Cdo patterns the musculature of the esophagus and is required for esophageal motility in mice

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Introduction:
Cdo is a multifunctional cell surface co-receptor that promotes Hedgehog signaling during gastrointestinal myogenesis by mediating and chaperoning signaling during skeletal myogenesis. We report here novel roles for Cdo in patterning of the murine esophageal musculature and esophageal motility disorders such as achalasia.

Defects in Cdo−/− esophagi occur postnatally

Expression of Cdo in the postnatal esophagus

Conclusions:
1) Cdo is required for a process of smooth muscle fascicular morphogenesis that drives formation of the mature pattern of the esophageal musculature.
2) Cdo is required to sensitize tonic smooth muscle in the LES to NO-induced relaxation; its absence results in achalasia.

Cdo−/− mice have mispatterned smooth muscles

Cdo is required for esophageal smooth muscle fascicles to alter their shape and orientation

Normal density of myenteric neurons in the Cdo−/− LES

The Cdo−/− LES fails to relax in response to EFS or nitroprusside

Adult Cdo−/− esophagi have mispatterned smooth muscle

Skeletal myogenesis occurs in a transition zone in the postnatal esophagus

Expression of Cdo in the postnatal esophagus

Failure of skeletal myoblasts to move distally in Cdo−/− esophagi

Defects in Cdo−/− esophagi occur postnatally

Expression of Cdo in the postnatal esophagus

Confirmation of defects in Cdo−/− esophagi

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