

**Master 2 internship project
Year 2023-2024**

Laboratory/Institute: IBS

Director: M. Weissenhorn

Team: Entrée et Bourgeonnement des Virus à Enveloppe **Head of the team:** M. Weissenhorn

Name and status of the scientist in charge of the project: Boscheron **HDR:** yes no

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Program of the Master's degree in Biology:

- Microbiology, Infectious Diseases and Immunology Structural Biology of Pathogens
 Physiology, Epigenetics, Differentiation, Cancer Neurosciences and Neurobiology

Title of the project:

Membrane coated helical ESCRT-III polymer cleavage

Objectives (up to 3 lines):

Explore the kinetics of tubular filament cleavage by Vps4B.

Investigate the contribution of ESCRT-III amphipathic helices in membrane cleavage

Assess the significance of lipid composition for membrane constriction.

Abstract (up to 10 lines):

The evolutionary-conserved machinery known as the "endosomal sorting complex required for transport" (ESCRT-0, -I, II, -III, and VPS4) plays a crucial role in various membrane remodeling processes, including the formation of multi-vesicular endosomes, cytokinesis, and enveloped virus budding. ESCRT-III proteins, existing as cytosolic monomers, polymerize into tubular filaments on membranes, which are subsequently remodeled and recycled by the ATPase VPS4. These filaments predominantly participate in inside-out budding events, such as virus and vesicle budding. In our recent study, we uncovered the molecular interactions between ESCRT-III proteins and lipids, revealing the involvement of N-terminal amphipathic helices. Our objectives are as follows: (i) to investigate the kinetics of disassembling membrane-coated ESCRT-III polymers, (ii) to examine the role of ESCRT-III amphipathic helices in inducing membrane constriction and fission, and (iii) to assess the influence of lipid composition on these processes.

Methods (up to 3 lines):

Production of ESCRT-III and Vps4B proteins

Optimization of microscopy setting for imaging membrane-coated ESCRT-III.

Real-time microscopy of membrane coated ESCRT-III for membrane fission analysis.

Up to 3 relevant publications of the team:

Azad, K., D. Guilligay, C. Boscheron, S. Maity, N. De Franceschi, G. Sulbaran, G. Effantin, H. Wang, J.P. Kleman, P. Bassereau, G. Schoehn, W.H. Roos, A. Desfosses, and W. Weissenhorn. 2023. Structural basis of CHMP2A-CHMP3 ESCRT-III polymer assembly and membrane cleavage. *Nat Struct Mol Biol.* 30:81-90.

Maity, S., C. Caillat, N. Miguet, G. Sulbaran, G. Effantin, G. Schoehn, W.H. Roos, and W. Weissenhorn. 2019. VPS4 triggers constriction and cleavage of ESCRT-III helical filaments. *Sci Adv.* 5:eau7198.

Requested domains of expertise (up to 5 keywords):

Biochemistry and microscopy. We warmly welcome serious, curious, and dynamic students!