



Molecular Genetics

UNIVERSITY OF TORONTO

FACULTY CANDIDATE SEMINAR

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CANDIDATE FOR
ASSISTANT PROFESSOR,
MOLECULAR BIOLOGY &
GENETICS

**Thurs, April 24,
2025**

**2:00 PM -
3:00 PM**

Red Seminar Room

Donnelly CCBR
160 College Street

CRISPy Chickens: Genetically coordinated cell fate transitions in neural tube development

Development relies on the coordinated differentiation of stem cells in dynamically changing environments. An excellent example is vertebrate neural tube formation. Here, stem cells transition through a dynamic signalling landscape to form neural tissue where the detailed gene regulatory mechanisms remain ill-defined. To address this, we developed and performed a multiplexed in vivo single-cell perturbation screen in chick embryos of genes that change in their expression with acquisition of the neural tube lineage. This revealed a role for the gene *MLLT3*, a component of the super elongation complex, in specification of neural identity. Perturbation of *MLLT3* resulted in knockout cells adopting a lateral plate mesoderm fate over that of the neural tube causing kinked spines. We discovered that *MLLT3* depletion caused misregulation of genes involved in Wnt and Retinoic Acid (RA) signalling, key regulatory pathways of neural fate. We then compared the effect of *MLLT3* loss to the forced expression of mutant *RARα*, either lacking the *MLLT3* binding domain or consisting of only the *MLLT3* binding region. In all cases, neural tube progenitors were depleted, resulting in smaller neural tubes. However, only *MLLT3* loss caused disruption of the stem cell compartment, indicating a dual role of stem cell maintenance coupled with RA driven neural fate acquisition. Together this data demonstrates a system appropriate for performing in vivo CRISPR screens in chick embryos and identifies a previous unanticipated role for *MLLT3*. More broadly, it highlights a mechanistic gene regulatory strategy of lineage emergence in a dynamic signalling landscape.