TANGIER DISEASE

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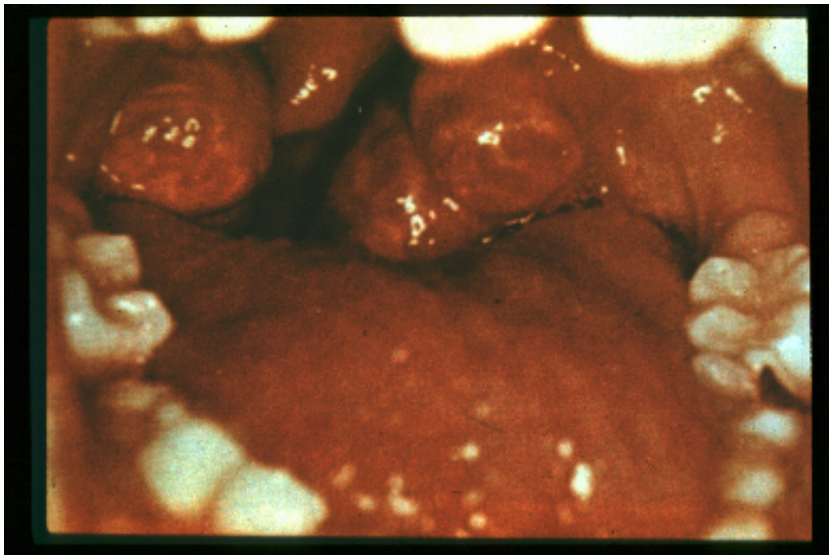
BIOC 118Q

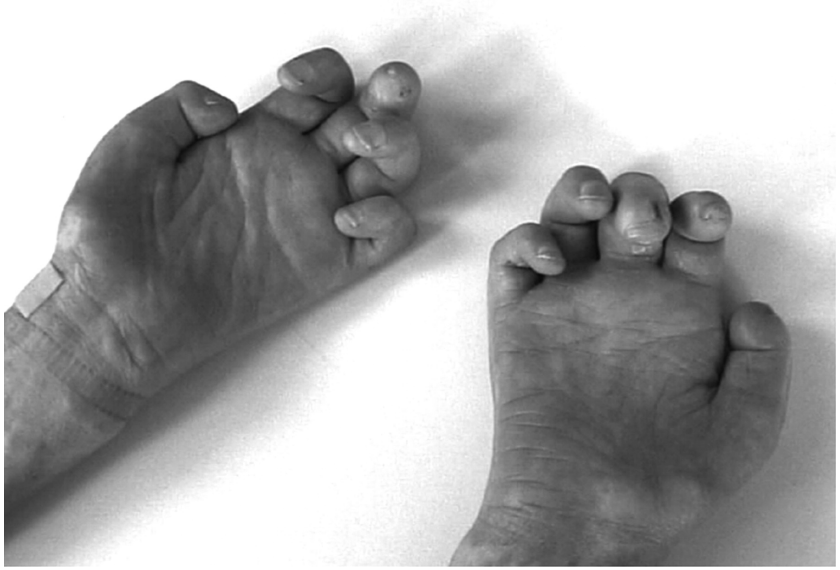
Background Information

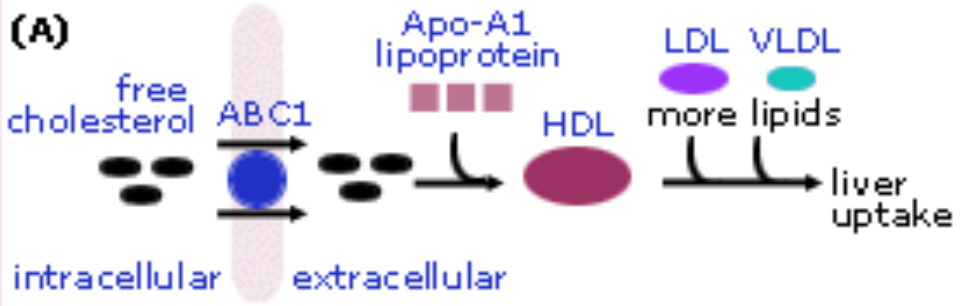
- Genetic disorder of cholesterol transport
- Characteristics include:
  - Orange tonsils
  - Low levels of HDL-C and apoA1
  - Enlarged liver or spleen
  - Build up of cholesterol



Effects

- Moderate increased risk of developing heart/cardiovascular disease
- Buildup of cholesterol can be toxic to cells
- Individuals have a 4-6x increased chance of developing coronary artery disease





