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Poster Submissions

Poster Title

Thyroid Conversion of Mouse ESC-Derived Anterior Foregut through Transient Overexpression of Nkx2-1

Authors and their Affiliation

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Abstract Submission

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Would you like your abstract to be considered for an oral presentation (students and post docs only)?

Yes

Introduction:
Thyroid lineages are derived from mouse embryonic stem cells (mESCs) through brief BMP4/TGF-β signaling inhibition at the definitive endoderm stage leading to anterior foregut endoderm (AFE), followed by FGF2/BMP4 treatment. These cells are characterized by expression of Nkx2-1, a homeodomain transcription factor expressed in the developing lung, thyroid, and forebrain. Currently, little is known about the specification process and the yield of progenitors derived is low.

Methods:
For this project, we utilized a mESC line double knock-in GFP-T/hCD4-Foxa2 with a doxycycline-inducible Nkx2-1 transgene (Tet-On).

Results:
Activation of the Nkx2-1 transgene for 24 hours at the AFE stage induces and maintains high levels of endogenous Nkx2-1 (up to 80% Nkx2-1^{+} cells) as well as thyroid-specific markers including Pax8 (up to 60% Nkx2-1^{+},Pax8^{+} cells), Tg, Foxe1, Hhex, Nis, and Tshr at later stages (day 22+) in our protocol. These cells can be cultured in three-dimensional matrix, where they mature and organize into the distinctive follicle structure.
Critical determinants of this thyroid lineage specification have been revealed by variations in developmental stage timing, signaling pathways, and sorting of subpopulations. Specifically, these experiments highlight a very narrow developmental time window of cellular competence to respond to exogenous Nkx2-1. They also show essential aspects including the derivation of anterior foregut endoderm populations with varied competence (marked and sorted by Foxa2 expression) and the necessity of dual FGF2/BMP4 signaling activation.
To provide further insights into the mechanisms of this thyroid specification from AFE, we are analyzing RNA-Seq data sets acquired from relevant stages to identify potential targets of Nkx2-1 and changes in global gene expression.

Conclusion:
The results demonstrate that Nkx2-1 can act as a stage-specific inductive signal during mESC differentiation to thyroid follicular cells. This method has provided novel insights into the thyroid specification process and exemplifies the potential of a more efficient system for deriving and studying thyroid cells, which can be used for *in vitro* modeling of development and disease.