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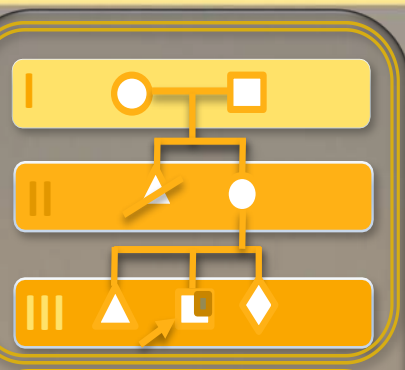

From the desk of Editor

The genetic division of the Pediatric Department publishes a monthly newsletter for all Medical Professionals. The newsletter is related to genealogical parlance and is a deliberate attempt to enhance awareness of genetic disorders with recent updates.

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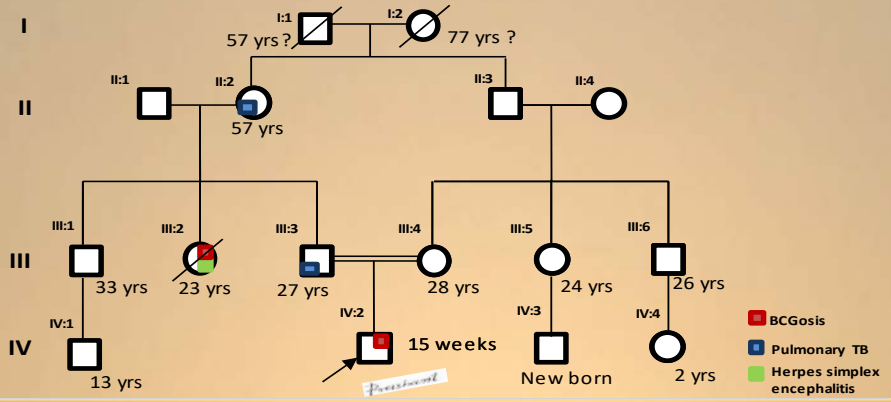
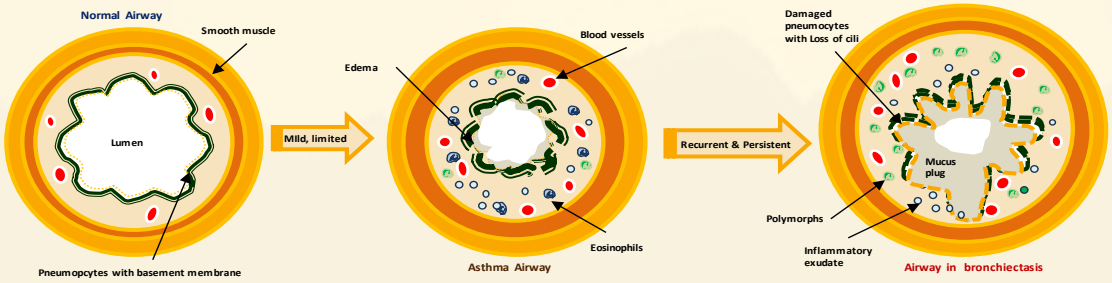
Pulmogenetics-VII / Hereditary Immuno-deficiency & Bronchiectasis as one of the characteristic phenotype/ STAT1



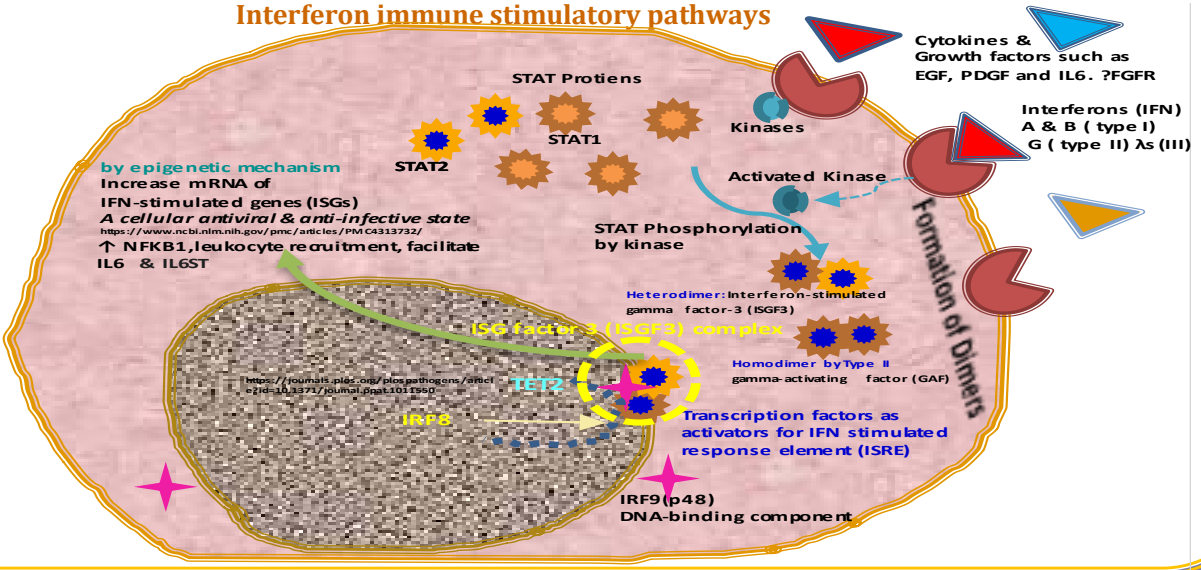
Impact on airways due to variable dysfunction of genes & pathways related to immunity regulation