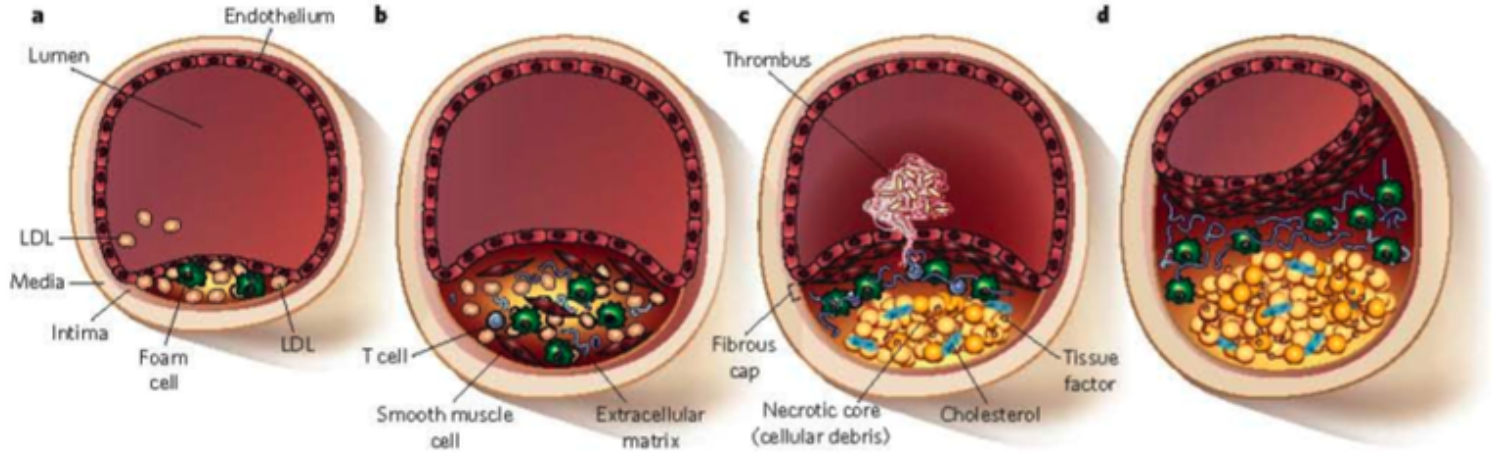
(A) In normal cells ABC1 helps cholesterol exit the cell where it combines with lipid poor Apo-A1 lipoprotein to form high density lipoprotein (HDL). HDL picks up more lipids from low density (LD) and very low density (VLDL) lipoproteins and transfers the cholesterol to the liver, where it is processed.

(B) In Tangier disease, mutations in ABC1 cause cholesterol to accumulate within the cell.

[Adapted from Young and Fielding (1999) Nat Genet. Aug;22(4):316-8, with permission]

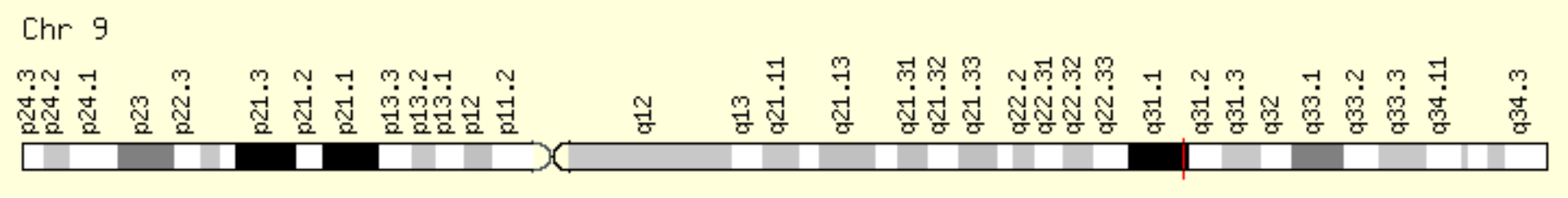
Classic Diagnostic

- Peripheral neuropathy (loss of sensation/movement)
- Syringomyelia-symptoms (widespread loss of pain, and temperature sensation)
- Progressive muscle wasting and weakness
- Corneal clouding, visual impairment,
- Hypocholesterolemia (low HDL)
- Enlarged lipid-laden tonsils
- Atherosclerosis (build up of cholesterol)



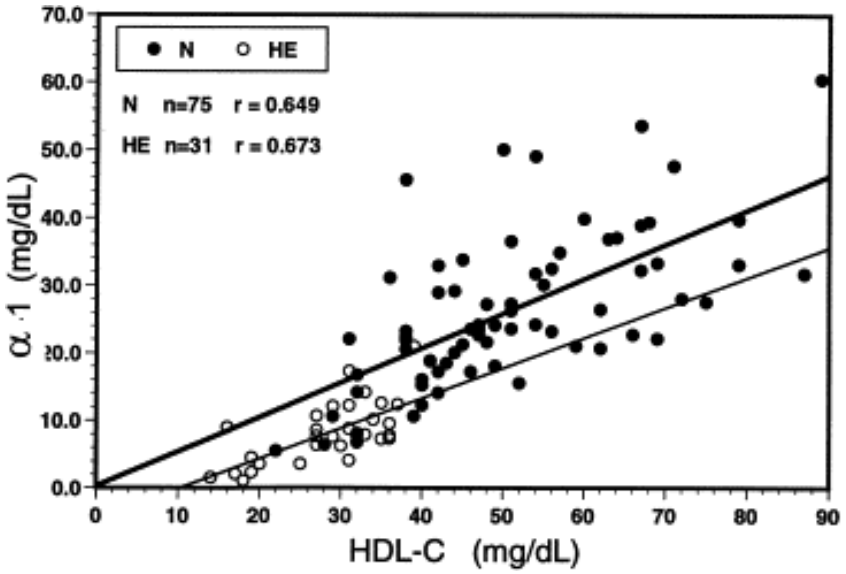
Novel Diagnostic

- Caused by mutation of ABCA1 (ATP-binding cassette) gene on chromosome 9q31
- Discovered in 1999
  - 50 mutations related to Tangier disease that disrupt function
- Only 3 labs that test according to NCBI
- ABCA1 regulates the cholesterol efflux protein, which play an important role in reverse cholesterol transport



Classic Treatment

- Removal of spleen/tonsils if enlarged
- Arteriosclerosis can be treated through angioplasty/bypass surgery
  - Attempted HDL treatment, though generally ineffective



Novel Treatment

- Still exploring
- Problem is in cell transportation, which processes we need to research more
- Could possibly transfer ABCA1 gene to macrophages or bone marrow cells to help the disease