CSC 334: TOPICS IN COMPUTATIONAL BIOLOGY

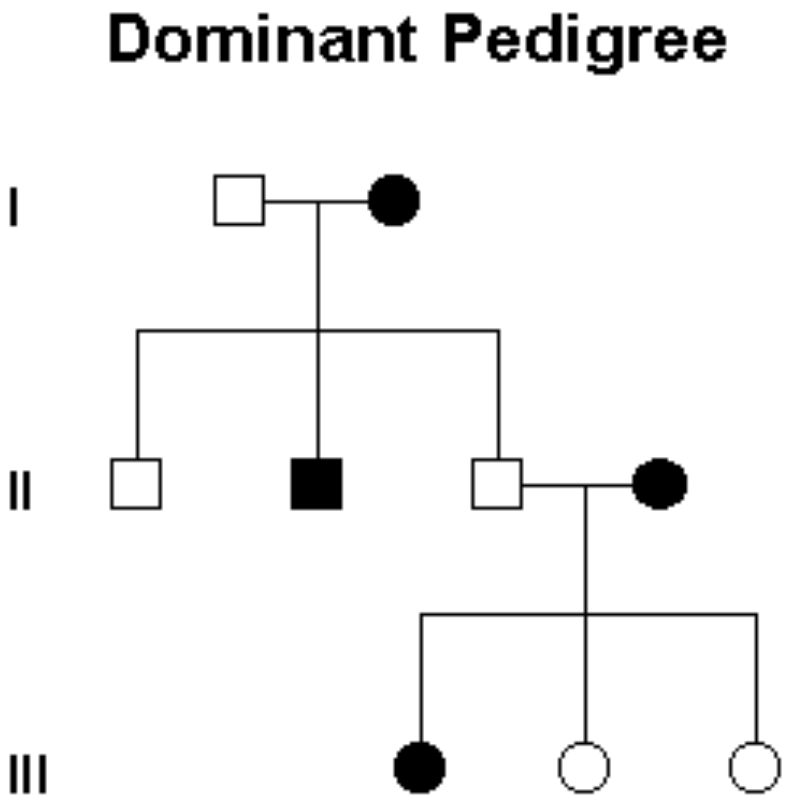
"Algorithms for Genomic Data"

