Curriculum

A. Eckly is a research director at the Blood Transfusion Center and a group leader at UMR-S1255 in Strasbourg, France. Her team is interested in deciphering the *in vivo* passage of megakaryocytes from the bone marrow through the sinusoid vessel wall towards the blood circulation, a process referred to as intravasation. The research focuses on megakaryocyte interactions with their microenvironment, including endothelial cells and the extracellular matrix. To this end, she has acquired expertise in 3D imaging of bone marrow, including 3D electron microscopy and photonic imaging combined with ultrastructural information.

Overview of the presentation

Title: The Platelet Factory: Unlocking the Secrets of Megakaryocytes in 3D

Platelet formation depends on the strategic positioning of mature megakaryocytes (MK) at sinusoidal sites, which facilitates the polarized release of platelets into the bloodstream. Unlike other hematopoietic cells, MKs extend cytoplasmic protrusions through basement membranes and endothelial layers, a process called intravasation. This presentation will explore recent advancements in understanding the interactions between megakaryocytes and the vascular niche, enabled by cutting-edge 3D imaging techniques.

We will focus on two critical aspects of platelet biogenesis:

1. **MK Anchoring and ECM Regulation**: We will discuss how megakaryocytes construct a three-dimensional extracellular matrix (ECM) cage at sinusoid interfaces. This ECM cage integrates with the endothelial basement membrane, creating a physical scaffold that anchors

the MKs while allowing controlled protrusions of proplatelets. We will examine how this ECM cage, regulated by β1/β3 integrins and matrix metalloproteinases (MMPs), is involved in MK maturation and intravasation.

2. Mechanism of Actin-Based Podosomes in Megakaryocyte Transendothelial Migration: Our research has identified an actomyosin-driven podosome network (PodoPZ) that facilitates MK passage through endothelial barriers. We will explore how PodoPZ induces fusion of the apical-basal membrane, creating pores through which proplatelets extend into circulation.

By integrating these findings, we will demonstrate how the interplay between integrin-mediated signaling, MMP activity, and podosome dynamics regulates ECM properties and controls MK maturation and interactions at the bone marrow-blood interface. This presentation will highlight the power of advanced 3D imaging in unraveling the complexities of niche-regulated hematopoiesis and discuss the implications for understanding defects in thrombopoiesis.