The RFX family of transcription factors and the regulation of cilia biogenesis

Cilia are cell surface associated microtubule-based filamentous organelles that function in fluid transport, cellular locomotion and in signal transduction. Given these multifarious roles, defective motile and primary cilia can cause a number of human diseases, collectively called ciliopathies. A key question in the field of ciliary biology is how the primary and motile ciliogenic programs are transcriptionally initiated and regulated\(^1\).

The laboratories of Dr. Peter Swoboda at the Karolinska Institute in Stockholm, Sweden, and Dr. Sudipto Roy at the IMCB in Singapore have complementary expertise in analyzing cilia formation and function. Dr. Swoboda’s lab has been the pioneer in the analysis of the *C. elegans* RFX transcription factor, DAF-19, and its role in controlling cilia formation\(^2\), while Dr. Roy’s group has the expertise in analyzing the transcriptional regulation of vertebrate ciliary development and function using the zebrafish embryo as the model system\(^3\).

The first aspect of this joint proposal for an A*STAR Graduate Scholarship (Overseas) aims to use genetic analysis in the zebrafish embryo to identify *rfx* genes with critical roles in controlling vertebrate ciliogenesis. This will involve making systematic knock-outs of all *rfx* family members in the zebrafish embryo and examination of the resulting ciliary phenotypes. Following this, the contribution of the different RFX proteins to the regulation of ciliary genes will be investigated. This will involve microarray-based genome-wide expression profiling of embryos deficient in RFX proteins, as well as transgenic embryos designed to over-express RFX proteins. The second aspect of this joint proposal aims to characterize protein interaction partners of the *C. elegans* RFX protein DAF-19, which exists in four different isoforms. The situation in *C. elegans* is relatively simple as compared to the scenario in vertebrates, where all the different RFX proteins exist in even larger numbers of isoforms. Our working model assumes that different RFX isoforms have different protein partners to differentially regulate their respective groups of ciliary target genes. The complementary approaches outlined in this proposal will provide new insights into the transcriptional networks responsible for ciliary biogenesis in invertebrates and vertebrates.

References:


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