Uncovering the Biological Programs that Govern Development

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The developmental process by which complex tissues, organs and organisms develop begins with pluripotency: the ability of so-called naïve embryonic stem cells to generate the full spectrum of adult cell types, as well as the germline. Understanding how these cells differentiate to diverse fate-restricted lineages is key both to understand the biological programs that govern development, but also to utilise the power of these cells for regenerative medicine. Fate decisions arise as the consequence of a complex interplay between regulatory factors, and while experiments have revealed critical genes and possible interactions between them, our understanding of stem cell decision-making remains fragmentary. Against this backdrop, automated reasoning provides a powerful strategy to navigate this complexity and to derive interaction networks that are consistent with experimental specifications. These networks can subsequently be used to formulate predictions of untested behaviour that guide experiment and inform model refinement. In this talk, I will describe such a reasoning methodology, which has been applied to investigate stem cell pluripotency through an iterative computational and experimental strategy. Furthermore, I will show how this approach has generated insight into how fate-restricted cells can be reprogrammed to the embryonic stem-like state.