



*" May Reduce Your
Cholesterol"*



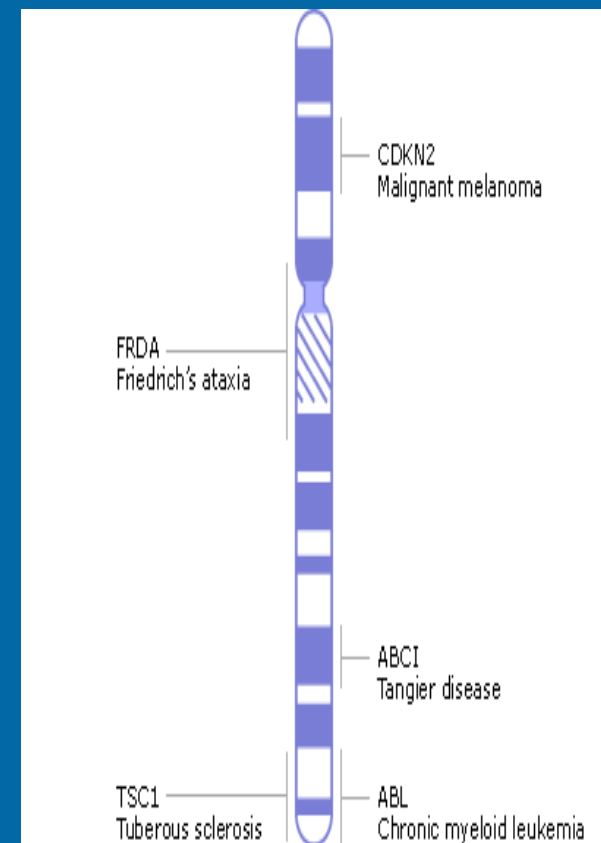
Tangier Island, Virginia

- Settled 1686, now descendants of inhabitants from British Isles, maintain dialect
- Fredrickson et al., 1961
 - Enlarged, orange tonsils
 - Low levels of high density lipoproteins (HDL)

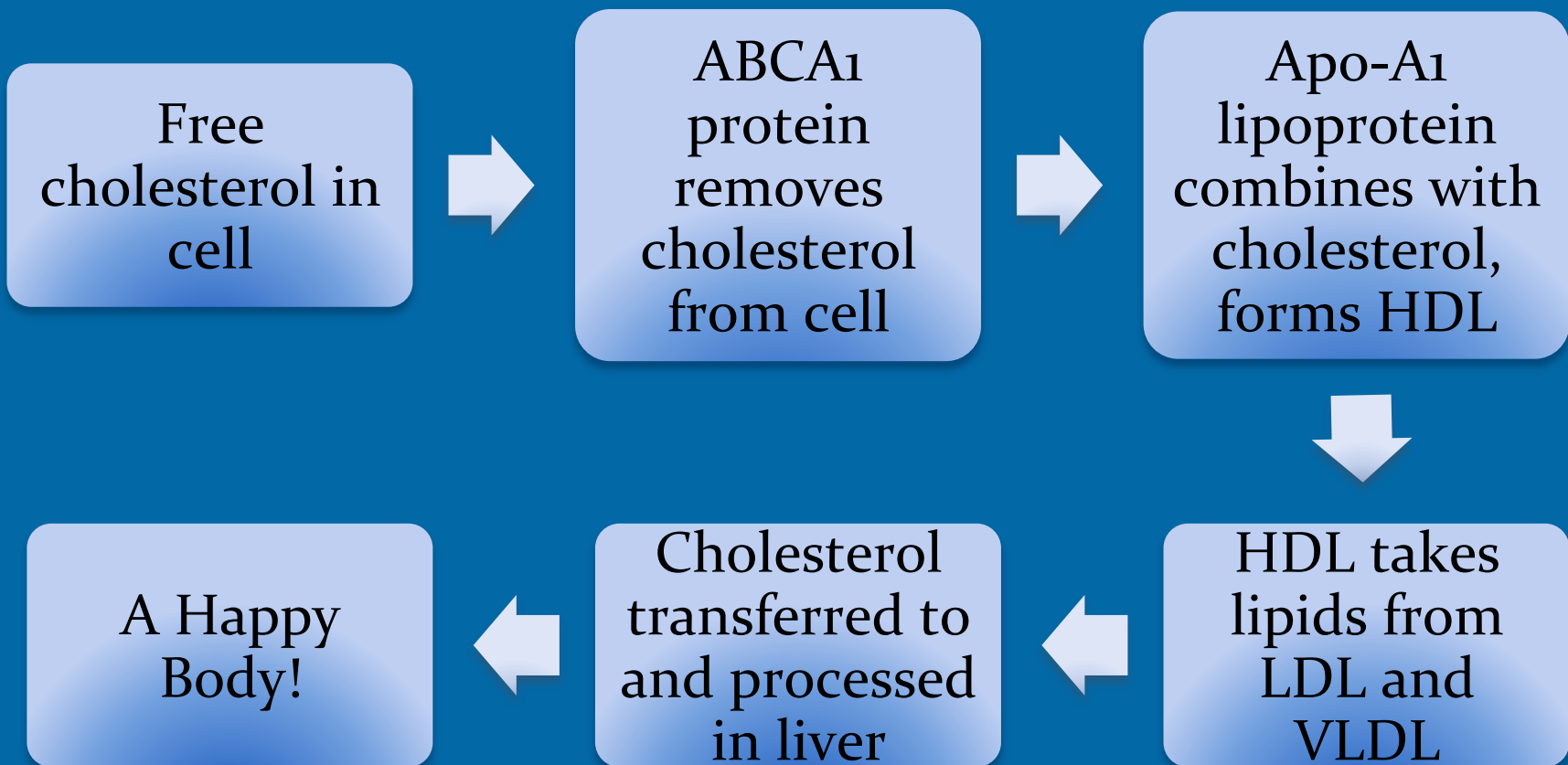
Two hallmarks as initial basis for recognition/diagnosis of Tangier Disease

Tangier Disease

- 1998-mapped to 9q31; rare, autosomal recessive metabolic disorder
- 1999-mutations in ABCA1 gene: ATP binding cassette gene
- Amino acid substitutions, unable to eliminate cholesterol from cells



Normal Pathway



Tangier Disease

- Cholesterol build-up: enlarged tonsils, hepatomegaly, splenomegaly, retinitis pigmentosa, polyneuropathy
- Low HDL: risk for premature atherosclerosis
- Heterozygotes: no clinical symptoms
- Genetic knowledge and diagnosis: molecular testing, HDL test

Treatment

- Continues to be based on severity: heart surgery, organ removal
- Benefits of genetic knowledge: structural vs. pathway disorder and gene therapy, preventing incorrect diagnosis
- Implications of understanding cholesterol transport pathway, HDL and heart disease

References

- Genes and Diseases
- Gene Tests and Reviews
- Genetic Home Reference
- Karolinska Library
- National Center for Biotechnology Information
- Online Mendelian Inheritance in Man
- The Online Metabolic and Molecular Bases of Inherited Disease