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Bacterial “vision” and how its study unmasked a long-sought human enzyme

In many organisms, light triggers the synthesis of carotenoids to quench the reactive species formed upon illumination and minimize cell damage. Light induces a transcriptional response leading to carotenogenesis in the Gram-negative soil bacterium *Myxococcus xanthus* via two light-sensing and signaling mechanisms. In one mechanism, photoexcitation of the heme precursor protoporphyrin IX, a photosensitizer, generates highly reactive singlet oxygen, which signals a complex genetic circuit with several factors to activate genes for carotenogenesis. The membrane-associated protein CarF acts early in this signaling pathway. Although CarF homologs are rare in bacteria and largely restricted to myxobacteria, these proteins with unknown functions are prevalent in animals (invertebrates and vertebrates including humans, where it is called TMEM189) and in plants. We have discovered that CarF and its animal homologs, including human TMEM189, but not those in plants, are plasmanylethanolamine desaturases whose identity has been unknown for almost fifty years. CarF-TMEM189 enable the biosynthesis of plasmalogens, a special class of glycerophospholipids, with the hallmark sn-1 vinyl ether linkage, which are abundant in the brain, heart, and leukocytes, and in nearly all subcellular membranes. They have proposed membrane organization, signaling and antioxidant roles, and their deficiency correlates with various human disorders including cancer and Alzheimer’s disease. Our discovery of the long-sought desaturase indispensable for human plasmalogen biosynthesis opens a crucial door to study the biogenesis, functions, and roles of these lipids in disease. Moreover, besides unearthing an elusive human enzyme, our studies have revealed a novel and crucial role of plasmalogens in bacterial light-induced signaling.

Publicaciones recientes:

- Anaerobic bacteria need their vitamin B12 to digest estrogen.
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- A bacterial light response reveals an orphan desaturase for human plasmalogen synthesis.
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