Fall 2015

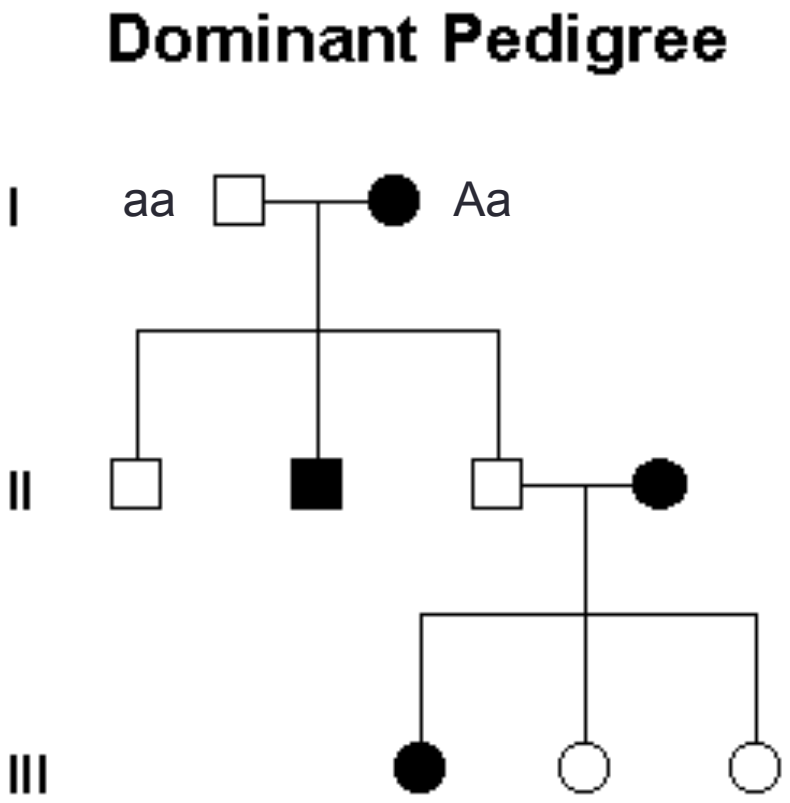
Smith College

Instructor: Prof. Sara Sheehan

Before GWAS: pedigree analysis



Before GWAS: pedigree analysis



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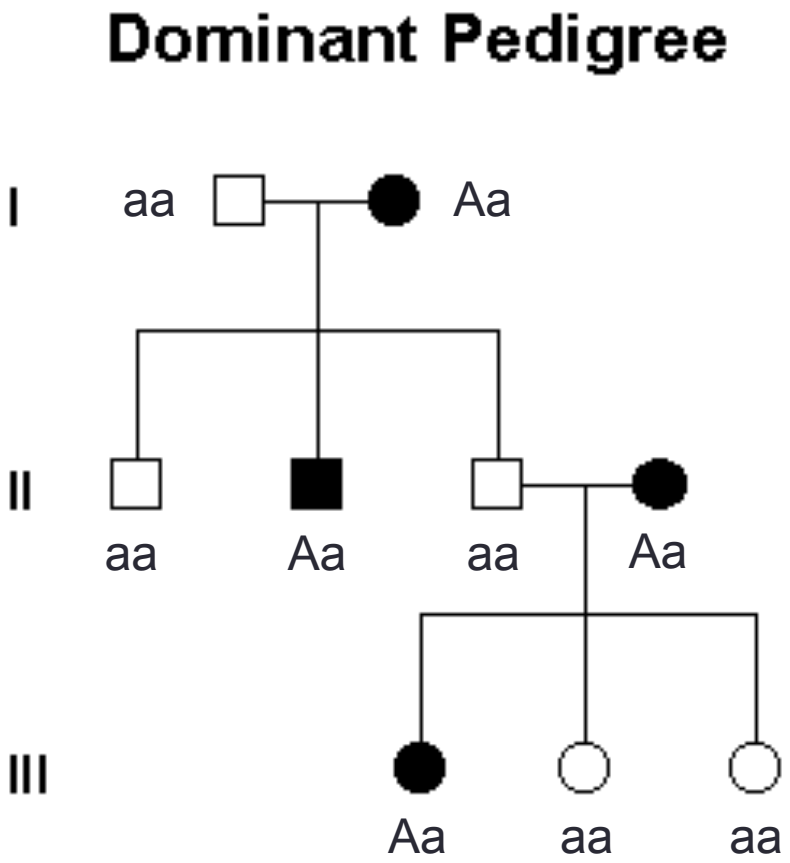

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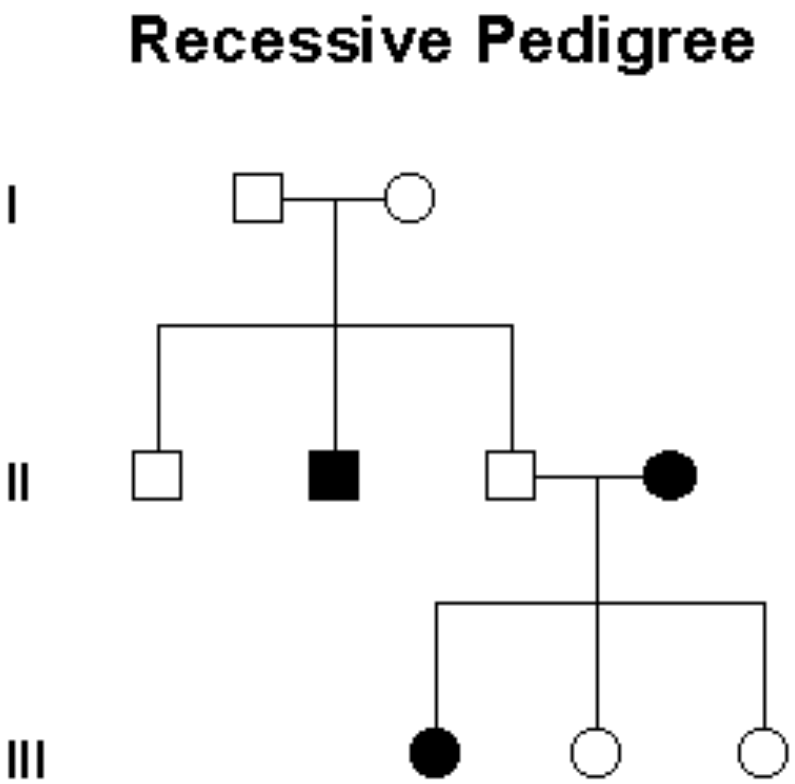

