Project Title: Gene therapy approaches to restore ciliary function in CRISPR-Cas9 zebrafish mutant models of Primary Ciliary Dyskinesia

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Summary:
The vertebrate body-plan displays highly conserved left-right asymmetry in the location of internal organs. In humans, the heart is placed on the left side and the liver on the right. These organs are positioned in this way because during embryonic development there was a transient organ named left-right organizer (LRO) where the LR instructions are laid down. The first effectors of these instructions are motile cilia that must create a fluid flow that will be directional and heterogeneous in terms of flow-speed. To monitor how these motile cilia achieve their job we have set up high-speed videomicroscopy in our lab to visualize live cilia in motion. However, more challenging, to understand the function of the ciliary constituents we need to mutate particular proteins present in the ciliary cytoskeleton and then be able to repair them.

The aim of this project is to 1) Characterize zebrafish mutants, that are models for human PCD mutations, so that we can evaluate their function and better understand the disease causes; 2) investigate gene therapy approaches to rescue those same mutations that we have produced and evaluate the restored ciliary function. The student will be expected to travel to the UK for application of the same principle in primary human cell cultures. These pre-clinical studies aim to precede clinical trials in the future.

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