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Department Of Pediatric Genetic -division

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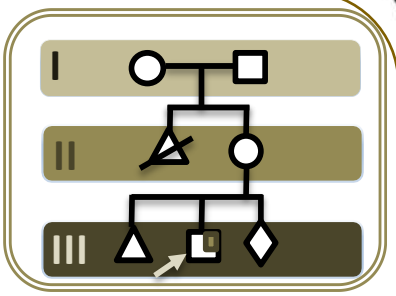
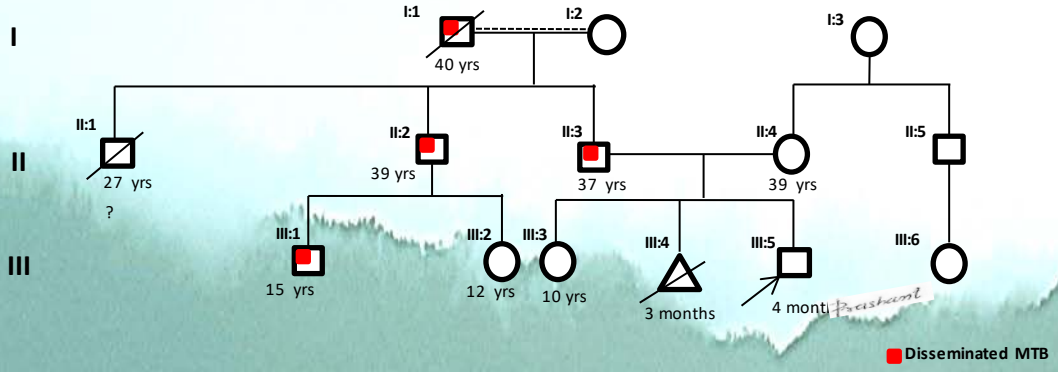


From the desk of Editor

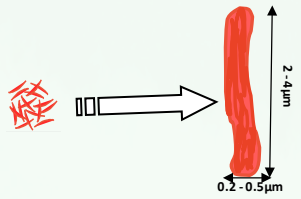
The genetic division of the Pediatric Department is publishing a monthly newsletter for faculty and residents. The newsletter is related to genealogical parlance and is a deliberate attempt to enhance awareness of genetic disorders with recent updates.

Pulmogenetics-(III)

Tuberculosis / Human Genetics/ sensibility and response- General



Mycobacterium Tuberculosis Bacterium (MTB)



High magnification M. TB

- High G+C Gram-positive bacteria in the family Mycobacteriaceae
- An obligate aerobic organism
- Sanger Institute (2013) Strain: H37Rv (Ref Seq: GCF_000195955.2)
- Genome size 4.4 Mb and Genes: 4,008
- Subspecies- around 100

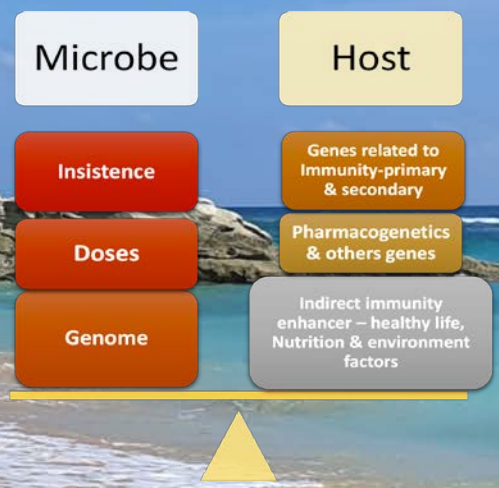
Insight:

1. How does human genetics interact with tuberculosis infection?
2. What is the Phenotypic series (PS) in OMIM entries for the host susceptibility and tuberculosis?
3. What is the updated knowledge regarding genes related to the vulnerability of tuberculosis?
4. What factors decide the drug response for TB infection?
5. What will be the pretest genetic counseling for case III:5?