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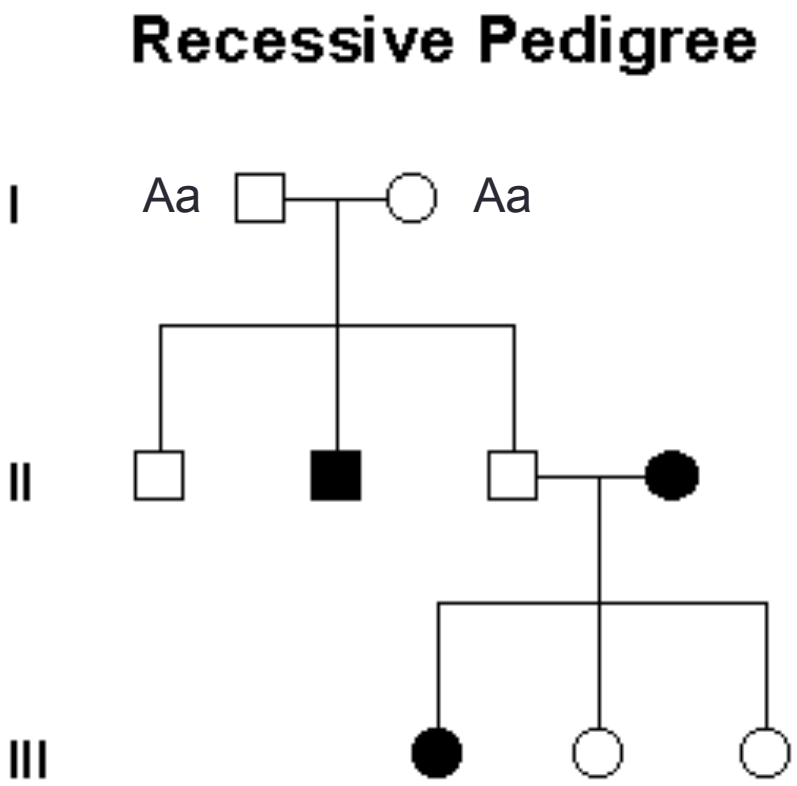

