood in custom-made models.

The supervision team consists of Prof. J Samitier who will lead the membrane design, Prof. Rodriguez-Emmenegger, who is a specialist in biointerfaces and hemocompatibility, and Prof. Gratacós who is a pioneer in fetal medicine and surgery and leading the CaixaResearch Placenta Artificial project. The three groups have a successful history of collaboration.

3. Job position description:

The PhD program will have 3 phases: (i) design of 3D printed membranes that cause minimal resistance to flow and pressure drop, (ii) introduction of interactive hemocompatible nanocoatings, (iii) build an oxygenating membrane that could be potentially integrated among the components of an artificial placenta system and test it for proof-of-concept. For (i) the candidate will develop new polymer inks compatible with 3D printing, model different structures (e.g gyroids) seeking for the best fluid conditions and print the first prototypes and test gas exchange. The fluidic conditions will be modelled and experimentally evaluated with tomography (KIT Germany). The (ii) will use brush-like polymer brushes that are stealth to blood and thereby do not allow platelet adhesion. The brushes will be functionalized with molecules to prevent the activation of contact system (inhibitors of FXIIa, FXIa) as well as the kinin-kallikrein to modulate blood activity. They will also integrate the ability to digest clots, neutrophile extracellular traps and we will investigate the introduction of NO release using endogenous components. With this we seek to mimic some of the salient functions of endothelium. The nanoscale coatings will be studied using a number of surface sensitive technique including XPS,¡ToF-SIMS, AFM, SPR, etc. Each of these functions will be tested in vitro using dynamic models that mimic the fetal flow. Finally, in (iii) the candidate will assemble the system and perform in vitro hemocompatibility tests to evaluate the overall performance. Additionally, the groups will seek for additional funding opportunities to support in vivo animal models.

This is a highly interdisciplinary project that builds on very strong macromolecular and surface chemistry, joining concepts of engineering, nanotechnology, fluid dynamics, biochemistry, and fetal medicine. These are all expertise of the participating groups.

Group Leaders at IBEC

1. Title: PhD, ICREA Research Professor
2. Full name: César Rodriguez-Emmenegger
3. Email: crodriguez@ibecbarelona.eu
4. Research Group: Bioinspired Interactive Materials and Protocellular Systems

1. Title: Prof PhD
2. Full name: Josep Samitier
3. Email: jsamitier@ibecbarcelona.eu
4. Research Group: Nanobioengineering

Group Leader at SJD

1. Title: Professor Dr.
2. Full name: Eduard Gratacós Solsona
3. Email: eduard.gratacos@sjd.es
4. Research group: Fetal Medicine and Surgery