

## Track « Integrative Biology, Physiopathologies »

Proposal for a Master 2 internship – 2024-2025

**Title :** Effects of macrophage polarization modulated by sevoflurane in vitro on epithelial alveolar viability

**Laboratory:** iGReD, Université Clermont Auvergne, CNRS, INSERM (Team « Translational approach to epithelial injury and repair »)

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### **Summary :**

Acute respiratory distress syndrome (ARDS) is a major cause of respiratory failure and death, such as during COVID-19, that still lacks specific therapy. The fibro-proliferative phase allows alveolar repair, but dysfunction can lead to refractory ARDS and fibrotic sequelae. Repair depends on epithelial viability and the interaction between macrophages and epithelial cells.

Sevoflurane, a volatile anesthetic, could have protective effects on ARDS pathogenesis. Preclinical and clinical studies suggest decreased inflammation, improved oxygenation, and modulation of macrophage polarization towards an anti-inflammatory phenotype.

The current project aims to test the hypothesis that sevoflurane could have a protective effect on alveolar epithelial viability, notably through an anti-apoptotic effect, by inducing anti-inflammatory macrophage polarization and thus promoting the beneficial effects of such polarization on epithelial cells during ARDS. Freshly isolated primary human alveolar epithelial type 2 cells, exposed or not to pro-inflammatory cytokines and treated or not with sevoflurane, will be cultured in complete medium or sevoflurane-treated, primary human macrophage-conditioned medium to assess epithelial viability and markers of apoptosis.

This project fully aligns with the desire from our team to pursue collaborative translational research in the era of precision medicine.

**Methodologies (key words):** cell culture; immunofluorescence; multi-analyte ELISA (ELLA); western blot; viability assay; cytotoxicity assay.

### **Publications of the research group on the proposed topic (3 max.)**

- Jabaudon M et al. Inhaled sedation in the intensive care unit. *Anaesth Crit Care Pain Med* (2022).
- Garnier M. et al. Macrophage polarization favors epithelial repair during acute respiratory distress syndrome. *Crit Care Med.* (2018).
- Zhai R. et al. Effects of sevoflurane on lung epithelial permeability in experimental models of acute respiratory distress syndrome. *J Transl Med.* (2023).