NANYANG TECHNOLOGICAL UNIVERSITY

School of Biological Sciences

Reg. No. 200604393R

Research Theme: Cell and Structural Biology

Research Project Title: Structure and higher-order organisation of caveolae studied by correlative light and electron microscopy

Principal Investigator/Supervisor: A/Prof Alexander Ludwig

Co-supervisor/ Collaborator(s) (if any): NA

The goal of this PhD project is to investigate the structure and cellular organisation of caveolae inside cells using state-of-the-art imaging. Caveolae are specialised membrane domains with key roles in endothelia, adipocytes and muscle cells (1,2). Caveolae exist as flask- or cup-shaped invaginations in the plasma membrane but are also frequently found to form large interconnected networks of unknown function. Loss or dysfunction of caveolae causes human diseases, with profound effects on the cardiovascular system, lipid and glucose metabolism and muscle function. On the molecular level, caveolae have been implicated in the control of membrane tension and mechanotransduction, signaling and trafficking. We are interested in a) understanding how caveolar proteins assemble to make caveolae, b) how these protein assemblies are regulated to control the shape and function of caveolae, and c) in the dynamic assembly and function of caveolar networks.

The proposed project is based upon our previous work in which we showed that the caveolar membrane bulb is shaped by a distinct protein complex, which we termed the caveolar coat complex (3,4). The primary goal of this PhD project is to determine the 3D structure of the caveolar coat inside cells using cryo-electron tomography. In addition, the cellular organisation and dynamic assembly of caveolar networks will be investigated using correlative light and electron microscopy (CLEM).

The candidate will gain expertise in molecular and cell biology, protein biochemistry, and state- of-the-art high-resolution microscopy techniques including correlative light and electron microscopy, 3D tomography and cryo-imaging.

Literature

1. Parton RG, del Pozo MA. Caveolae as plasma membrane sensors, protectors and organizers. Nat Rev Mol Cell Biol 2013;14(2):98-112.
2. Shvets E, Ludwig A, Nichols BJ. News from the caves: update on the structure and function of caveolae. Current opinion in cell biology 2014;29C:99-106. 3.
3. Ludwig A, Howard G, Mendoza-Topaz C, Deerinck T, Mackey M, Sandin S, Ellisman MH, Nichols BJ. Molecular composition and ultrastructure of the caveolar coat complex. PLoS Biol 2013;11(8):e1001640.
4. Ludwig, A, Nichols, BJ, Sandin, S. Architecture of the Caveolar Coat Complex, **J Cell Sci**, 2016 Jul, doi: 10.1242/jcs.191262

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