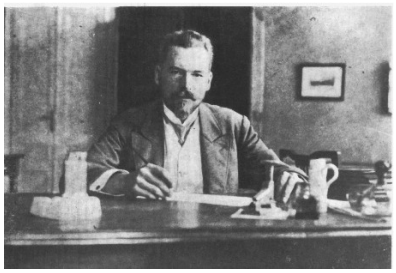

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Catalytically optimized search strategy

Monday, 25 September 2023 14:40 (25 minutes)

Understanding how information is transmitted from the exterior to the interior of living cells is essential for developing new therapeutic strategies. Despite recent structural advances, the mechanisms that govern interactions of membrane-bound receptors with intracellular arrestin molecules at the plasma membrane remain elusive. Here [1], we combine single-molecule microscopy with molecular dynamics simulations to dissect the complex sequence of events involved in b-arrestin interactions with both receptors and the lipid bilayer.

We carefully characterize the spatiotemporal co-dynamics of receptors and arrestins. We show that receptor and arrestin diffusion has multiple states that are linked to biological function.

Unexpectedly, our results reveal that b-arrestin spontaneously inserts into the lipid bilayer and transiently interacts with receptors via lateral diffusion on the plasma membrane. Moreover, they indicate that following receptor interaction, the plasma membrane stabilizes b-arrestin in a longer-lived membrane-bound state, allowing it to diffuse to clathrin-coated pits separately from the activating receptor.

This constitutes a new mechanism for the target-search strategy that combines surface-mediated diffusion with catalytic activation.

These results open the way to new questions in search strategies and expand our current understanding of b-arrestin function at the plasma membrane.

[1] Lanoiselée, Grimes, Koszegi et al.
Plasma membrane preassociation drives β-arrestin coupling to receptors and activation. Cell. 2023

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