

Deciphering Neuronal Development & Vulnerability in the Hypothalamus



Thomas Kim Lab
- DANDRITE & Biomedicine

Exploring Neuronal Fate, Microglial Interactions, and Pathological Modeling

Who We Are

We investigate how hypothalamic neurons form, differentiate, and function, with a focus on both intrinsic mechanisms and extrinsic influences.

Our work spans normal development to pathological conditions like Alzheimer's Disease and maternal obesity, aiming to uncover the mechanisms underlying neuronal vulnerability and neuroinflammation.

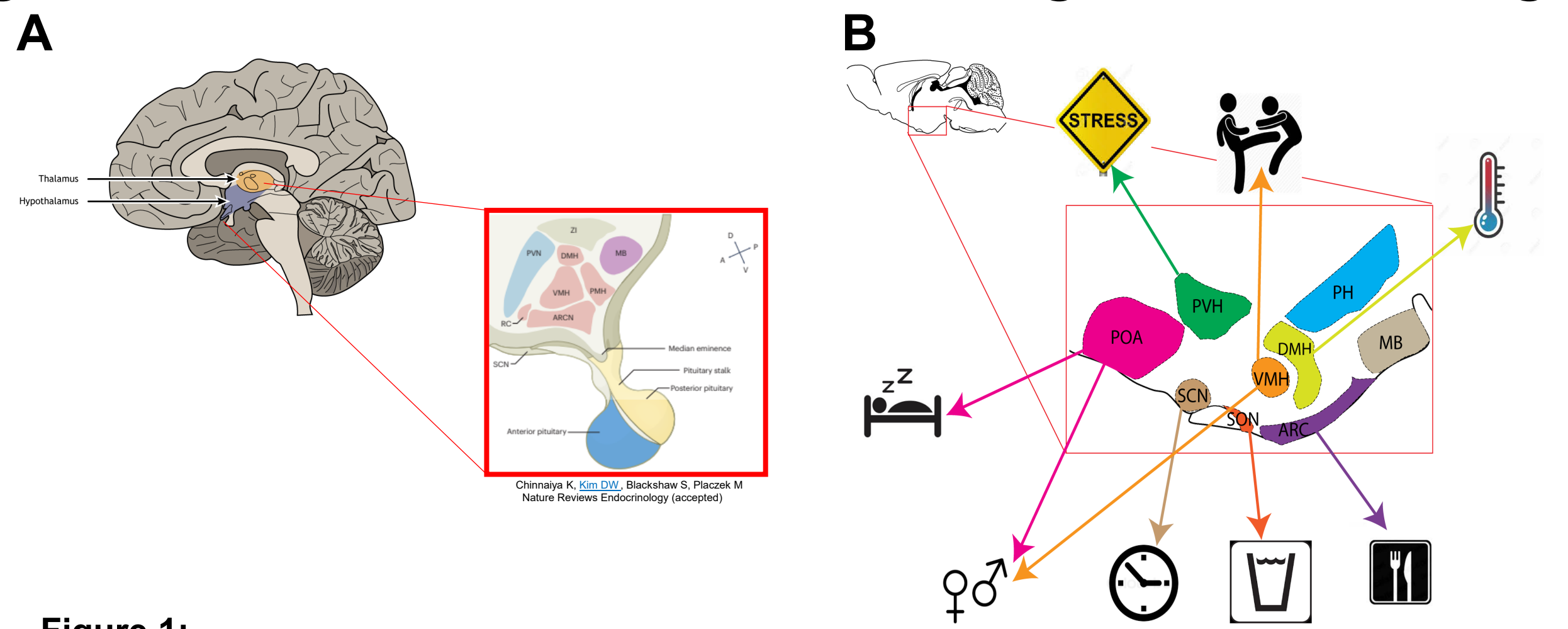


Figure 1:

A) Anatomical location of the hypothalamus within the brain, highlighting its proximity to key regions
B) Overview of hypothalamic functions, including regulation of homeostasis, and metabolism

Our Approach and Methods

Approach 1: Characterizing Development

We aim to uncover how neurons & microglia mature during early life.

- Intrinsic Mechanisms: Single-cell omics reveal how genes shape neuronal fate and function.
- Extrinsic Influences: Microglial activity guides circuit formation and neuronal interactions.

