Different course of lung disease in two siblings with novel 
*ABCA3* mutations.

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Mutations in the gene for adenosine triphosphate-binding cassette transporter subfamily A member 3 (*ABCA3*) have been reported in infants and children with surfactant deficiency and interstitial lung disease. *ABCA3* is a lipid transporter, which plays an essential role in lung surfactant metabolism and lamellar body biogenesis in type II alveolar epithelial cells.

We report a case of siblings found to be compound heterozygotes for two novel *ABCA3* gene mutations (Asp⁵⁰⁷del CA Ter⁵⁰⁸ in exon 13 and Asp⁶⁹⁶Asn in exon 17) but developing very different course of lung disease. The index case is a baby girl with severe interstitial lung disease that manifested on the first days of life. Her 4-year-old brother carrying the same mutations has no signs of lung disease so far.

Our findings suggest the contribution of other genetic, epigenetic or environmental factors to discordant phenotype observed in patients carrying the same mutations in the *ABCA3* gene. As seen with cystic fibrosis, a typical monogenic autosomal recessive disorder with widely varying clinical presentations, polymorphic variants in genes besides *CFTR* can determine the severity of disease. Otherwise, alternative splicing of *ABCA3* may lead to an in-frame exclusion of the mutated exon or position, which is translated into modified but still functional protein. The clinical course of the index case suggests benefit of combined medical therapy in treating infants with *ABCA3* deficiency.

Reference