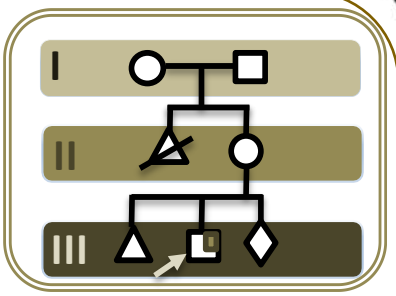
Rishi Vansh

All India Institute of Medical Science Rishikesh AIIMSR

Department Of Pediatric Genetic -division

Volume 4 **Issue 42, Nov 2023**



From the desk of Editor

The genetic division of the Pediatric Department is publishing a monthly newsletter for faculty and residents. The newsletter is related to genealogical parlance and is a deliberate attempt to enhance awareness of genetic disorders with recent updates.

Pulmogenetics-(VI)

Human Genetics/ Genetics– Surfactant dysfunction & Lung disorders

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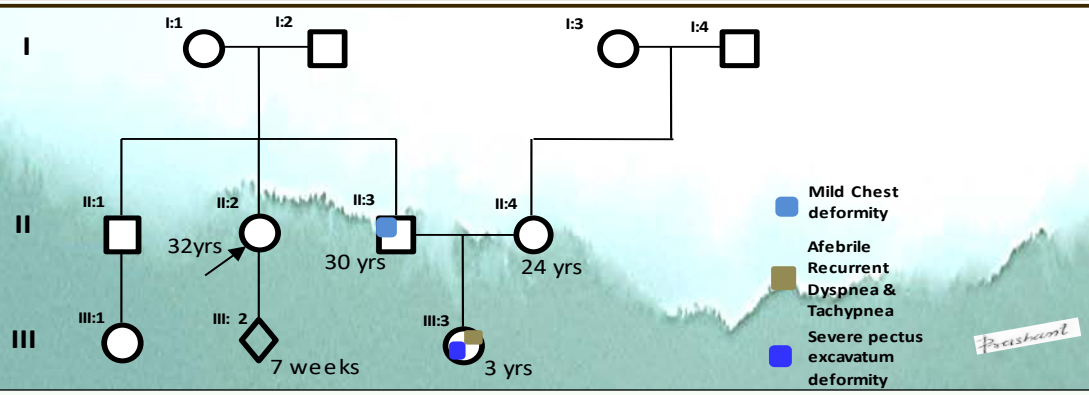
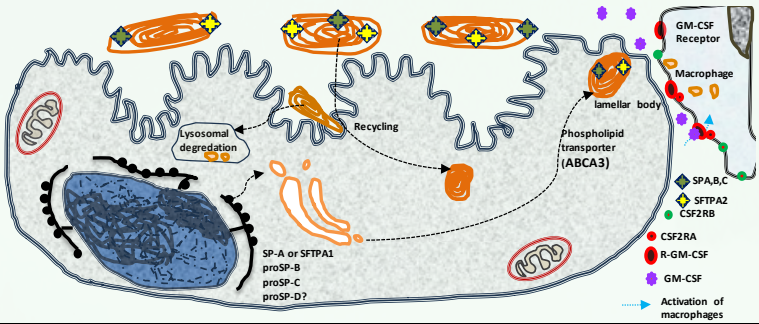
DOI: 10.13140/RG.2.2.12054.93769



Pneumocyte -Type II & Surfactant Proteins

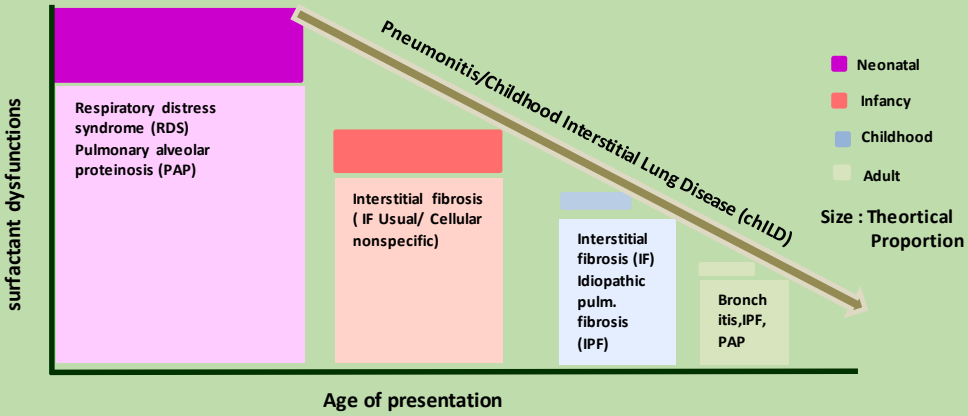


- Alveolar type II cell: a cuboidal cell
- Synthesis of major components of surfactant
- Surfactant is a mixture of amphipathic surfactant proteins essential for lung function and homeostasis, specifically for
  - Reduce surface tension at the air-liquid interface
  - Innate immunity

Insight:

1. What is the phenotypic spectrum of surfactant deficiency?
2. What is the age of presentation of various surfactant dysfunctions?
3. How do anti-GM-CSF antibodies induce acquired Pulmonary alveolar proteinosis (PAP)?
4. Is there any role of serum or BAL GMCSF level in the case of PAP?
5. What would be the counseling plan for the family of case: III2?

