

SYSCILIA



A systems biology approach to dissect cilia function and its disruption in human genetic disease

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Introduction

This project aims to apply systems biology approaches to cilia, long-known organelles of growing biomedical importance. A cilium can be regarded as a relatively small, experimentally tractable, isolated system that is ideally suited to such analyses. Primary cilia are basically signaling hubs (Fig. 1), and their disruption leads to striking developmental defects. Some ciliopathy-associated proteins have recently been revealed to be physically or functionally associated in several distinct groupings, with limited connections to other crucial biological processes. The project will focus on the core systems biology activities of data generation, integration, assay development, model building and model refinement. The models and associated discoveries will ultimately be employed to accurately diagnose and therapeutically target the growing number of human diseases associated with ciliary dysfunction.

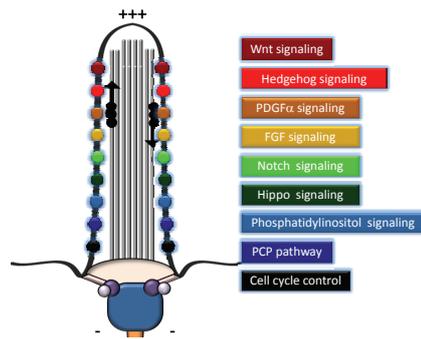


Figure 1 Scheme of a cilium and its basic involvement in cellular and developmental processes

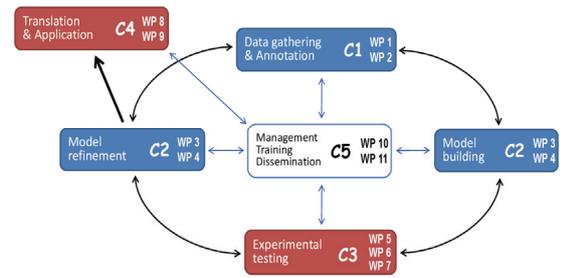


Figure 2 The SYSCILIA workflow. The work is organized into five and 11 workpackages.

- C1 Defining the elements and variables of ciliary systems
- C2 Modelling the variables of ciliary systems
- C3 Assessing and manipulating the variables of ciliary systems
- C4 Applying ciliary systems to human health towards improved diagnostics and therapy
- C5 Project management, training, and dissemination of data, including translation to the industry

Strategy

The Systems Biology workflow of SYSCILIA involves iterative cycles of quantitative data generation, model building, experimental testing and model refinement. The work is divided into four scientific components, and a fifth component involving project management, training, and dissemination of data, including translation to the industry (Fig. 2 & 3)

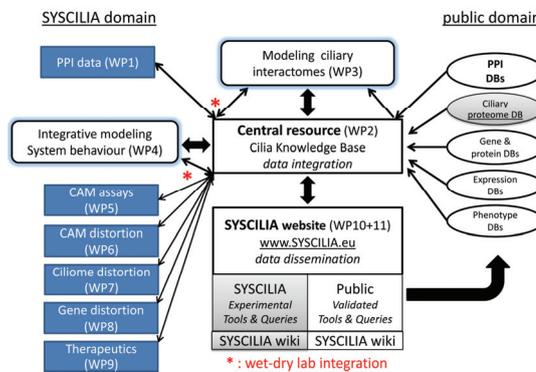


Figure 3 SYSCILIA integrative knowledge management through the central resource. Boxes in blue indicate wet-lab science; clear or gray boxes indicate computational efforts/resources



Figure 4 Screenshot of the SYSCILIA website: www.SYSCILIA.org

Systems biology... is about putting together rather than taking apart, integration rather than reduction. It requires that we develop ways of thinking about integration that are as rigorous as our reductionist paradigms, but different... It means changing our philosophy.

– Denis Noble, *The Music of Life: Biology beyond the genome* –

Consortium

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Picture of consortium members taken during the annual meeting 2011

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