

Polyunsaturated fatty acids mediate cholesterol trafficking in *C. elegans*

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Proper cholesterol transport is crucial for the functionality of cells. In *C. elegans*, certain cholesterol derivatives called dafachronic acids (DAs) govern the entry into diapause. In their absence, worms form a developmentally arrested dauer larva. Thus, cholesterol transport to appropriate places for DA biosynthesis warrants the reproductive growth. Recently, it was reported the discovery a novel class of glycosphingolipids, PEGCs, required for cholesterol mobilization/transport from internal storage pools. Here, we identify other components involved in this process. We found that strains lacking polyunsaturated fatty acids (PUFAs) undergo increased dauer arrest when grown without cholesterol. This correlates with the depletion of the PUFA-derived endocannabinoids 2-arachidonoyl glycerol and anandamide. Feeding of these endocannabinoids inhibits dauer formation caused by PUFAs deficiency or impaired cholesterol trafficking (e.g. in Niemann-Pick C1 or DAF-7/TGF- β mutants). Moreover, in parallel to PEGCs, endocannabinoids abolish the arrest induced by cholesterol depletion. These findings reveal an unsuspected function of endocannabinoids in cholesterol trafficking regulation.