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Department Of

Pediatric Genetic -division

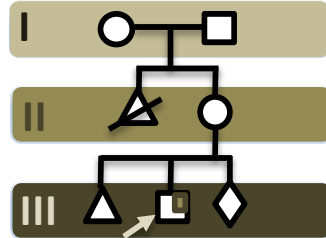
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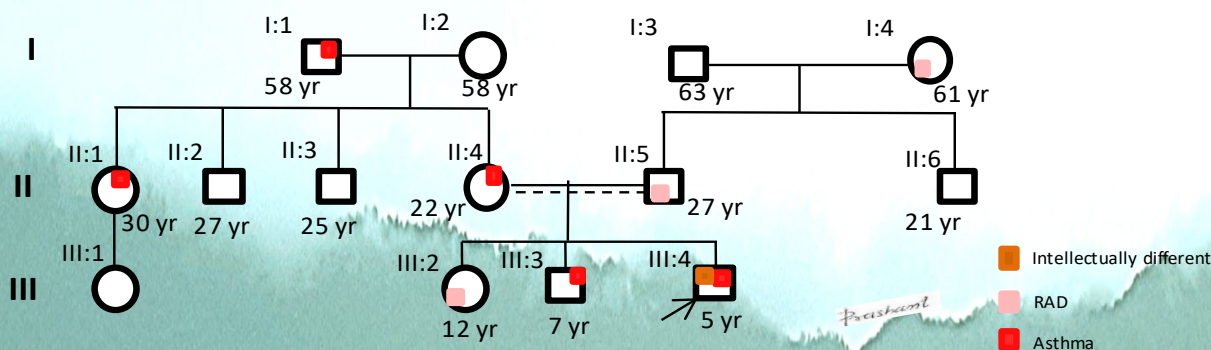


From the desk of Editor

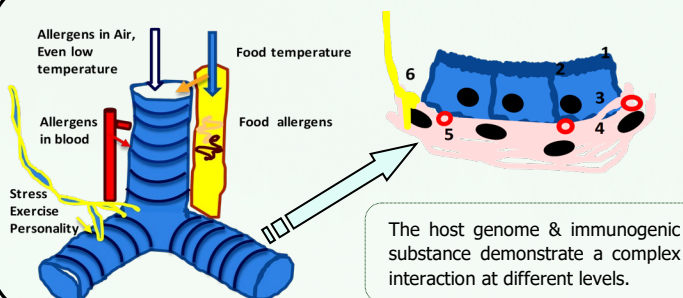
The genetic division of the Pediatric Department is publishing a monthly newsletter for faculty and residents. The newsletter is related to genealogical parlance and is a deliberate attempt to enhance awareness of genetic disorders with recent updates.

Pulmogenetics-(IV)

Asthma/ Human Genetics/ "Asthma-related traits" (ASRT)



Asthma (Pathophysiology- Possible Genetics pathways)



1. Mucous contents and regulatory pathways of secretion
2. Cilia function pathway (non-syndromic tissue-specific)
3. Inflammatory regulatory and metabolic pathways including the **PD1 pathway**
4. Autocrine and paracrine signaling pathways
5. Antigen processing pathways of the immune system
6. **GABAergic pathway**; extra & intraneuronal transport and synaptic metabolism defects

Insight:

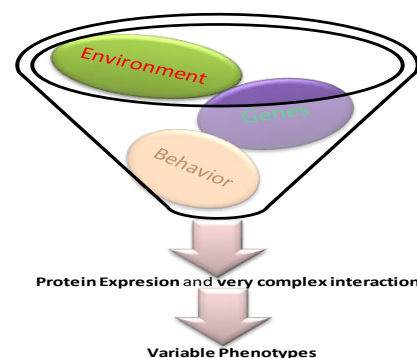
1. What is the basic pathogenesis of complex or multifactorial disease?
2. What are the genes' functions linked with **ASRT**?
3. What is the best way to manage an asthmatic case?
4. What are possible non-inflammatory pathways linked with asthma?
5. How would you counsel the family for phenotypic variabilities in the Pedigree?

