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Journal club

COMING TO GRIPS WITH CELL SURFACE POLARITY

Towards the end of the 1970s, I was working at the EMBL with Ari Helenius and Henrik Garoff, studying Semliki Forest virus as a simple model of biological membranes, which led to our pioneering discoveries of the mechanisms of viral entry and viral membrane assembly. I then left the Semliki Forest virus model to Ari and Henrik, as I was striving to find a more suitable experimental model that would allow me to pursue my new research interest — cell polarity.

I made little progress at first; this changed dramatically after an astounding paper from Enrique Rodriguez-Boulan and David Sabatini was published, which showed that influenza virus buds from the apical membrane in a Madin–Darby canine kidney (MDCK) cell line, whereas vesicular stomatitis virus (VSV) is released basolaterally from these cells. I thought: what a cool experimental system! Daniel Louvard had just joined the EMBL, and luckily he had the MDCK cells in his suitcase. I was ready to go!

> “cells forced to grow on plastic or glass are only partially polarized”

However, the beginnings were troublesome. It turned out that not all cells in the monolayer were polarized, despite our frantic efforts, and VSV proteins were often seen at the apical membrane, instead of only basolaterally. I was beginning to think that I had made the wrong choice. The project was rescued by another paper from the Sabatini lab that reported on the use of semi-permeable filters to grow MDCK cells, which exposes the basal cell surfaces to the medium (Cereijido *et al.*).

When we fed radioactive amino acids to the filter-grown cells from their apical side, no label was taken up, in contrast to cells that were grown in a culture dish. At first this was puzzling, but then it dawned on us that epithelia feed from their basal side *in vivo*, which is exposed to the blood, and so the mechanisms for the uptake of nutrients in epithelial cells should be located basolaterally. We then found that filter-grown cells are fully polarized, whereas cells forced to grow on plastic or glass are only partially polarized, as otherwise they would starve to death. Accordingly, we showed that VSV was unable to infect the filter-grown cells from the apical side, and that the virus had to be applied through the filter pores. This led to the establishment of filter-grown MDCK cells as a model system to study epithelial cell polarity, using viruses as tools (Simons & Wandinger-Ness).

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ORIGINAL ARTICLES Rodriguez Boulan, E. & Sabatini, D. D. Asymmetric budding of viruses in epithelial monolayers: a model system for study of epithelial polarity. *Proc. Natl Acad. Sci. USA* **75**, 571–575 (1978) | Cereijido, M. *et al.* Polarized monolayers formed by epithelial cells on a permeable and translucent support. *J. Cell Biol.* **77**, 853–880 (1978) | Simons, K. & Wandinger-Ness, A. Polarized sorting in epithelia. *Cell* **62**, 207–210 (1990)