

The Palmitoylation Cycle – How Cells Fight Entropy to Enrich Proteins on Specific Membrane Compartments

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We have described a cycle of lipid modification reactions (palmitoylation/depalmitoylation) that enables cells to enrich proteins on specific subcellular membranes and to rapidly shuttle them between these compartments. The cycle counteracts entropy-driven distribution of palmitoylated proteins over all membranes without any requirement of receptor interactions. Prominent examples are members of the Ras GTPase family of proto-oncogenes: the de-/repalmitoylation cycle not only controls their specific subcellular localization but also their isoform-specific activity profiles on different subcellular compartments upon growth factor stimulation of cells [1,2,3].

Using a chemical-biological approach to directly monitor dynamic lipid modifications in living cells we have further characterized the palmitoylation mechanism and found a surprisingly low substrate specificity of the reaction. Our findings allowed us to postulate a generic cellular sorting mechanism that can account for the continuous enrichment of any palmitoylatable peripheral membrane protein along the Golgi apparatus, secretory pathway, plasma membrane and interconnected endosomal compartment [4].

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3. F.J. Dekker, O. Rocks, N. Vartak, et al, *Nat Chem Biol* **6**, 449-456 (2010)
4. O. Rocks et al., *Cell*, **141**, 458-471 (2010)