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Women and Future in Science Seminar

Dynamic interplay of cytoskeletal motors during neuronal migration in confined brain tissue

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Dynamic interplay of cytoskeletal motors during neuronal migration in confined brain tissue

Cell migration is important in various physiological and pathological events such as morphogenesis, immune surveillance, and cancer metastasis. The nucleus is the largest and stiffest cargo and presents the biggest physical challenge for the cell to pass through the interstitial space between other cells and extracellular matrices. During brain development, newborn neurons in the mammalian brain migrate a long distance from the germinal layer to the specific layer in the cortex. It is agreed that the nuclear translocation in neurons is orchestrated by the pulling force of minus-end directed microtubule motor dynein (cytoplasmic dynein) and contractile force of actomyosin, yet the actual force generated by these cytoskeletal components remains elusive.

A major effort of my lab has been devoted to live-imaging of cytoskeletal dynamics in migrating neurons. A high spatio-temporal resolution imaging has revealed unexpected dynamic behaviors of the nucleus by complex interplays of cytoskeletal motors. Unlike the prevailing view of dynein-driven constant forward movement, the nucleus exhibits complex movement in order to advance in narrow interstitial spaces. The stochastic and inconsistent movement is driven by bidirectional microtubule motors which dynamically anchor and pull small points on the nuclear envelope via the LINC complex proteins. In contrast to the steering forces of the microtubule motors, actomyosin instead exerts strong contractile force in the front and rear of the nucleus. Neurons sense the space confinement via a mechanosensor Piezo1 and switch the force generation mechanism by recruiting distinct actomyosin networks. Thus, neurons are equipped with multiple cytoskeletal engines and migrate through diverse extracellular environment by switching the migration modes.

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