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MITOSIS

Where did the membrane go?

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> …the total surface area of a cell decreases during mitosis-induced cell rounding as a consequence of blocked endosomal recycling.

Many adherent cells round up during prophase and metaphase and only regain their extended, flattened shape at cytokinesis. Boucrot and Kirchhausen now report that to accommodate the rounding-up shape change, endosomal uptake continues as normal but endosomal recycling is blocked, thereby reducing the overall surface area of the cell. Furthermore, the recovery of the surface area, which begins at the start of anaphase, is due to the reactivation of endosomal recycling.

Previous studies have investigated what happens to the cell membrane during mitosis, but have returned inconclusive results. Some studies have suggested that the overall cell-surface area decreases to accommodate the surface-to-volume ratio change, whereas others have suggested that the membrane develops ruffles of villi to compensate. Using live-cell imaging, Boucrot and Kirchhausen fluorescently stained the cell membrane at different stages during cell division to resolve the contradiction. Their findings showed that rounding up during mitosis caused a significant reduction (twofold in human HeLa cells and six- to eightfold in monkey BSC1 cells) in overall surface area. (By contrast, rounding up as a result of trypsin exposure caused increased membrane ruffling but no change in surface area.)

To examine how the surface area is reduced, the authors fluorescently labelled the σ2 subunit of the AP2 adaptor, a crucial element in clathrin-mediated endocytosis, and monitored it by live-cell imaging. They observed that the time needed for clathrin-coated pits to form and bud, as well as the size of clathrin-coated pits, remained constant throughout mitosis. Therefore, endocytosis is thought to remain normal throughout mitosis. By contrast, when the authors monitored endosomal recycling throughout mitosis, they observed that protein recycling back to the cell membrane (such as recycling of the transferrin receptor) was reduced during prophase and metaphase. However, recycling resumed at the same time that the cell began to recover plasma membrane.

To confirm the role of endosomal recycling, the authors inactivated VAMP3 and VAMP7, two proteins that are involved in the fusion of early and late endosomes to the cell membrane. Indeed, inactivation of either protein blocked the recovery of the cell membrane at the end of mitosis and prevented cells from undergoing cytokinesis. By treating cells with brefeldin A, which inhibits transport in the Golgi, the authors also ruled out the possibility that the Golgi contributes newly synthesized membrane at the end of mitosis.

Through live-cell imaging, Boucrot and Kirchhausen have shown that the total surface area of a cell decreases during mitosis-induced cell rounding as a consequence of blocked endosomal recycling. Starting in anaphase, endosomal recycling is reactivated and the two daughter cells reacquire enough plasma membrane to undergo cytokinesis. However, the question of how endosomal recycling is modulated and coordinated with mitosis remains to be addressed.

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ORIGINAL RESEARCH PAPER Boucrot, E. & Kirchhausen, T. Endosomal recycling controls plasma membrane area during mitosis. *Proc. Natl Acad. Sci. USA* **104**, 7939–7944 (2007)