Surfactant related disorders: Possible Genotype -phenotype corelation



Genes related to surfactants with their function and respected phenotypes

Gene/Locus/ Location / Phenotype	Clinical spectrum/s (MOI)/ onset age	Phenotype OMIM no.	Gene function
SFTPB / 2p11.2/ Surfactant metabolism dysfunction, pulmonary, 1 (**SMDP1**)	ILD, pulmonary alveolar proteinosis (PAP), desquamative interstitial pneumonitis (DIP), or cellular nonspecific interstitial pneumonitis (NSIP)/**AR/ neonatal**	**265120**	Pulmonary-associated surfactant protein B (SPB), as amphipathic proteins enhance stability and spreading
SFTPC/8p21.3/ **SMDP2**	ILD, PAP RDS in prematurity/**AD/infancy, child adult**	**610913**	Pulmonary-associated surfactant protein C (SPC), as highly hydrophobic proteins work on the peripheral air spaces.
ABCA3/ 16p13.3/ **SMDP3**	RDS/ **AR/ Neonatal**	610921	Help in synthesis by catalyses the ATP-dependent transport of phosphatidylcholine and phosphoglycerol from the cytoplasm into lamellar bodies
CSF2RA/ Xp22.33 / **SMDP4**	PAP / **X linked/** Infant, young child	300770	Receptor for granulocyte-macrophage colony-stimulating factor. Crucial part of GM-CSF signaling pathway
CSF2RB/22q12.3/ **SMDP5**	PAP/ AR /adolescent, adult	138981	Differentiate monocytes into macrophages
SFTPA1/10q22.3/ Interstitial lung disease 1 (**ILD-1**)	ILD, RDS, Idiopathic Interstitial Pneumonia, Idiopathic pulmonary fibrosis / **AD, AR** / adult	619611	Related to alveolar innate immunity, and control inflammation (dual mode function) Also contributes to lower the surface tension
SFTPA2/ 10q22.3/ **ILD-2**	ILD, RDS, Idiopathic pulmonary fibrosis **/AD/** adult	178500	Innate immunity of alveoli lower the surface tension 138981
MUC5B/ 11p15.5/ **Pulmonary fibrosis, idiopathic, susceptibility to**	ILD, and Extrinsic Allergic Alveolitis/AD/adult	178500	Gel-forming mucin in mucus
SFTPD/ 10q22.3 /	/Not defined	178635	innate immunity and surfactant turnover

Pulmonary alveolar proteinosis (PAP): surfactant & its metabolic products accumulate within alveoli, leading to gaseous exchange malfunction.
Types of PAP: **Defective production:** Hereditary mutations in surfactant proteins.
Defective clearance: Dysfunction of alveolar macrophage by Auto-immune with anti-GM-CSF antibodies (Most common ~90% PAP cases), hereditary mutations in receptor & associate proteins of granulocyte macrophage-colony stimulating factor (High serum & BAL level of GMCSF), hematological disorders and toxins
Investigation of choice: bronchoalveolar lavage fluid (BALF) study, & **Gold standard:** Lung biopsy **(chILD)**

Counseling the family for case III:2- 1. Need phenotyping: Clinical details of proband and her parents; 2. Confirming the diagnosis: biochemical or histopathological & Molecular report, 3. Examination of case II:2 & her husband, & genotyping of case II:2 (If family carries the mutation/variant), 4. Follow up with the report and the option of antenatal testing need to be discussed with the family in case of significant findings. 5. Case II:2 must follow routine standard protocol also.

Thought Riveting:

- ***What are the sailent differences in fetal, infantile, and adult surfactant proteins?***
- ***Is it clinically useful to thoroughly evaluate, & investigate for chronic lung disease in children with Isolated pectus excavatum deformity without skeletal dysplasia, & respiratory distress?***
- ***How does COVID-19 affect surfactant metabolism?***
- ***What could be the likely phenotype of GMCSF gene mutations in humans?***
- ***Is there any possible-oxygen dependent locus control region for surfactant proteins?***

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