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Title: Discs Large licenses Pins to orient mitotic spindles

Abstract

Oriented cell divisions are critical to animal development. Division orientation determines the placement of daughter cells, and thereby promotes cell diversity and helps to organize and expand tissues. The direction in which a cell divides is established by the orientation of the mitotic spindle at metaphase. Spindle orientation in animals typically relies on an evolutionarily conserved machine comprised of at least four proteins: in flies, these are called Partner of Inscuteable (Pins), Gαi, Mushroom body defective (Mud), and Dynein. The canonical model is that Pins acts as a cortical anchor for Mud and Dynein, which exert a pulling force on astral microtubules that reels the spindle into alignment. Another established, but poorly understood, component of this machinery is Discs large (Dlg), an apical-basal polarity factor that interacts with phosphorylated Pins. Whereas previous work from our lab and others suggested that Dlg is required for Pins localization, I show here that Pins localization is unaffected by the loss of Dlg. My results indicate that Dlg works to activate, rather than localize Pins function. These results suggest that the canonical model is incomplete, raising the question of how the spindle orientation machinery is regulated.