Grenoble Alliance for Integrated Structural & Cell Biology

GRAL Research proposal for PhD projects

Institute and Group: IBS- EBEV / BIG- BGE

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Title of the thesis project: **Alix control of exosome cargoes entry**

Keywords: Alix/ESCRT, endophilin, exosomes, VSV, drosophila

Summary of the project:

Exosomes are 40–100 nm membrane lipid vesicles secreted into the extracellular milieu by all eukaryotic cells. They bind to and are internalized by neighboring or distant cells, thus allowing their cargos (lipids, proteins and RNAs) to modify the phenotype of receiving cells. Today, exosomes are extensively studied for their role in intercellular communication in normal and diseased organisms, as well as for their possible use to transfer genetic material and molecules of therapeutic interest. This project proposes to unravel the molecular mechanisms needed for exosomes to transfer biologically active cargoes into receiving cells. We will concentrate our effort on the protein Alix, which was shown to be used by some viruses which hijack the exosome system to release their nucleoplasmid in the cytoplasm of infected cells. Our own preliminary results show that Alix ko fibroblasts are resistant to Vesicular Stomatitis Virus infection and cannot be modified by exogenous RNAs contained in exosomes. The student will perform structure/function studies using Alix mutants to complement Alix ko cell lines for exosomes and VSV transfer and use Drosophila wing development as a living system model which requires exosome transfer of differentiation and growth factors. Thus, this project should reveal the fundamental molecular mechanisms allowing exosomes to shuttle biologically active material between cells.