

P019 Zebrafish fat-free, a gene required for intestinal lipid absorption and is essential for Golgi apparatus structure
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The zebrafish fat-free (*ffr*) mutation was identified in a physiological screen for genes that regulate lipid metabolism. *ffr* mutant larvae are morphologically indistinguishable from wild type (*wt*) sibling larvae, but their absorption of NBD-cholesterol and other fluorescently labeled lipids is severely impaired (Farber et al., 2001). Through positional cloning, we have identified a causative mutation in a highly conserved and ubiquitously expressed gene within the *ffr* locus. The Ffr protein contains a Dor-1 like domain typical of the mammalian oligomeric Golgi complex (COG) gene, *cog8*. Golgi complex ultrastructure is disrupted in the *ffr* digestive tract, a finding that supports a role for the Ffr protein in intracellular trafficking. Consistent with a possible role in COG-mediated Golgi function, *wt* Ffr-GFP and COG8-mRFP fusion proteins partially colocalize in the zebrafish blastomeres, and an apolipoprotein A1-mRFP fusion protein is mislocalized when ectopically expressed in *ffr* deficient embryos. In addition, truncated *ffr* mutant mRFP fusion proteins concentrate in one area of the trans Golgi network (TGN). In contrast, *wt* Ffr-GFP fusion proteins mainly localized in the perinuclear region though it overlaps with mutant mRFP fusion protein. Furthermore, enterocyte retention of the styryl dye AM1-43 in *ffr* larvae support the idea that altered lipid trafficking contributes to this defect. Together, these data indicate that *ffr* is a novel gene required for both Golgi structure and ultimately lipid transport.