Pleasantine Mill, PhD
University of Edinburgh
Group Leader, MRC Human Genetics Unit, Institute of Genetics and Cancer

Talk Title: **Cilia in Development and Disease: Dynamics, Diversity and Reversing Disease Phenotypes**

Abstract:
The Mill lab aims to understand genetic disease and disease mechanisms arising from dysfunction of mammalian cilia, termed the ciliopathies. While mammalian cilia are ubiquitous and highly conserved structures, the clinical features associated with cilia dysfunction are highly pleiotropic with varying degrees of severity and penetrance among tissues. The cellular and developmental basis to this phenotypic complexity is poorly understood and remains controversial. However, it is quite clear that not all cilia are created equal. In order to better understand the functional and structural diversity of the mammalian cilia repertoire, our strategy has been to engineer genetic tools to allow us to deeply molecularly phenotype cilia with organelle-resolution in vivo, using cutting-edge proteomics and imaging.

I will present some of our recently published work (Ford et al 2018 *Dev Cell*; Van Kerckvoorde et al 2021 *MiMB*), where we have developed a multi-component fluorescent biosensor that allows us to simultaneously 'light up' both cilia and stage in the cell cycle in mice. This allows live 'single cell' resolution of how these two processes are interconnected in health as well in models of human ciliopathies and cancer initiation/progression. We have asked fundamental questions about how long cilia remain prior to mitosis in primary cells or in vivo, and challenge the dogma that cilia act akin to 'brakes' to the cell cycle and must be resorbed prior to re-entry. I will also update on some of ongoing work to use these tools in our mouse models of human ciliopathies to understand disease phenotypes as well as our endogenous proximity labeling strategy to molecularly profile different cilia and their sensitivity to disease-causing mutations.