Three distinct classes of myenteric ganglia in mice and humans

INSIGHTS FROM QUANTITATIVE ANALYSES

BACKGROUND

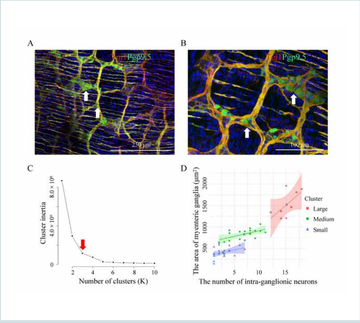
The myenteric plexus primarily consists of the myenteric ganglia, which include enteric neurons, synaptic neuropils, and glial cells. Abnormal myenteric plexus formation can result in gastrointestinal disorders. Comprehensive morphological classification studies of myenteric ganglia remain limited.

METHODS

Whole-mount immunofluorescence staining was used to label myenteric ganglia in the colon tissue of mice and children. The ganglionic area and the number of intraganglion neurons were quantified by the K-means clustering algorithm. The guts of an embryonic day 11.5 (E11.5) mouse were cultured and immunostained to observe the characteristics of developing myenteric ganglia.

RESULTS

Myenteric ganglia can be categorized into three groups in the colon tissues of mice and healthy children. A similar classification was observed for Tuj1-positive neuronal cell clusters in the midgut of the E11.5 mouse. Culture of the E11.5 mouse midgut revealed that the area of post-cultured clusters of developing neurons also fell into three distinct categories, with a noticeable increase compared to pre-culture.

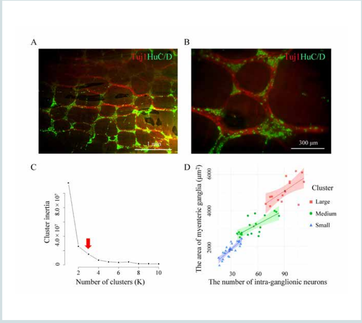


Three classes of mouse colonic myenteric ganglia.

(A and B) Tuj1 and Pgp9.5 labeled the ganglia and neurons within the myenteric plexus in the colons of 4-week-old mice, (A) representative image of the overall myenteric plexus network at 200× magnification, (B) representative image of a specific ganglion at 400× magnification; white arrows indicated the myenteric ganglion. Three mice were used, six images were produced, and 49 paired data were generated.

(C) The Elbow Method was used to determine the optimal K-value (red arrow) of (A and B).

(D) The Classification graph of K-means clustering for (A and B). Linear regression analysis was performed within each group, resulting in trend lines, and the colored areas represented 95% confidence intervals.

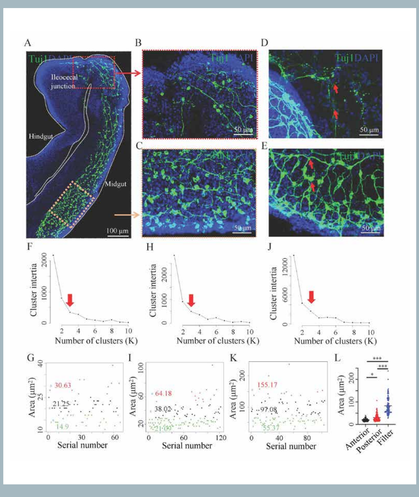


Classification of human colonic myenteric ganglia.

(A and B) Tuj1 and HuC/D labeled the myenteric plexus and neurons within the muscularis propria of normal colon from two patients. Twenty-four images were produced, and 58 paired data were generated.

(C) The Elbow Method was used to determine the optimal K-value (red arrow).

(D) The Classification graph of K-means clustering.



Whole-mount staining of embryonic mouse gut and culture in vitro.

(A) Enteric neuron precursors and neurons were labeled with Tuj1 at E11.5. Three mice were used, five images were produced, and three sets of area data (66, 122, and 104, respectively) were generated.

(B and C) Local magnifications of the red and yellow boxes in (A), respectively.

(D) The Tuj1-positive neuron precursors and neurons (red arrows) migrating onto the filter membrane.

(E) The clusters of Tuj1-positive cells (red arrows) within the gut.

Determination of the optimal K-value (red arrow) for the area of Tuj1-positive cell clusters in the anterior midgut (F), posterior midgut (H), and the midgut on the filter (J) using the Elbow Method.

Classification graph of area of Tuj1-positive cell clusters in the anterior midgut (G), posterior midgut (I), and the midgut on the filter (K) using K-means Clustering. (L) Statistical analysis for area of Tuj1-positive cell clusters among the above three groups using one-way ANOVA for multiple comparisons. Anterior, anterior midgut section; posterior, posterior midgut section; filter, **posterior midgut section on the filter membrane after culture. *, p = 0.0200, ***, p < 0.001.**

CONCLUSION

The myenteric ganglia in mice and humans can be categorized into three groups based on both the ganglionic area and intraganglion neuron count, and distinct classes of myenteric ganglia may be present during early development.

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