{ASTHMA, SUSCEPTIBILITY TO} * (OMIM phenotype 600807)- (MOI-AD inheritance) with Phenotype mapping key- 3 - The molecular basis of the disorder is known

** Braces- "{}" - used for variations that add to susceptibility to complex disorders or conditions such as infection*

Gene/Locus/ Location	Other Phenotype/s (MOI)	Gene function
HNMT/ 2q22.1	Intellectual developmental disorder, autosomal recessive 51 (AR)	Inactivates histamine by N-methylation
MUC7/4q13.3	{Asthma, protection against} (AD)	Enhance bacterial clearance & attachment for <i>P. aeruginosa pili</i> .
IL13/ 5q31.1	{Allergic rhinitis, susceptibility to} (AD)	Regulate the allergic inflammation
SCGB3A2/ 5q32	-	Down-regulate inflammation of respiratory epithelium
ADRB2/ 5q32	Beta-2-adrenoreceptor agonist, reduced response to {Asthma, nocturnal, susceptibility to} {Obesity, susceptibility to} (AD/ AR)	Attach epinephrine and activating adenylate cyclase
TNF/ 6p21.33	{Migraine without aura, susceptibility to} (AD) {Dementia, vascular, susceptibility to}, {Septic shock, susceptibility to}, {Malaria, cerebral, susceptibility to} (?)	Proinflammatory cytokine
PLA2G7/6p12.3	Platelet-activating factor acetyl hydrolase deficiency (AR) {Atopy, susceptibility to} (AD)	Activate polymorphic WBCs & enhance vascular permeability
ALOX5/10q11.21	{Atherosclerosis, susceptibility to} (?) {Asthma, diminished response to antileukotriene treatment in} (AD)	Leukotrienes synthesis (initial two steps)
CCL11/ 17q12	{HIV1, resistance to} (?)	Attract eosinophils accumulation in presence of allergen

Pathogenesis for multifactorial disorders



- ⌘ Exposure to a particular antigen for a susceptible person led to hypersensitivity (Exposure time and duration α pathogenicity of genetic variation)
- ⌘ Personalized medicine is the best way to manage asthma for better patient care.
- ⌘ **Rx Triad:** the healthy lifestyle (Including specific diet & nutrition), **prevention of precipitating factors (environmental), and drugs (bronchodilator & disease modifier as a local steroid)**
- ⌘ Care giver's understandability of the disease pathophysiology, drug action, & administration steps is the secret of successfulness of therapy.

Asthma Susceptibility Related Traits with Phenotype mapping key- 2 - The disorder was placed on the map by statistical methods (MOI- Not defined)

Gene/Locus/ Location	MIM No	Phenotype/s	Gene function
IRAK3/ 12q14.3	611064	{Asthma susceptibility 5}	Regulating the immune receptors signalling
CHI3L1/ 1q32.1 (ASRT)	601525	{Asthma-related traits, susceptibility to, 7} Schizophrenia, susceptibility to (AD)	Help in tissue plasticity with surrounding & macrophage differentiation
ASRT4/ 1p31	610906	{Asthma-related traits, susceptibility to, 4}	Not well defined
NPSR1/ 7p14.3 (GPRA)	608584	{Asthma, susceptibility to, 2}	G-protein coupled receptor for Neuropeptide S(NPS) ligand, regulate cell growth and calcium mobilization
PTGDR/14q22.1	604687	{Asthma, susceptibility to, 1}	Receptor of Prostaglandin D2 (PGD2), promotes mast cell maturation and degranulation
Not known/ 2p16	609958	{Asthma-related traits, susceptibility to, 3}	Not well defined- bronchial hyper responsiveness
Not known/ 9q33	613207	{Asthma-related traits, susceptibility to, 8}	Not well defined-coherence between airway tissues
Not known/17q21	611403	{Asthma-related traits, susceptibility to, 6}	Not well defined- predisposition in smokers
HLA-G/ 6p22.1	600807	{Asthma, susceptibility to}	Harmonizing immune tolerance

Counseling the family for phenotypic variabilities- The phenotype of Multifactorial disease usually varies within the families because of the presence or absence of modifiers besides environmental factors. Combine phenotype of unexplained Intellectually different with reactive airway disease in the family may be associated with mutation of the **histamine N-methyltransferase (HNMT) gene**. Further counselling depends upon detail phenotyping & molecular testing.

Thought Riveting:

- ⌘ How are turmeric powder and garlic associated with PD1 pathway?
- ⌘ What are ASRTs have age-depended penetration?
- ⌘ Can targeting the GABAergic pathway altered the disease response?
- ⌘ How have the Yoga techniques altered the protein function beyond the epigenetic mechanism (cytoplasmic protein regulation)?
- ⌘ What is the possible mechanism for the alternation of the circadian cycle of beta-2-adrenergic receptors (ADRB2), located on smooth muscle cells, in a patient with nocturnal asthma?

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