Why does Xia-Gibbs Syndrome affect so many parts of the body?

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Xia-Gibbs Patients demonstrate Pleiotropic Ectoderm and Mesoderm Heterozygous Phenotypes—Why?

Ectodermal

Dysmorphic Faces Autism Language Ataxia Micrognathia Seizures Aplasia cutis (absence of skin)

Mesodermal

Hypotonia Independent walking gastrointestinal Skeletal abnls.



Jiang et al. 2018

The varied morphology of surface skin





Regional 'GPS' Positioning Map Encoded with the Mesoderm during Development



Regional 'GPS' Positioning Map Encoded with the Mesoderm during Development helps to pattern brain development and body plan





Regional mesodermal controls left-right, anterior-posterior, and dorsal-ventral surface ectoderm patterning, and is the major integrator of positioning information



After Johansson and Headon 2014

After birth, the same regional mesodermal responds to environmental cues for adult neurodevelopment, skin, and muscle homeostasis



What does the regional mesoderm GPS have to do with Xia-Gibbs Syndrome?

Using induced pluripotent cells, we find Xia-Gibbs Syndrome gene (AHDC1) product Gibbin helps the mesoderm read "positional and timing cues"



Annie Collier PhD



Collier et al, Nature 2022

In skin organoids, Gibbin-mutant Basal Keratinocytes display normal basal markers, but defective stratification program





3-D Organoid Culture

In vivo CRISPR chimeras demonstrate ectodermal and mesodermal defects consistent with Xia-Gibbs phenotypes



Collier et al, Nature 2022

AHDC1 binds to gene promoters and interacts with transcription factors that sense position and timing information.



Patient induced pluripotent cells will help us understand which "regional patterning signals" can be useful to ameliorate symptoms



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