"Dosage-sensitive modifiers of Notch signaling in a mouse model of Alagille syndrome"

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Alagille syndrome (ALGS, OMIM #118450) is a multi-system developmental disorder affecting the hepatobiliary and cardiovascular systems, among others. The majority of ALGS patients harbor dominant mutations in components of the Notch signaling pathway (~95% JAG1, ~1-2% NOTCH2). However, there is extreme variability in disease presentation and prognosis that cannot be explained by the nature of the causative mutations. Moreover, no mechanism-based therapies are available. Using a mouse model for ALGS which we established several years ago, we seek to identify and characterize dosage-sensitive genetic modifiers of the ALGS phenotypes, hoping to shed light on its pathophysiology and to establish potential therapeutic targets.

References: