#### News Release

## Title

Elasticity-based boosting of neuroepithelial nucleokinesis via indirect energy transfer from mother to daughter.

### **Key Points**

1. We identified novel mechanism for nucleokinesis of neural progenitor cells.

2. Subapical area of developing cerebral cortex has unique elastic properties.

3. Mother cells' rounding up for cytokinesis transiently deforms surrounding subapical microzone. The restoring force from the microzone is received by newborn daughter cells, thereby boosting their basalward nucleokinesis.

#### Summary

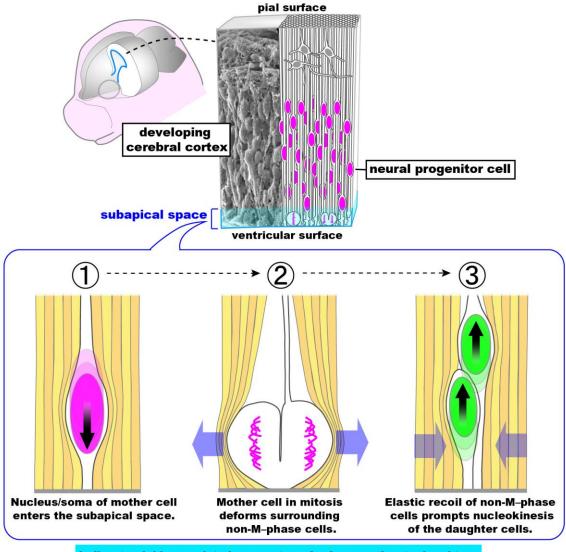
For the normal development of animal organs in a limited time and space, production of cells must be efficiently coordinated with tissue-forming cellular logistics. In the proliferative zone of the embryonic mammalian cerebral cortex, cell production occurs at the inner surface of the wall. Previous studies suggested that inward movements of progenitors' nuclei before division may induce passive outward displacement of daughter cells' nuclei. But, how such passive nuclear traffic is achieved remained unknown. In the present study reported by Professor Takaki Miyata, Assistant professor Tomoyasu Shinoda in Nagoya University Graduate School of Medicine (dean: Kenji Kadomatsu, M.D., Ph. D.) showed that a microzone where progenitor cells undergo mitosis is elastic due to a dense packing of flexible fiber-like cellular processes via actomyosin-dependent horizontal narrowing of the inner surface. Each mother cell's rounding up for division via actomyosin laterally pushed this elastic microzone, thereby storing mechanical energy there. Experiments to add or remove mechanical stress reveled that this mother-derived mechanical energy transiently stored is then given back to the mother's daughter cells, thereby helping the prompt outward movement of the daughter cells' nuclei in an energy saving-manner. Mathematical simulations showed that timely departure of newly generated daughter cells is critical for the overall tissue structure of the cerebral proliferative zone. This study was published online in PLOS Biology on April XX, 2018.

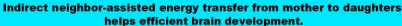
### **Research Background**

For the normal development of animal organs in a limited time and space, production of cells must be efficiently coordinated with tissue-forming cellular logistics. In the proliferative zone of the embryonic mammalian cerebral cortex, cell production occurs at the inner surface of the wall. Previous studies suggested that inward movements of progenitors' nuclei before division may induce passive outward displacement of daughter cells' nuclei. But, how such passive nuclear traffic is achieved remained unknown.

### **Research Results**

We found that a microzone where progenitor cells undergo mitosis is elastic due to a dense packing of flexible fiber-like cellular processes via actomyosin-dependent horizontal narrowing of the inner surface. Each mother cell's rounding up for division via actomyosin laterally pushed this elastic microzone, thereby storing mechanical energy there. Experiments to add or remove mechanical stress reveled that this mother-derived mechanical energy transiently stored is then given back to the mother's daughter cells, thereby helping the prompt outward movement of the daughter cells' nuclei. Mathematical simulations showed that timely departure of newly generated daughter cells is critical for the overall tissue structure of the cerebral proliferative zone.





# **Research Summary and Future Perspective**

Our findings revealed a novel system for the efficient production logistics in cerebral proliferative zone, by physical collaboration of M-phase and non-M-phase cells. Understanding such physical/mechanical aspect in the brain morphogenesis will benefit the progression of tissue engineering for ongoing regenerative medical treatment, especially for the central nervous system.

# Publication

Shinoda T, Nagasaka A, Inoue Y, Higuchi R, Minami Y, Kato K, Suzuki M, Kondo T, Kawaue T, Saito K, Ueno N, Fukazawa Y, Nagayama M, Miura T, Adachi T, Mitata T. Elasticity-based boosting of neuroepithelial nucleokinesis via indirect energy transfer from mother to daughter. PLOS Biology, April 20, 2018.

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# Japanese ver.

https://www.med.nagoya-u.ac.jp/medical\_J/research/pdf/PLOS\_B\_20180423.pdf