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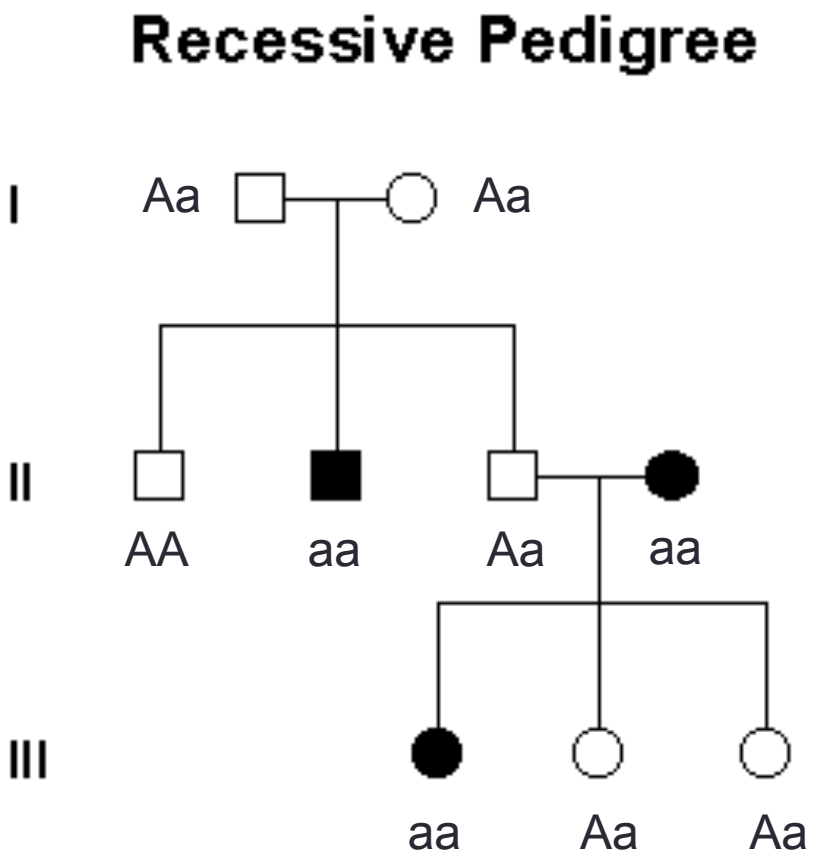
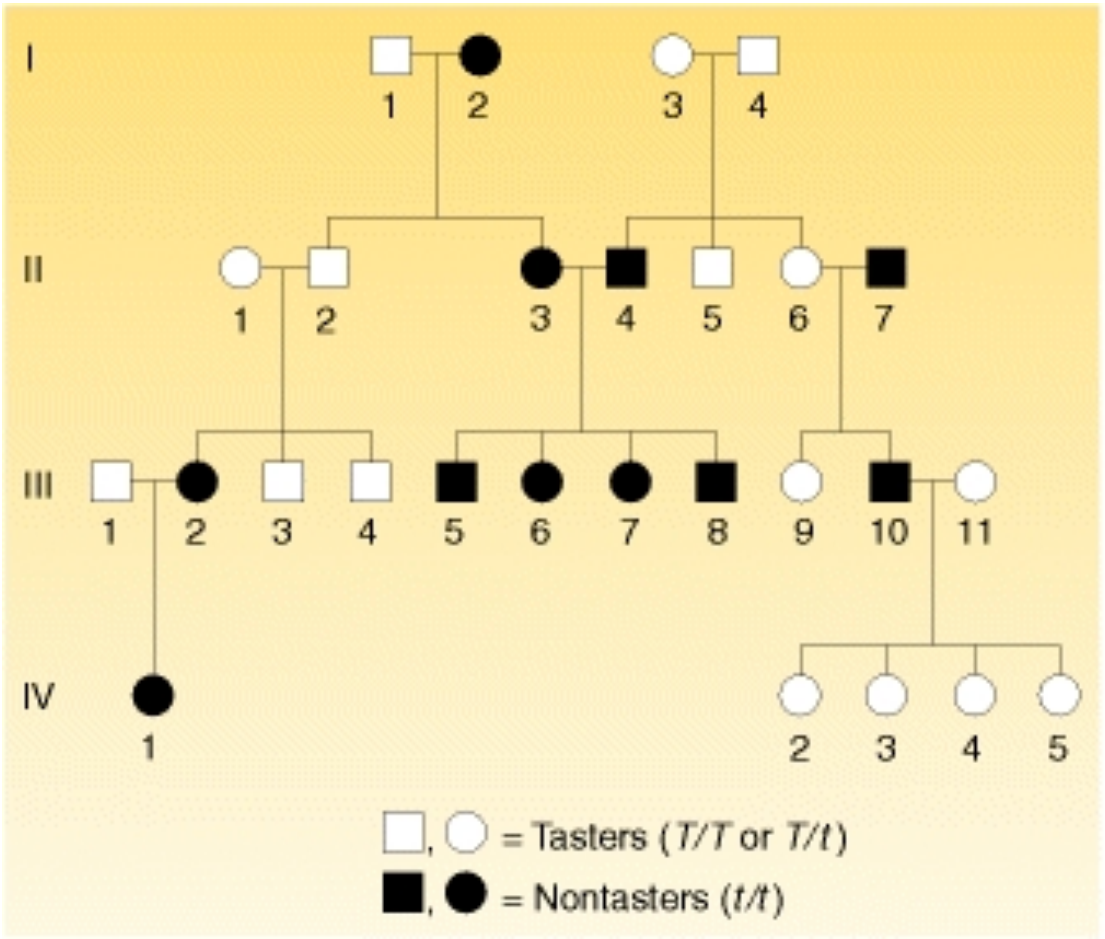


