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Signaling cascades in regulation of fat absorption and remodeling of lipid droplets' proteome in small intestine

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Short summary

Lipid-rich diets increase incidents of obesity, diabetes, inflammatory diseases, and cancer. Absorption of lipids in the intestine is a multistep process, initiated by the micellization and digestion of lipids in the lumen of the intestine, uptake of fatty acids (FAs) and glycerides by enterocytes followed by re-synthesis of triglycerides (TGs) at the endoplasmic reticulum. In enterocytes, TGs might be either directed into chylomicrons for the subsequent secretion or stored in lipid droplets (LDs). Dynamic processes of deposition and degradation of TGs stored in LDs buffer FAs levels in the cytoplasm at the postprandial and fasting states. Degradation of TGs (lipolysis) stored in LDs into FAs is mediated by multiple enzymes, like adipose triglyceride lipase (ATGL) or hormone-sensitive lipase (HSL). Since FAs at certain concentrations are toxic for cells, regulation of LDs dynamics is central to maintaining intestinal homeostasis. Our previous study showed that upon lipid ingestion protein kinase D2 (PKD2) promotes chylomicron-mediated TGs transport to the general circulation. Our new data show that PKD2 regulates also LDs dynamics in enterocytes and is a part of the signaling machinery regulating changes in enterocytes' proteostasis in response to lipid ingestion. We demonstrated that ingestion

of lipids promotes rapid changes in the proteome of enterocytes mediated by posttranslational mechanisms, also by PKD2. These changes include the degradation of LDs-associated lipases to prevent toxic effects of FAs. These data suggest that enterocytes utilize a mechanism preventing excessive flux of FAs into the cytosol after consumption of lipids, which is required for preserving enterocytes' function.

List of publications:

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8. Oury F*, Sumara G*, Sumara O, Ferron M, Chang H, Smith CE, Hermo L, Suarez S, Roth BL, Ducy P, Karsenty G. Endocrine Regulation of Male Fertility by the Skeleton. *Cell*. 2011 Mar 4;144(5):796-809. *equal contribution

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