Institute of Medical Biology
A*STAR

Seminar Announcement

- All Are Welcome -

Speaker : **Dr Barry Coull**
University of Maastricht

Title : ***"Birt-Hogg-Dubé syndrome is a novel ciliopathy"***

Date : **5 June 2014 (Thursday)**

Time : **11:00am – 12:00pm**

Venue : **Aspiration Theatrette, Matrix Level 2M**

Host : **Prof Maurice van Steensel**
(Tel: 64070191; e-mail: maurice.vansteensel@imb.a-star.edu.sg)

Abstract:

Birt-Hogg-Dubé (BHD) syndrome is an autosomal dominant disorder where patients are predisposed to kidney cancer, lung and kidney cysts and benign skin tumours. BHD is caused by heterozygous mutations affecting folliculin (FLCN), a conserved protein that is considered a tumour suppressor. Over the past 15 years multiple roles for FLCN in cellular physiology have been described, yet it remains unclear how these translate to BHD lesions. As formation of cysts in the lung and kidney are hallmark characteristics of ciliopathies, we speculated that FLCN might also have a role in primary cilia. Our data indicate that FLCN localises to motile and non-motile cilia, centrosomes and the mitotic spindle. Alteration of FLCN levels can cause changes to the onset of ciliogenesis, without abrogating it. In three-dimensional culture, abnormal expression of FLCN disrupts polarised growth of kidney cells and deregulates canonical Wnt signalling. Our findings further suggest that BHD-causing FLCN mutants may retain partial functionality. Thus, several BHD symptoms may be due to abnormal levels of FLCN rather than its complete loss and accordingly, we show expression of mutant FLCN in a BHD-associated renal carcinoma. We propose that BHD is a novel ciliopathy, its symptoms at least partly due to abnormal ciliogenesis and canonical Wnt signalling.

About the Speaker:

Barry Coull, PhD, studied Molecular Biology at the University of Aberdeen, followed by a Masters in Molecular Microbiology at the University of Nottingham. Next he moved to the laboratory of Professor Alan Lehmann in the MRC Cell Mutation Unit (later Genome Damage and Stability Centre) at the University of Sussex to study for his PhD. In Alan's Lab, Barry worked on the bypass of UV induced DNA damage by the Human Polymerase iota. After completion of his PhD, he spent a short time working in industry with Unilever, before deciding to return to academic lab based research at the National University of Ireland Galway (NUIG). At NUIG in the laboratories of Prof Ciaran Morrison and Prof Noel Lowndes, Barry continued the theme of working on DNA damage, examining dysfunction of DNA damage and checkpoint pathways in DT40 knockout cells. After NUIG, he moved to his current position at the University of Maastricht, where he has spent the last few years trying to uncover the molecular mechanism behind the cancer causing disorder Birt-Hogg-Dubé (BHD).