A bipartite module in the pericentriolar matrix scaffold mediates phosphoregulated binding to the γ-tubulin complex

Centrosomes consist of a centriolar core surrounded by a pericentriolar material (PCM) matrix that docks γ-tubulin complexes (γTuCs) to nucleate microtubules. During mitotic entry, Polo-Like Kinase 1 (PLK1) phosphorylates the N-terminus of the PCM scaffold protein SPD-5 to promote γTuC recruitment essential for chromosome segregation. Here,we show that the SPD-5 N-terminus exhibits two phosphoregulated γTuC binding elements, PRGB1 and PRGB2, both of which independently bind γTuCs upon PLK1 phosphorylation. Selective inhibition of either element impairs γTuC recruitment, while deleting both elements increases centrosome separation defects, recapitulating the complete loss of γTuCs. In the absence of PLK1, monomeric PRGB1 interacts with dimeric PRGB2, forming an autoinhibited conformation that prevents γTuC binding. PLK1 phosphorylation disrupts this interaction and relieves the autoinhibition through a conformational change without altering its oligomerization status. These results reveal a bipartite phosphoregulated module within the PCM scaffold that mediates γTuC recruitment to activate microtubule nucleation at mitotic centrosomes.

Generation of a micro-intestine system by reproducing interstitial flow and its application in viral infectious disease

Recent advances have enabled in vitro modeling of the human intestine, but it remains a challenge to recapitulate fully its structural and functional characteristics. We hypothesized that interstitial flow plays a vital role in intestinal development. We aimed to construct an in vivo-like multilayered intestinal tissue model (micro-intestine system) by differentiating human ES/iPS cells into intestinal cells on a microfluidic device. Numerical simulations demonstrated that interstitial flow could be replicated by gently perfusing medium through the microfluidic device's pores. Single-cell RNA-sequencing analysis revealed that intestinal epithelial cells, fibroblasts, and enteric neurons were simultaneously differentiated from human ES/iPS cells in micro-intestine systems. Interstitial flow within the microfluidic device enhanced the maturation of intestinal cells, leading to the development of a villi-like epithelium and an aligned mesenchymal layer. Furthermore, enterovirus infection studies showed that the micro-intestine system would be a useful tool for recapitulating the pathophysiology of infectious diseases. Our micro-intestine system not only overcomes the limitations of conventional intestine models but also offers a unique opportunity to study the pathophysiology of intestinal disease.