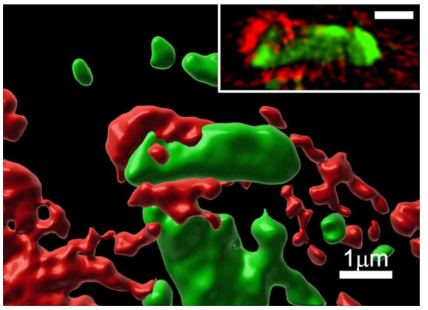
# This Week in The Journal

## Retinal Pigmented Epithelium "Nibbles" Away Outer Segment Tips

Ankita Umapathy, Gil Torten, Antonio E. Paniagua, Julie Chung, Madeline Tomlinson, et al.

(see pages 2653–2664)

The retinal pigmented epithelium (RPE) serves a remarkable support role in the retina, nourishing and maintaining photoreceptor cells in ways that are crucial for vision. This includes "nibbling" away at the tips of the outer segment (OS) of rods and cones. Photoreceptors are made up of stacks of membranous discs that contain photoreceptive proteins. As these discs are added at the base of the OS, the tip must be removed and recycled to make way. Deficits in this membrane ingestion and degradation by the RPE can lead to retinal degradation and blindness. Scientists have long marveled at this process, but little is known about how it occurs, although some proteins required for the activity have been identified. Now, Umapathy et al. investigate using high-speed 3D live-cell imaging in mice to visualize the spatiotemporal details of the phagocytic event. The researchers created a culture of primary RPE cells together with OSs and then transiently transfected RPEs with F-tractin-RFP to label actin filaments. Peak coordinated ingestion occurred over 30–45 min but could be observed for up to 90 min. Actin filaments extended apical membranes from RPE cells, which enveloped the tip of an OS and engulfed the separated cellular matter, suggesting a scission event mediated by dynamic actin filaments. The specific events suggested a process called trogocytosis. Inhibition of actin polymerization prolonged but did not prevent the scission process. The authors then honed in on which proteins played a part in the scission events—specifically the Bin-Amphiphysin-Rev domain-containing proteins formin-binding protein 17 (FBP17) and amphiphysin-1 (AMPH1), which sense and bind to curved membranes and can induce further curvature. Live imaging revealed that fluorescently labeled FBP17 and AMPH1 were associated with membrane "cups" of RPE cells containing OS tips, albeit in slightly different localization patterns. The study finds once and for all that, rather than the OS passively shedding its distal discs for phagocytosis, RPE cells actively trogocytose, or nibble away, the tips.




Inset, fluorescently labeled f-actin (red) of a phagocytic cup engulfing the tip of an OS labeled with antibody (green); the larger image is a 3D rendering of the interaction.

## Abstract Sequential Monitoring Occurs in the Prefrontal Cortex

Nadira Yusif Rodriguez, Theresa H. McKim, Debaleena Basu, Aarit Ahuja, and Theresa M. Desrochers

(see pages 2741–2755)

Imagine walking into a kitchen stocked with ingredients, tools, and appliances—but to make a successful meal, you'll need a recipe. The cognitive processes needed to keep track of such sequential, abstract instructions requires an active process called sequence monitoring. The neural underpinnings of such abstract monitoring remain mostly unknown, but brain-imaging studies in humans indicate that it includes activity in the left or bilateral rostrolateral prefrontal cortex (RLPFC), and studies in nonhuman primates suggest that the dorsolateral PFC (DLPFC) mediates abstract thought and sequential information. This week, Yusif Rodriguez et al. explore the possibility in monkeys that area 46 of the DLPFC, an area analogous to human RLPFC, monitors abstract visual sequential information. The authors conducted functional magnetic resonance imaging in three awake adult male rhesus macaque monkeys that fixated on a central spot while viewing fractal images in four-item visual sequences. No responses were required, and monkeys received continuous liquid reward as long as they maintained fixation. Visual stimuli were presented in blocks that either followed or deviated from sequential rules. The imaging data suggested that both the right and left sides of area 46 of DLPFC monitors abstract visual sequence structure. Interestingly, the right and left sides seemed to track the abstract information with differing dynamics, with onset-based activity on the right and ramping dynamics during the presentation on the left. Importantly, the data show that similar brain areas in humans and nonhuman primates mediate abstract sequence monitoring, although in humans the activity is more consistent bilaterally. The work brings us a step closer to deciphering the neural substrates of abstract sequential cognitive processes.

*This Week in The Journal was written by Stephani Sutherland*

https://doi.org/10.1523/JNEUROSCI.twij.43.15.2023