Insight:

1. What is the impact of recurrent inflammation on the innate immune system at the cellular level?
2. What are genes responsible for bronchiectasis related to immune regulatory pathways?
3. How do the interferon immune stimulatory pathways act at the cellular level?
4. What is the possible phenotype for case IV: 2?

Interferon immune stimulatory pathways



Genes related to immune regulation & responsible for bronchiectasis due to Recurrent Respiratory tract infections +/- Multisystem inflammatory disease

Gene/location /MOI	Gene function	Phenotypes / *Miscellaneous*
STAT1/ 2q32.2/ AD, & **AR**	Signal transducer and transcription activator, for interferon-alpha/beta (IFNA/B) and interferon-gamma (IFNG) signalling pathways	Immunodeficiency (ID) 31 A, 31 C (AD) 31 B (AR) *Severe recurrent respiratory tract infections of the, including mycobacterial disease*
IRF8/16q24.1 /AD & AR	Regulate expression of genes stimulated by type I interferon	ID 32A (AD)- Mycobacteriosis ID 32B (AR)- Recurrent viral disease
IGHM/14q32. 33/**AR**	The IGHM gene encodes the Constant region of immunoglobulin heavy chains	Agammaglobulinemia 1 - Infantile *onset & neutropenia*
TPP2/ 13q33.1/**AR**	A dynamic supramolecular structure, proteasome like function, epitope generation for MHC class I antigen presentation	ID 78 with autoimmunity(AI) & developmental delay *Ectodermal changes: Paronychia. Alopecia, dermo-hypodermitis, & dermatitis*
IRF9/14q12/ **AR**	Mediates signalling by type I IFNs	ID 65 *Pivot role in anti-viral immunity*
NFKB1/4q24/ **AD**	NFKB is a transcription regulator as activators or repressors	ID, common variable (CV), 12 *Type I diabetes mellitus, Pernicious anemia, Hepatitis, & Chronic enteropathy*

Continue…

Gene/location /MOI	Gene function	Phenotypes / Miscellaneous
LRBA/4q31.3/ **AR**	Involved in intracellular signalling by regulates CTLA4 & post bacterial lipopolysaccharides (LPS) exposure	ID, CV, 8, with AI *Early childhood onset, ITP, IBD, Asthma, & recurrent Conjunctivitis*
TAP2/6p21.3 2/**AR**	Intricate in antigen presentation	Bare lymphocyte syndrome, type I *Emphysema, Localized cutaneous necrobiosis lipoidica*
IL6ST/5q11.2 /**AD & AR**	Initiating signal transmission for CNTF, IL11, IL6, LIF, CTF1, OSM and BSF3 as a part of the cytokine receptor complex	1.ID 94 with autoinflammation and dysmorphic facies (AD) 2.Hyper-IgE syndrome 4A, with recurrent infections (AD) 3. Hyper-IgE syndrome 4B, with recurrent infections (AR) 4. Stuve-Wiedemann syndrome 2 (AR) *Macrocephaly, Prognathia, Hypertelorism, Downslanting palpebral fissures, Small nose Granulomatous interstitial lung disease, & organomegaly*
LIG1/19q13.3 3/**AR**	DNA ligase, role in DNA replication, recombination, & the repair process	ID 96 *Early childhood onset, sensitive to DNA-damaging agents*
TET2/4q24/ **AR**	Activate the genes by DNA demethylation Convert methylcytosine to 5-hydroxymethylcytosine	ID 75 Myelodysplastic syndrome, somatic *Reported with various myeloproliferative disorders*

Possible phenotype for case IV: 2- Overall expected milder phenotype because of low penetrance, & have long term good prognosis.

Thought Riveting:

- ***What is the possible interaction of TPP2 & LRBA genes with IFN stimulated response element (ISRE)?***
- ***How does IFN signaling act on CTLA4 (Cytotoxic T-Lymphocyte Associated Protein 4)?***
- ***What is the predictable interaction of chloroquine with the LRBA gene in the pathological cellular stage?***
- ***Does any overactivity of the IL-17 pathway with STAT1 loss of function mutations protect from candida infection?***
- ***Do somatic mutations in the immune regulatory genes & their pathways lead to various autoimmune & inflammatory disorders?***