Master program: Pharmaceutical sciences
Master Course: Development of Drugs and Health Products – M1

Firm/Laboratory/public body: **UMR_S1176 - Hemostasis, Inflammation, Thrombosis (HITh), INSERM, University Paris-Saclay**

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Internship period: 5th of May - 5th of July

Title of the project: Characterization of a nanobody directed against the protein S in sepsis models

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Our team recently identified a nanobody directed against the anticoagulant protein S (PS). PS is a natural anticoagulant, which also directly contributes to the regulation of inflammation by promoting the efferocytosis of apoptotic cells, inducing thereby an immunomodulatory response. This effect lies in the ability of PS to bridge phosphatidylserine exposed on the surface of apoptotic cells to Mer, a receptor tyrosine kinase on the surface of macrophages. Cells and microparticles with phosphatidylserine on their surface play a crucial role in the pathology of sepsis as they are highly pro-inflammatory and pro-coagulant.
The anti-PS nanobody exhibits the particularity of enhancing the anticoagulant activity of the PS. In-vivo, it showed an antithrombotic effect in a mouse model of induced thrombosis, without increasing bleeding upon injury. In addition, preliminary results suggest that the anti-PS nanobody also likely promotes the phagocytosis of senescent cells by macrophages in-vitro, in a PS/Mer-dependent mechanism.
Hence, the anti-PS nanobody could be relevant in the treatment of septic shock by promoting both the anticoagulant and the anti-inflammatory activities of PS. Its antithrombotic activity, combined with its ability to favor the clearance of phosphatidyl serine-exposing cells, could regulate thrombo-inflammation without increasing the bleeding risk.
In this context, the objective of the short-term project (M1 internship) is to pursue in-vitro characterization of the anti-PS nanobody in cellular models of phagocytosis and inflammation. Concomitantly, murine models of septic shock are being developed to

evaluate the potential interest of the anti-PS nanobody in vivo. The M1 internship will also contribute to the characterization of these models, with plasma dosage of inflammatory cytokines and coagulation biomarkers.