Mycobacterium tuberculosis, susceptibility and protection against (OMIM phenotype # 607948)

Gene/ Locus / Location	MIM number	Other phenotypes	Gene function
NRAMP1 /2q35	600266	Susceptibility to Buruli ulcer	Sequestration of Fe (2+) and Mn (2+),
SP110/ 2q37.1	604457	Hepatic venoocclusive disease with immunodeficiency	Increases genes' transcription through retinoic acid response elements (RARE) and nuclear hormone receptor coactivator
CISH/3p21.2	602441	Susceptibility to malaria, bacteremia	Negative regulation of JAK-STAT5 signal pathway depended on cytokines & inhibit tyrosine phosphorylation of STAT5
TLR2/4q31.3	603028	Susceptibility to colorectal cancer, leprosy	Facilitate the innate immune by conjoins through LY96 and TLR1 or TLR6 in the presence of microbial cell wall components. In vitro, Prompt monocytes for M. TB, & also has a receptor function for M. TB lipoproteins
IRGM/5q33.1	608212	Inflammatory bowel disease (Crohn's disease) 19	Role in the innate immune system, Clear acute protozoan and bacterial infections by recognized GTPase activity. Prevent endotoxemia indirectly through macrophages' adhesion & motility, regulate autophagy & pro-inflammatory cytokine production,
IFNGR1/6q23.3	107470	Susceptibility to hepatitis B, h pylori, immunodeficiency 27 A & B	Receptor subunit for interferon-gamma/INFG & also need for IFNGR2 to form a functional receptor. Need to activation of downstream signaling components JAK1 and JAK2.
TIRAP/11q24.2	606252	Protection against bacteremia, malaria	An essential segment of the innate immune system by TLR2 and TLR4 signaling pathways. Controls TNF-alpha and interleukin-6 secretion
IFNG/12q15	147570	Rapid progression to AIDS, immunodeficiency, aplastic anaemia, response to therapy of hep C	Stimulate immune cells (like T & NK) for producing Type II interferon and enhancing antigen presentation and activating effector immune cells (antitumor responses), mostly act through transcription of IFNG-regulated genes, STAT1 & nuclear translocation
CCL2/17q12	158105	Modifier of coronary artery diseases, resistance to HIV-1, susceptibility to spina bifida	Prompts a strong chemotactic reaction (monocytes and basophils) and mobilization of intracellular Ca as a ligand for the C-C chemokine receptor CCR2
CD209/19p13.2	604672	Susceptibility to HIV-1, protection against dengue fever	Regulate DC-induced T-cell proliferation. Involved in initiation of the primary and adaptive immune response. Might be facilitate the endocytosis & transendothelial

- **TB is a chronic deliberating disease and affects one-third of humanity in any one of the forms: primary, primary progressive, or latent tuberculosis.**
- **Our immunity has inherited deficiency to eradicate it from our body.**
- **There is a complex interaction between the host genome and microbial genome not limited to each form of tuberculosis but also the response of therapy (pharmacogenetics).**
- **Besides, Complex genomic interaction among genes' polymorphisms or mutations (Epistasis) and significant environmental factors (reverse regulation of gene expression through proteins in various ways) are responsible for each form of tuberculosis disease and its response to therapy.**



Counseling the family for case III:5- **In view of infectious disease and lack of other unusual clinical or lab features. The yielding of genetic testing is still being determined because of the lack of data and the absence of specific phenotypes. So, first need to do detailed clinical, routine, and immunological workups for affected individuals.**
The decision on molecular testing depends upon family requests and institutional guidelines.

Thought Riveting:

- ***What could be the genes associated with progressive tuberculosis?***
- ***Is any role of genes related to b12 and iron metabolism with primary tuberculosis?***
- ***How could we strengthen our innate immunity through genetic & non-genetic engineering?***
- ***Does Yoga techniques heighten immunity by changing the epigenetic signature of immune system genes?***
- ***How intracellular or extracellular heavy metal concentration affects the immune system at various levels? Is this the science behind the Indian traditional medicines, which use dried burn extracted called "Bhasma," having a high concentration of different heavy metals?***

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