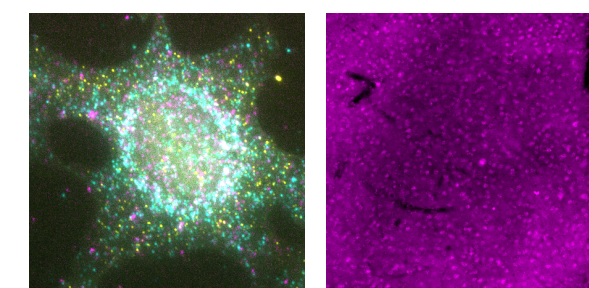


Figure 2:

Multiplex smFISH: An in-house developed method for efficient spatial transcriptomics

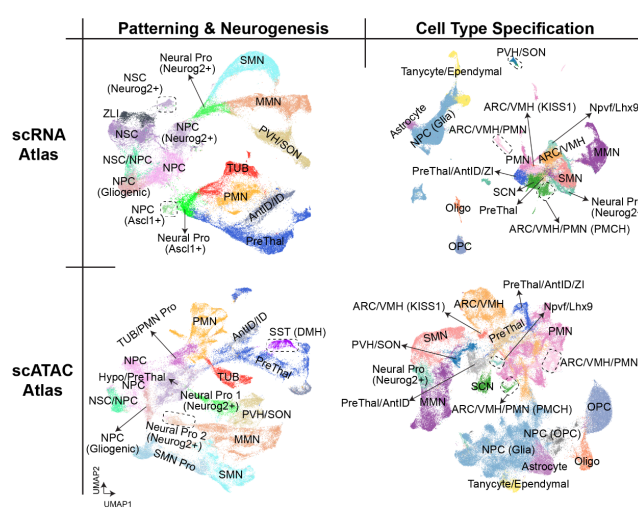


Figure 3:

Single-Cell Atlas: Comprehensive datasets mapping cell types, pathways, and gene networks during development, aging, and Alzheimer's in the hypothalamus

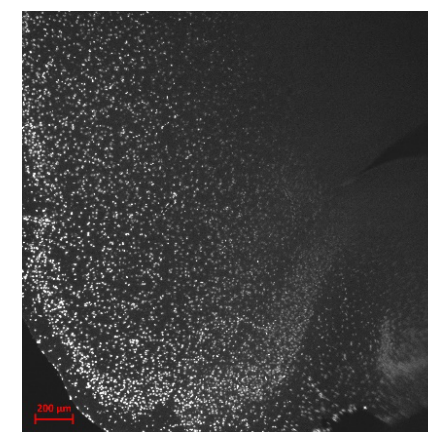


Figure 4:

Brain Clearing and Lightsheet Imaging



Figure 5:

Mouse models with dual-pathology (amyloidosis and tauopathy) & inducible Cre for microglia-specific *in vivo* CRISPR manipulations

Approach 2: Modeling Abnormal Conditions

We investigate how maternal obesity/infection, and Alzheimer's pathology disrupt hypothalamic function.

- Mouse Models: Alzheimer's models (APP/PS1 for plaques, Tau hyperphosphorylation for tangles).
- Focus: Identify brain regions and neuron types most vulnerable to developmental and inflammatory stressors.
- Goal: Unravel the origins of metabolic and neuroinflammatory imbalances tied to hypothalamic dysfunction.

Approach 3: Manipulating Key Components

We leverage advanced tools to test hypotheses about neuronal and microglial function.

- Models: Transitioning from *in vitro* cell lines and iPSCs to *in vivo* mouse models.
- Methods: CRISPRa/i for gene regulation with viral delivery systems, and behavioral profiling

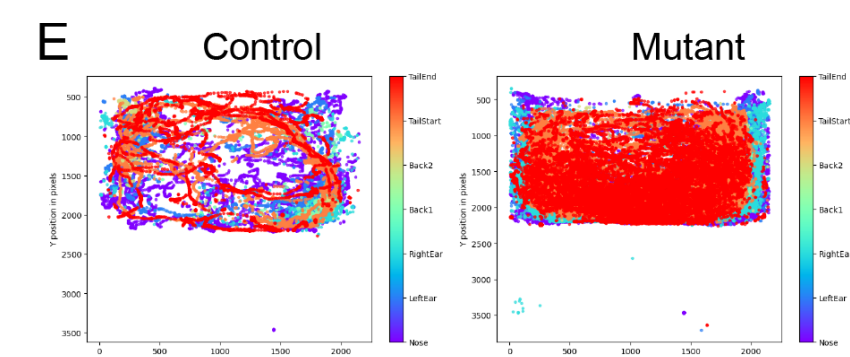


Figure 6:

Deep-Learning Behavioral Analysis

Student Opportunities

Join Our Research Efforts!

- Development: Uncover intrinsic & extrinsic factors shaping hypothalamic development
- Pathological Modeling: Study neuroinflammation and neuron-specific vulnerabilities in Alzheimer's disease
- Advanced Manipulation: Utilize CRISPRa/i and in-house microscopy to test hypotheses and validate findings.



Figure 7:

Our Lab Microscope

