Calibrated mitotic oscillator drives motile ciliogenesis

Cell division and differentiation depend on massive and rapid organelle remodeling. The mitotic oscillator, centered on the cyclin-dependent kinase 1–anaphase-promoting complex/cyclosome (CDK1-APC/C) axis, spatiotemporally coordinates this reorganization in dividing cells. Here we discovered that nondividing cells could also implement this mitotic clocklike regulatory circuit to orchestrate subcellular reorganization associated with differentiation. We probed centriole amplification in differentiating mouse-brain multiciliated cells. These postmitotic progenitors fine-tuned mitotic oscillator activity to drive the orderly progression of centriole production, maturation, and motile ciliation while avoiding the mitosis commitment threshold. Insufficient CDK1 activity hindered differentiation, whereas excessive activity accelerated differentiation yet drove postmitotic progenitors into mitosis. Thus, postmitotic cells can redeploy and calibrate the mitotic oscillator to uncouple cytoplasmic from nuclear dynamics for organelle remodeling associated with differentiation.
Smooth 2D manifold extraction from 3D image stack

Three-dimensional fluorescence microscopy followed by image processing is routinely used to study biological objects at various scales such as cells and tissue. However, maximum intensity projection, the most broadly used rendering tool, extracts a discontinuous layer of voxels, obliviously creating important artifacts and possibly misleading interpretation. Here we propose smooth manifold extraction, an algorithm that produces a continuous focused 2D extraction from a 3D volume, hence preserving local spatial relationships. We demonstrate the usefulness of our approach by applying it to various biological applications using confocal and wide-field microscopy 3D image stacks. We provide a parameter-free ImageJ/Fiji plugin that allows 2D visualization and interpretation of 3D image stacks with maximum accuracy.

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mTORC1 signaling and primary cilia are required for brain ventricle morphogenesis

Radial glial cells (RCGs) are self-renewing progenitor cells that give rise to neurons and glia during embryonic development. Throughout neurogenesis, these cells contact the cerebral ventricles and bear a primary cilium. Although the role of the primary cilium in embryonic patterning has been studied, its role in brain ventricular morphogenesis is poorly characterized. Using conditional mutants, we show that the primary cilia of radial glia determine the size of the surface of their ventricular apical domain through regulation of the mTORC1 pathway. In cilium-less mutants, the orientation of the mitotic spindle in radial glia is also significantly perturbed and associated with an increased number of basal progenitors. The enlarged apical domain of RGCs leads to dilatation of the brain ventricles during late embryonic stages (ventriculomegaly), which initiates hydrocephalus during postnatal stages. These phenotypes can all be significantly rescued by treatment with the mTORC1 inhibitor rapamycin. These results suggest that primary cilia regulate ventricle morphogenesis by acting as a brake on the mTORC1 pathway. This opens new avenues for the diagnosis and treatment of hydrocephalus.

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