News Release

Title

Differentiating cells mechanically limit progenitor cells' interkinetic nuclear migration to secure apical cytogenesis

Key Points

1. Developing brains use a mechanism like the Otoshi-buta (the drop lid), a kitchen wisdom.
2. Differentiating cells in embryonic cerebral walls form a dense filter-like layer to mechanically barrier nuclei of neural stem cells.
3. Loss of this barrier or fence results in abnormal popping out of neural stem cells' nuclei, leading to inability of neural stem cells to produce new cells.

Summary

Brain formation relies on production of new cells by neural stem cells, which abundantly exist in the embryonic period. Neural stem cells are thin and elongated like radish sprouts (Kaiware-daikon) or Enoki mushrooms. They move their nuclei depending on the status of cell production. They divide along the inner (apical) surface of the wall and their nuclei are therefore near the surface just before and after mitosis, while their nuclei are away from the surface when they synthesize DNA in preparation for subsequent division. The range of this elevator-like (to-and-fro) nuclear movement is about 100 μm even though the total length/height of each neural stem cell is ~300 μm. Why (for which biological significance) it should be limited and how this range limitation is established are both unknown. In the present study, Professor Takaki Miyata, Assistant Professor Takumi Kawaue, and a 6th year medical student Yuto Watanabe in Nagoya University Graduate School of Medicine (dean: Kenji Kadomatsu, M.D., Ph. D.) showed that a transient layer consisting of differentiating cells and their dense processes mechanically barriers nuclei of neural stem cells. Experimental drilling of this barrier-like layer resulted in abnormal popping out of neural stem cells' nuclei and the arrest of cell production by such nuclei-overshot stem cells. Thus demonstrated importance of mechanical limitation of nuclear movement during brain development is reminiscent of the usefulness of the Otoshibuta (Drop Lid) to limit a cooking space for condensing soap and avoiding undesired floating of ingredients. This study was published online in Development on June 26, 2018.

Research Background

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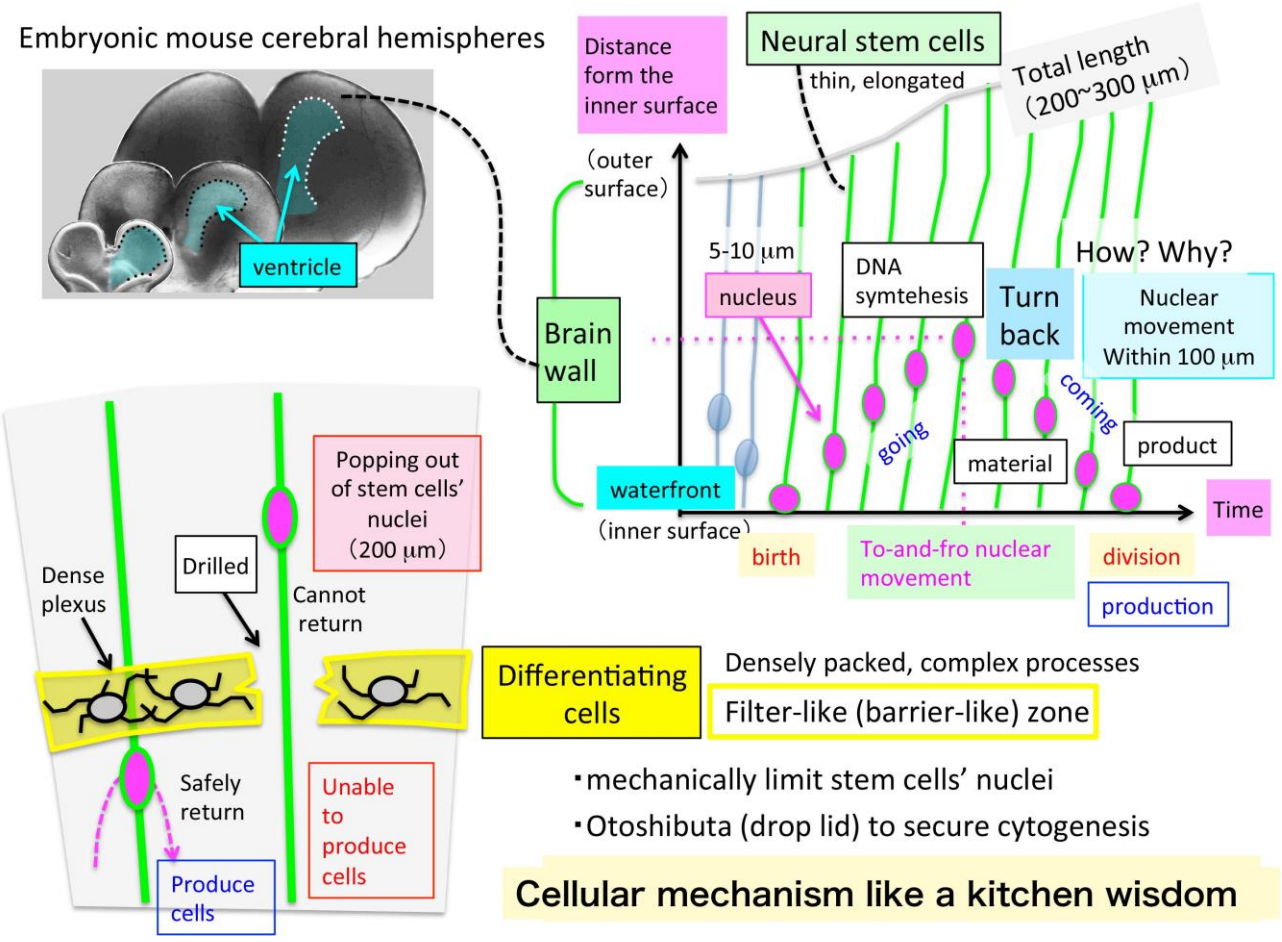

Research Results

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Research Summary and Future Perspective

Boomerangs or artificial satellites should turn back at an appropriate point. This study found that mouse neural stem cells' nuclei start to come back after a 100-μm going because they are mechanically fenced by differentiating cells there. Drilling of the fence resulted in abnormal popping out of stem cells' nuclei to 200 μm. Since the normal range of nuclear shuttling is much

greater in human (200 μm), this study provides a basis of future comparative studies aiming at elucidation of mechanisms underlying evolution of the human brain.

Publication

Yuto Watanabe, Takumi Kawaue, Takaki Miyata
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https://www.med.nagoya-u.ac.jp/medical_J/research/pdf/Development_20180627.pdf