Ability to taste the chemical PTC



From: Human Pedigree Analysis (1999)

Pedigree charts

Hemophilia in the royal family

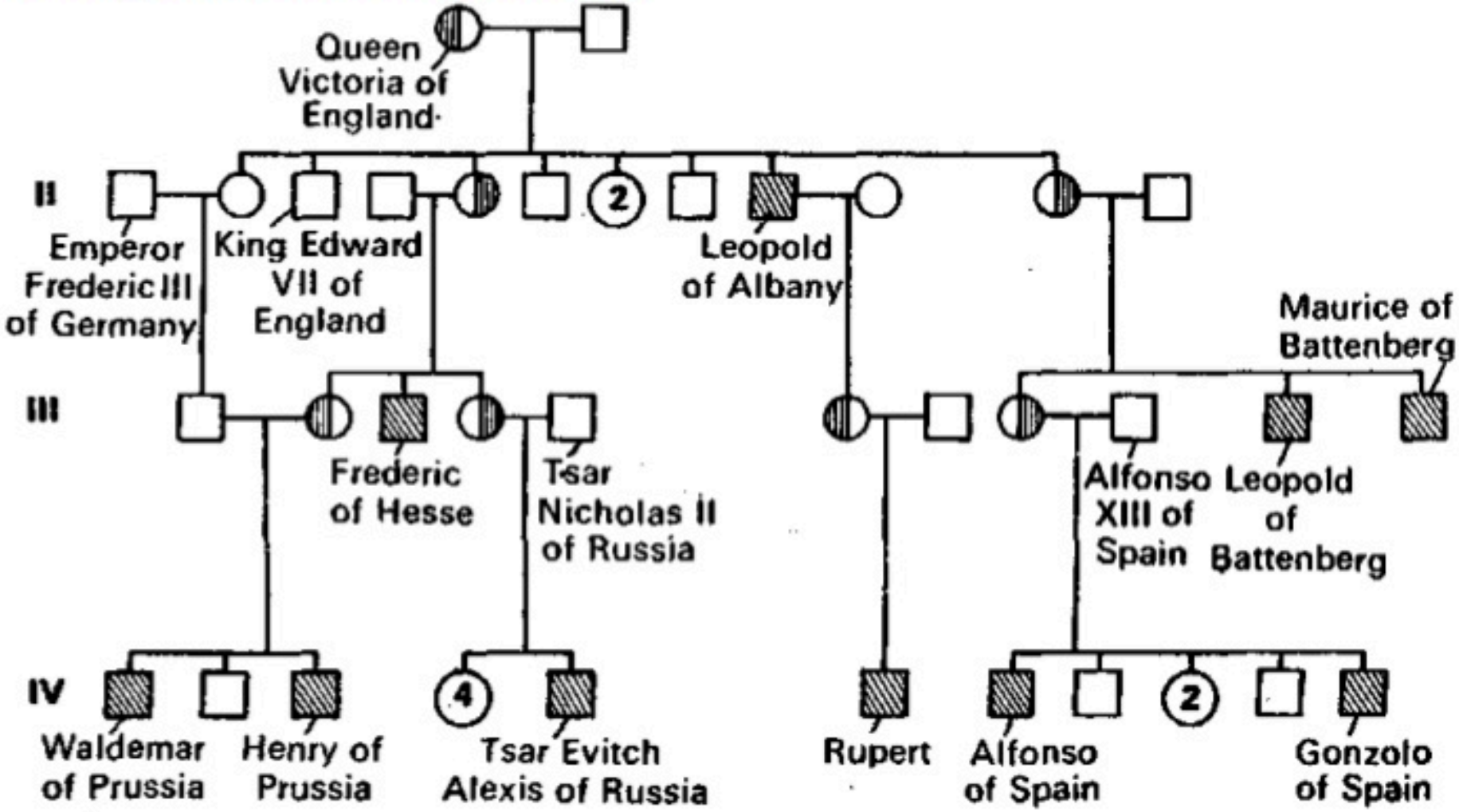
