Department of Biochemistry and Molecular Biology

PhD Oration

Friday 15th of June
3:30-4:30pm
Bio21 Institute Auditorium
30 Flemington Road, Parkville

Maryam Moslehi

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Dissecting the actions of doublecortin X (DCX) in cytoskeleton organisation

Doublecortin X (DCX), a microtubule (MT)-associated protein, is known to be essential for neuronal migration and cortical layering during brain development. DCX regulates neuronal migration via modulation of the cytoskeleton dynamics through direct interaction of doublecortin domains (DC1 and DC2) with MTs and indirect association with actin filaments (F-ACT). Whilst the association of DC domains with the cytoskeletal components, MTs and F-ACT, has been established, the dynamics of this association and the possible regulatory roles played by the flanking unstructured DCX terminal regions (DCX N-terminus and C-terminus) remain poorly defined. In my PhD studies, I have employed quantitative fluorescence recovery after photobleaching (FRAP) protocols, live- and fixed-cell imaging as well as biochemical studies to reveal that DCX shows remarkable rapid and near complete exchange within the MT network but that the removal of the C-terminal region significantly slows this exchange. My studies have further shown that in the absence of DCX C-terminal region, DCX protein is not able to respond to hyperosmotic stress by regulation of DCX dynamics. To evaluate the role of DCX N-terminal region, the impact of DCXSer28 phosphorylation, the only phosphorylation site within the DCX N-terminus, on DCX association with MTs and F-ACT was probed to reveal the new role for DCXSer28 as a regulatory switch for cytoskeletal organisation increasing association of DCX with F-ACT but decreasing DCX-MT association. To further study the DCX N-terminus, a recently identified DCX pathogenic mutant DCXE2K was assessed for its impact on the cytoskeleton organisation. The DCXE2K mutant reorganises cytoskeleton arrangements via slowing DCX dynamics in association with MTs and increasing the indirect association of DCX with F-ACT via an adaptor protein, spinophilin. Taken together, these results highlight the regulatory roles of the DCX terminal regions in association of DC domains of DCX with MTs and F-ACT.

ALL WELCOME. Please join us for Pizza to celebrate this PhD Oration!
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