Docket #: S23-071

Modeling human sensory ascending pathway in assembloids derived from human pluripotent stem cells

The ascending somatosensory pathway transmits sensory information, including pain, touch and itch, from the peripheral nervous system to the brain. Dysfunctions in this pathway are linked to disorders like peripheral neuropathy and autism spectrum disorder. Despite a significant need for effective therapeutics modulating pain and other somatosensory modalities, clinical translation remains challenging, which is likely related to species-specific features and the lack of in vitro models to directly probe and manipulate this polysynaptic pathway.

To remedy this issue, Stanford researchers have developed the first human ascending sensory pathway model using assembloids. The method involves differentiating human induced pluripotent stem (hiPS) cells into regionalized neural organoids resembling the components of the human sensory ascending pathway (Figure 1). This model provides a unique opportunity to directly study and manipulate the human sensory ascending pathway, overcoming previous challenges. This platform also enables functional analysis, including synchronized neural activity across the entire sensory pathway, offering a powerful tool for drug discovery targeting sensory disorders.

Figure:

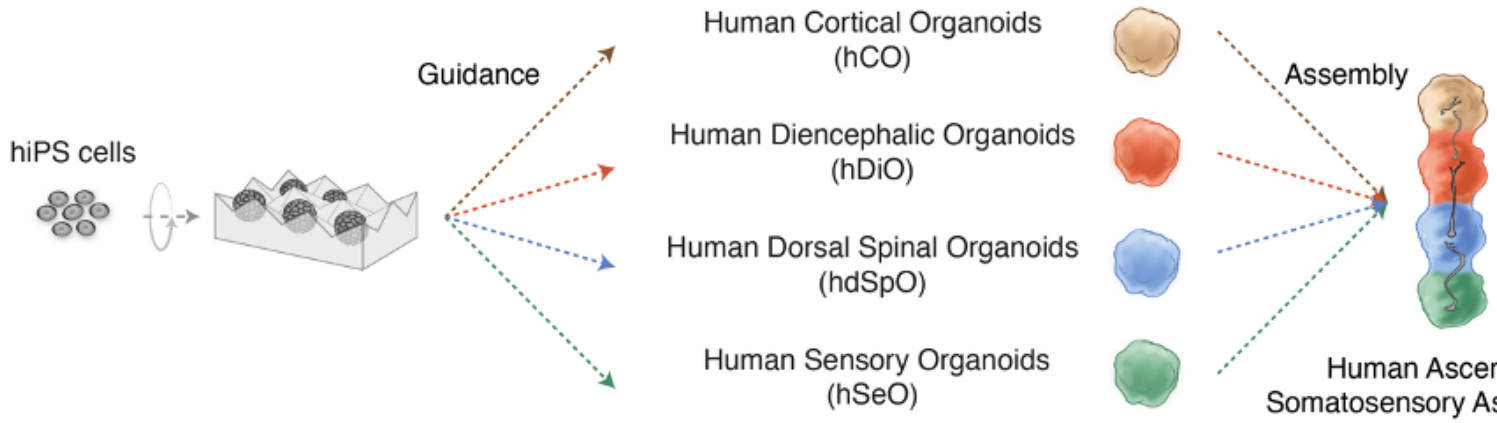


Figure description: Building human ascending somatosensory assembloid from human induced pluripotent stem cells.

Image Credit: inventors

Stage of Development
Proof of concept- models have shown to trigger and ascend the full sensory pathway

Applications

- Autism spectrum disorder
- Peripheral neuropathy
- Research mechanisms of sensory processing and pathogenesis
- Identification of novel therapeutic targets

Advantages

- First human cellular model of the ascending sensory pathway
- **Human-Specific Sensory Circuitry**: Provides the first in vitro model that resembles the human ascending somatosensory pathway, overcoming the limitations of species differences in animal models.
- **Comprehensive Functional Analysis:** Enables simultaneous monitoring of neural activity across multiple interconnected regions (sensory, spinal, thalamic, and cortical) through calcium imaging and extracellular recordings.
- **Targeted Disease Modeling and Therapeutic Screening:** Allows for the study of sensory disorders, such as pain insensitivity, through genetic manipulation (e.g., SCN9A knockout) and offers a platform for high-throughput

drug discovery targeting human sensory pathways.

Publications

- Kim JI, Imaizumi K, Thete MV, Hudacova Z, Jurjut O, Amin ND, Scherrer G, Pasca SP. Human assembloid model of the ascending neural sensory pathway. *bioRxiv* [Preprint]. 2024 Mar

Patents

- Published Application: WO2025165614

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