

## Intrinsic and extrinsic control of developmental timing in mouse and human stem cell models

**Project Code:** TRG-BABR-TR

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**Research area:** Evo-devo, Stem Cells and Developmental Biology

**BBSRC DTP main strategic theme:** Understanding the rules of life

**BBSRC DTP secondary strategic theme:** Transformative technologies, Bioscience for an integrated understanding of health

### Project outline:

How processes are temporally controlled is a fundamental question in developmental biology.

Understanding the rules that determine how cells and organisms can precisely initiate and terminate processes at specified times and how do they modulate the rate at which they tick will help us explain when processes go awry, for example in tissue overgrowth or deficits.

We have developed comparative stem cell differentiation models to spinal cord motor neurons from mouse and human embryonic stem cells to investigate the molecular mechanisms that control the rate of development (Rayon et al., 2020). In this project, the candidate will perform an in-depth analysis of the relevance of cell number and cell cycle length in developmental timing in mouse and human neural progenitors.

The specific aims of the project are:

1. To adapt the motor neuron differentiation protocol to geometrically confined conditions and assess the speed of differentiation in reproducible and spatially organized cell numbers in mouse and human.
2. To test if the speed of spinal cord motor neuron differentiation is similar across species independently of cell cycle by inducing cell cycle perturbations. We will apply modelling and statistical approaches to track the rate of progression in separate and co-cultured models.
3. To profile the secretome via mass spectrometry on such differentiations and identify extrinsic regulators of developmental timing.

Successfully identified candidates and downstream druggable cyclin targets will likely be translatable interventions to control development pace. Altogether, this project will help us unravel the role of cell cycle on developmental timing and propose a computational framework of how do tissues balance proliferation and differentiation to achieve their target size.