Mutations: Missing Spleen

Isolated congenital asplenia (ICA) is characterized by the absence of a spleen at birth in individuals with no other developmental defects. The patients are prone to life-threatening bacterial infections. The unbiased analysis of exomes revealed heterozygous mutations in RPSA in 18 patients from eight kindreds, corresponding to more than half the patients and over one-third of the kindreds studied. The clinical penetrance in these kindreds is complete. Expression studies indicated that the mutations carried by the patients-a nonsense mutation, a frameshift duplication, and five different missense mutations-cause autosomal dominant ICA by haploinsufficiency. RPSA encodes ribosomal protein SA, a component of the small subunit of the ribosome. This discovery establishes an essential role for RPSA in human spleen development.