

Single-nuclei RNA sequencing of the normal pituitary gland and pituitary neuroendocrine tumors



Joseph Oh, Rob Osorio, Jay Jung, Alex Ehrenberg, Aaron Diaz, Manish Aghi

BACKGROUND

- Pituitary neuroendocrine tumors (PitNETs) = common intracranial tumors of the anterior pituitary gland.
- The 2017 WHO classification introduced a new approach based on cell lineage using key transcription factors (TFs) for categorizing pituitary tumors.

- Still limited understanding of PitNET tumorigenesis and the dynamics of TF expression.

- Utilized single-nuclei RNA-sequencing, aimed to reconstruct a comprehensive atlas of the human pituitary gland and investigate the origin and trajectory leading to different subtypes of PitNETs

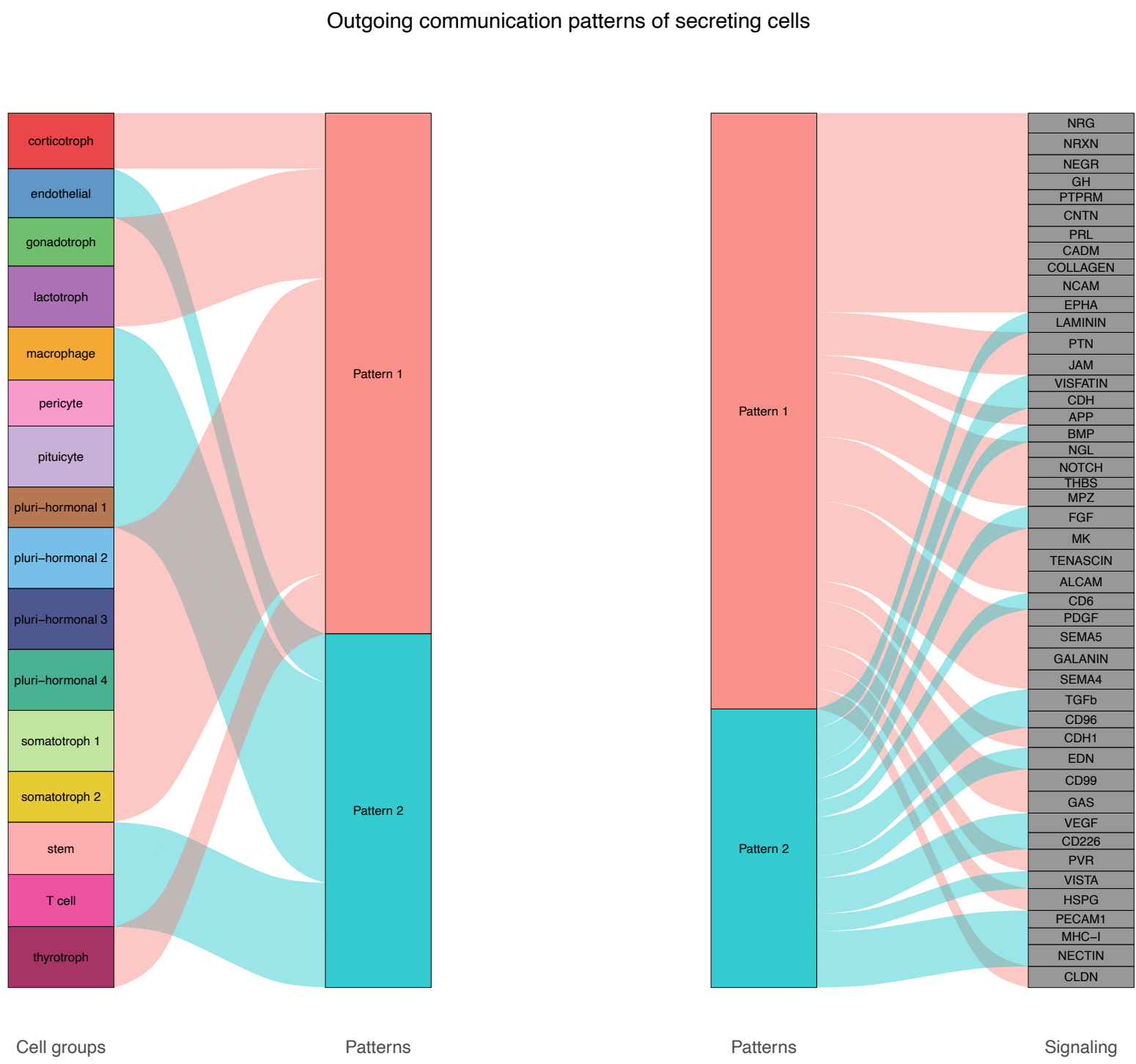
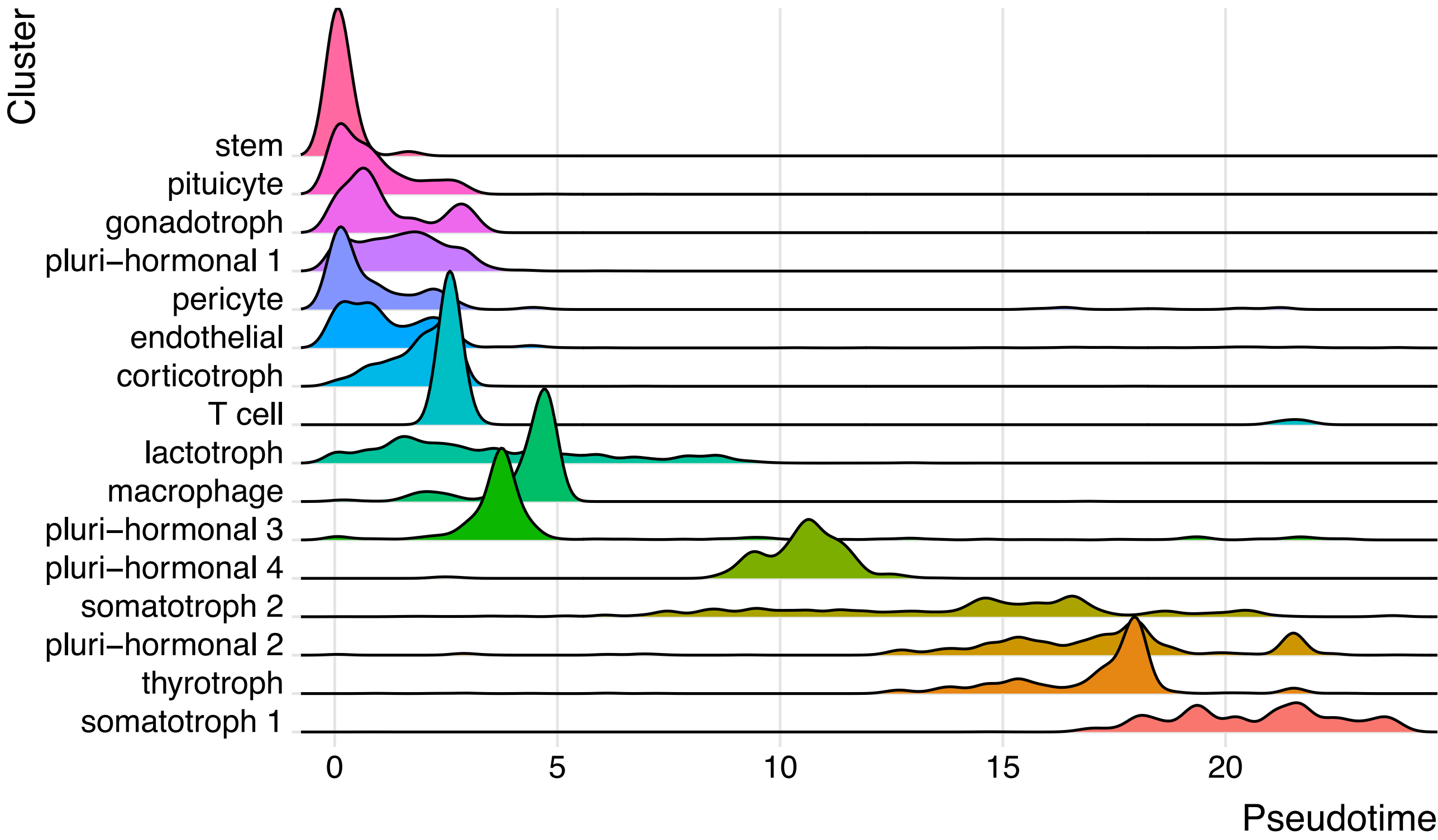
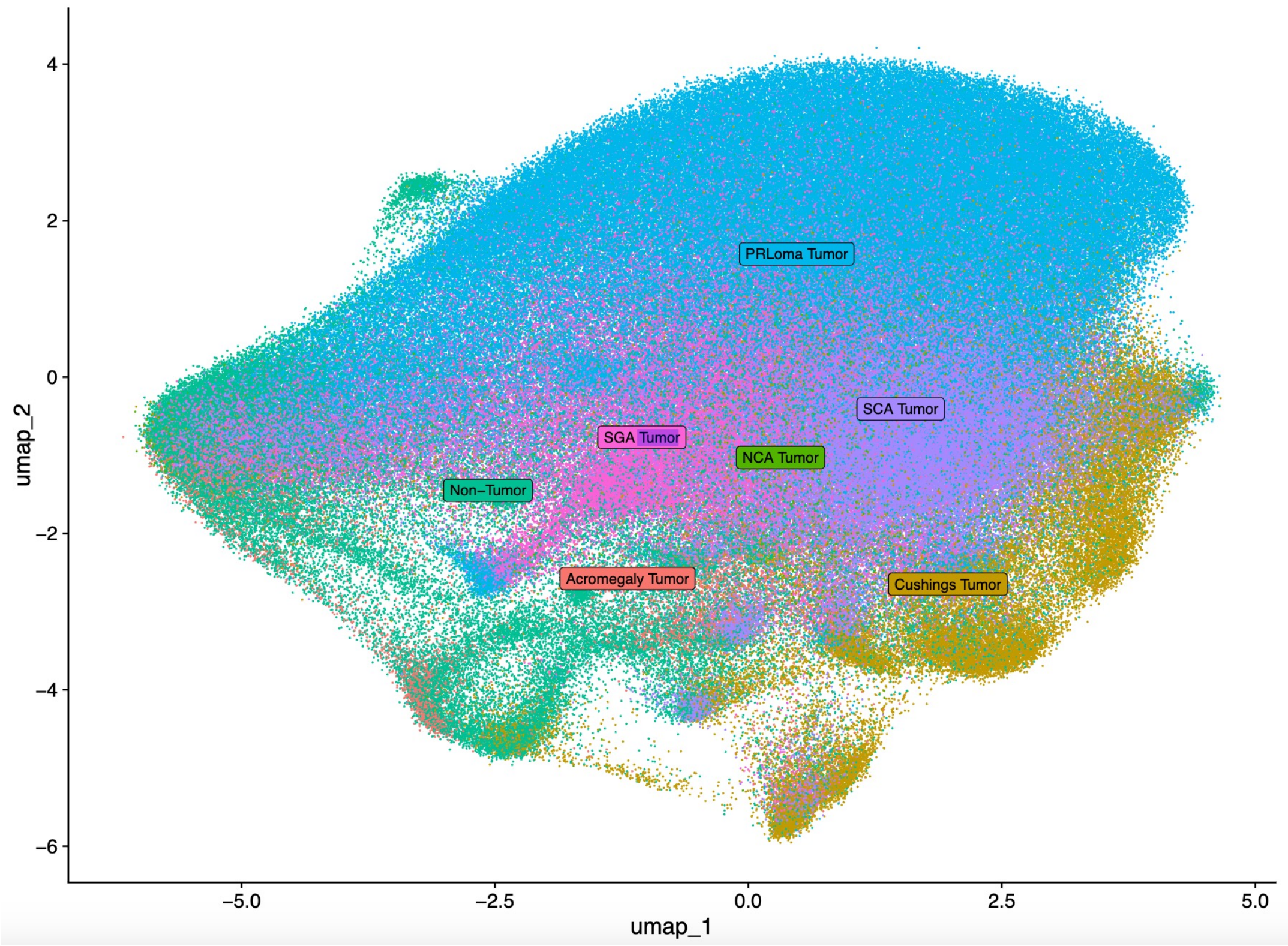
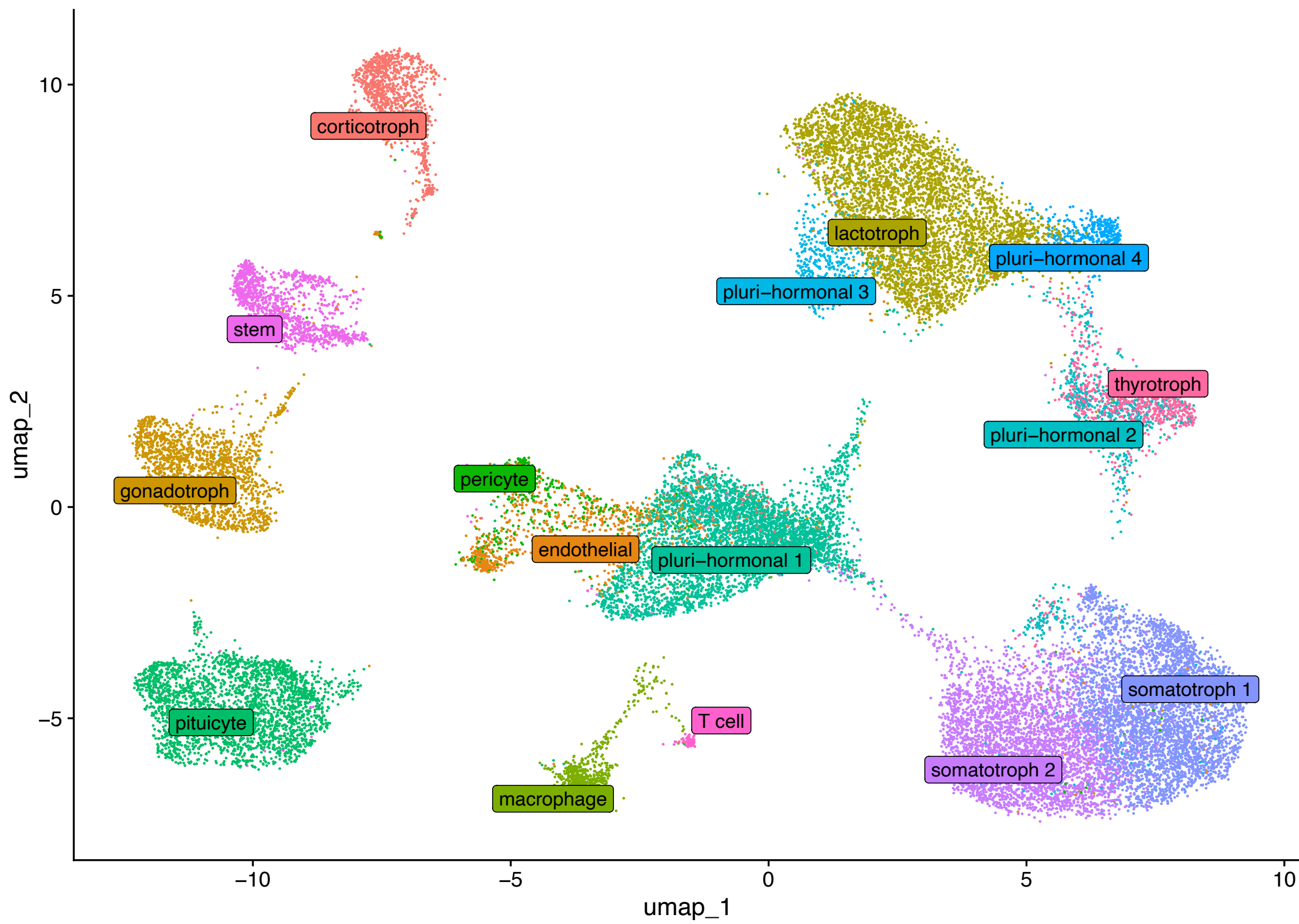
METHODS

-Normal pituitary glands (n=2) from the UCSF Memory and Aging Center

-Pituitary tumor samples (acromegaly n=2, Cushing's n=2, prolactinoma n=2, silent corticotroph n=2, silent gonadotroph n=2, and null cell n=2) from transsphenoidal surgeries at UCSF

-Flash-frozen and nuclei isolation, droplet-based single-cell RNA sequencing (scRNA-seq) library preparation using the Chromium Single Cell 3’ Library and Gel Bead and Multiplex Kit (10x Genomics).

-Uniform Manifold Approximation and Projection (UMAP), pseudotime analysis, and the exploration of cell-cell communication networks.



University of California
San Francisco

RESULTS

-n= 419,874 cells.

- Normal pituitary gland= 17 distinct clusters, representing different cell types including neuroendocrine cells (corticotroph, gonadotroph, lactotroph, thyrotroph, and somatotroph), immune cells (macrophages, T cells), stroma cells (pituicytes, pericytes, endothelial cells), and adult stem cells.

-Pluri-hormonal clusters expressing multiple neuroendocrine-type signatures were observed, indicating potential intermediate or transitional states between different cell lineages

- Through cell-chat analysis, 46 diverse signaling pathways involved in cell growth, hormonal signaling, immune interactions, and vasculature interactions were identified.

- Both preserved and altered transcription factor expression patterns in pituitary neuroendocrine tumors compared to those observed during gland development

DISCUSSION

This study provides comprehensive insights into the cellular heterogeneity, developmental dynamics, and communication networks within the adult human pituitary gland, as well as in pituitary neuroendocrine tumors.

Notably, we discovered distinct populations of neuroendocrine cells capable of producing multiple hormone types, representing intermediate stages of development.

The transcriptomic profile of pituitary tumor cells suggests a more fluid nature, indicating a spectrum of cellular identities rather than rigid classifications. This highlights the need for a flexible approach to classification and subtyping.

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