Comparative Photoaffinity Profiling of Omega-3 Signaling Lipid Probes Reveals Prostaglandin Reductase 1 as a Metabolic Hub in Human Macrophages

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**Photoaffinity Lipid Probes Decipher Docosahexanoic Acid Target**

**Significance:** Docosahexanoic acid (DHA) is an omega-3-polyunsaturated fatty acid (PUFA) and an endogenous signaling lipid with anti-inflammatory properties. However, its biological mechanism in the resolution of inflammation is poorly understood. Here, the authors developed two bio-orthogonal photoaffinity-click (pac) probes, pac-DHA and its 17-hydroxy metabolite pac-17-HDHA, to identify their targets in human macrophages.

**Comment:** The authors synthesized the PUFAs using Wittig olefination as a key reaction. Photoaffinity-based protein profiling revealed prostaglandin reductase 1 as the lipid-binding partner, which metabolizes 17-oxo-DHA – a metabolite of 17-HDHA. The authors also found that 17-oxo-DHA reduces the formation of pro-inflammatory lipids in human macrophages and neutrophils.