Introduction

Pulmonary surfactant metabolism dysfunction / pulmonary fibrosis comprise a genetically heterogeneous group of disorders that result in severe respiratory insufficiency or failure in full-term neonates, or infants. These disorders are associated with various pathologic entities, including pulmonary alveolar proteinosis (PAP), desquamative interstitial pneumonitis (DIP), cellular nonspecific interstitial pneumonitis (NSIP), or pulmonary fibrosis. A number of genes are associated with surfactant metabolism dysfunction, pulmonary (SMDP), including SFTPB (SMDP1 – autosomal recessive), SFTPC (SMDP2 – autosomal dominant), ABCA3 (SMDP3 – autosomal recessive), and CSF2RB (SMDP5 – autosomal recessive). The NKX2-1/TITF1 gene is associated with a neonatal respiratory distress syndrome and is autosomal dominant. The SFTPA2, TERC, and TERT genes are associated with pulmonary fibrosis.

Referrals

- Full term neonates with severe respiratory distress of unknown aetiology and older children with respiratory distress of unknown cause.
- Carrier testing can be offered to the adult relatives of patients once a disease causing mutation has been identified.

Prenatal testing

Prenatal testing is available for families in whom specific mutations have been identified or in whom appropriate family studies have been undertaken; please contact the laboratory to discuss.

Service offered

- Analysis of the ABCA3, CSF2RB, NKX2-1/TITF1, SFTPA2, SFTPB, SFTPC, TERC, and TERT genes by next generation sequencing (Agilent SureSelect and Illumina NextSeq). A minimum coverage of 30 reads is required to call a variant. In-house validation attributes a minimum sensitivity of 97.5% (with 95% confidence) for regions covered >30x. This assay is not currently validated to detect large deletions / duplications. All clinically relevant variants are confirmed by Sanger sequence analysis. Known benign polymorphisms and sequence variants which are unlikely to be pathogenic are not reported.
- Detection of known mutations in relatives of patients with confirmed mutations by Sanger sequencing.

Target reporting time

8 weeks for NGS screening. 2 weeks for routine testing of specific mutations. Please contact the laboratory for urgent cases.