Institute of Molecular and Cell Biology

A*STAR

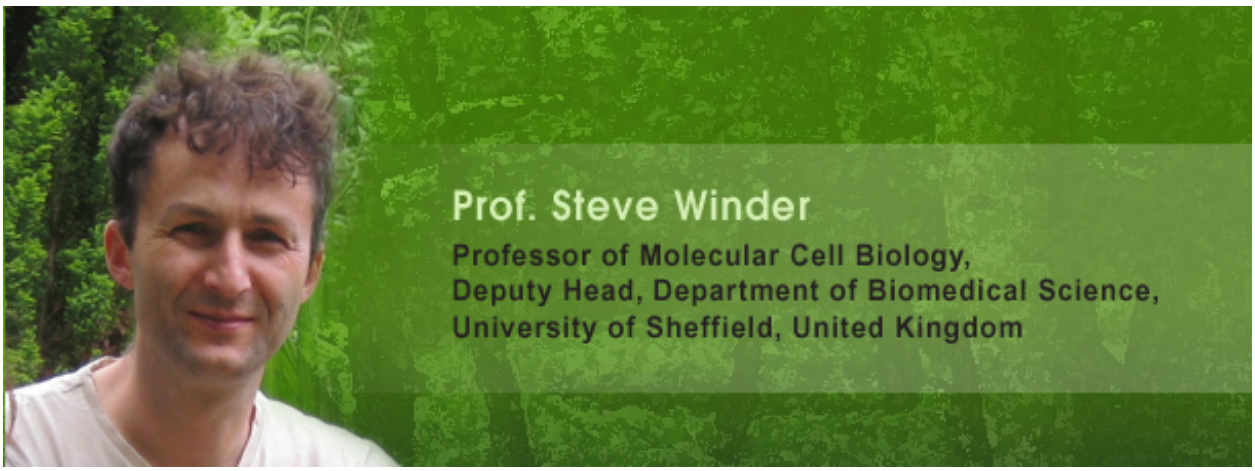
SEMINAR ANNOUNCEMENT

DATE: 12 March 2012, Monday

TIME / VENUE: 11:00AM @ Level 3, IMCB Seminar Room 3-46, Proteos, Biopolis

SPEAKER: Prof. Steve Winder

TITLE OF SEMINAR: **Dystroglycan phosphorylation as a therapeutic target for DMD**



Dystroglycan (DG) is a heterodimeric transmembrane glycoprotein, which in skeletal muscle forms a central role in the dystrophin-associated glycoprotein complex (DGC). This complex links dystrophin to the extracellular matrix, helping to provide stability to muscle fibres. Loss of functional components of the DGC or dystrophin leads to muscular dystrophy. Post-translational processing of DG is important to its cellular function. Modifications include, cleavage into alpha and beta subunits, phosphorylation and extensive glycosylation. Here we focus on the role of phosphorylation of beta-DG in muscular dystrophy. Recent work has shown that phosphorylation of a c-terminal tyrosine in beta-DG can cause redistribution of the protein from the cell membrane to endosomal compartments, possibly as a prerequisite to degradation. Furthermore phosphorylation of beta-DG acts as a molecular switch to control the binding partners and functions of beta-DG in myoblasts and muscle fibres and directs dystroglycan to different cell adhesion structures or ultimately for degradation. In normal muscle, binding of dystrophin to the c-terminal tyrosine would block phosphorylation, meaning that phosphorylation of beta-DG could be key in the disease process in DMD. We are using a combination of in vitro cell biology, and animal models in mice and zebrafish to dissect more finely the mechanisms involved.

Host: Prof. Philip Ingham

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