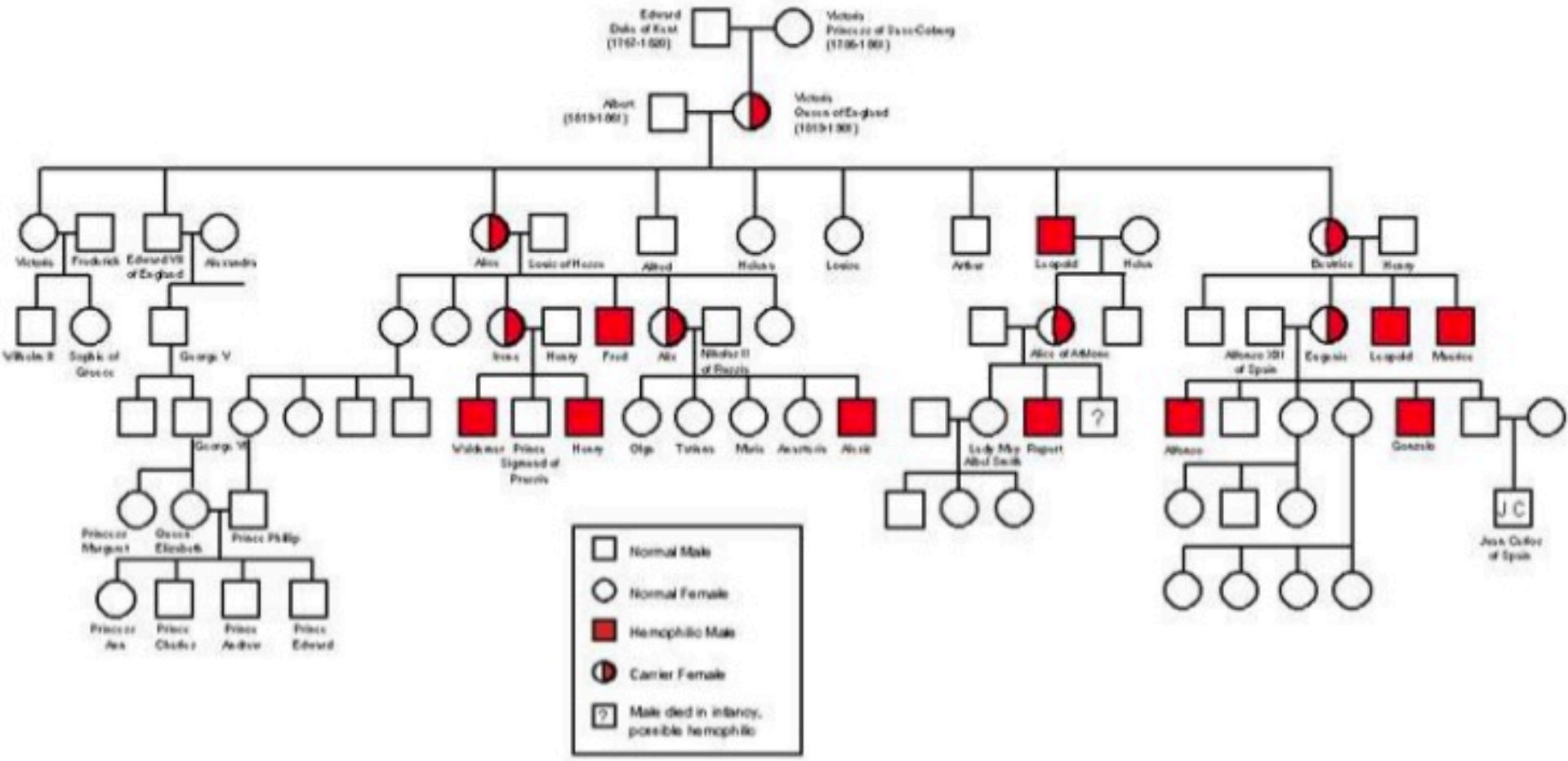


Fig. 41.11. Pedigree of Queen Victoria to illustrate the transmission of haemophilia

Hemophilia

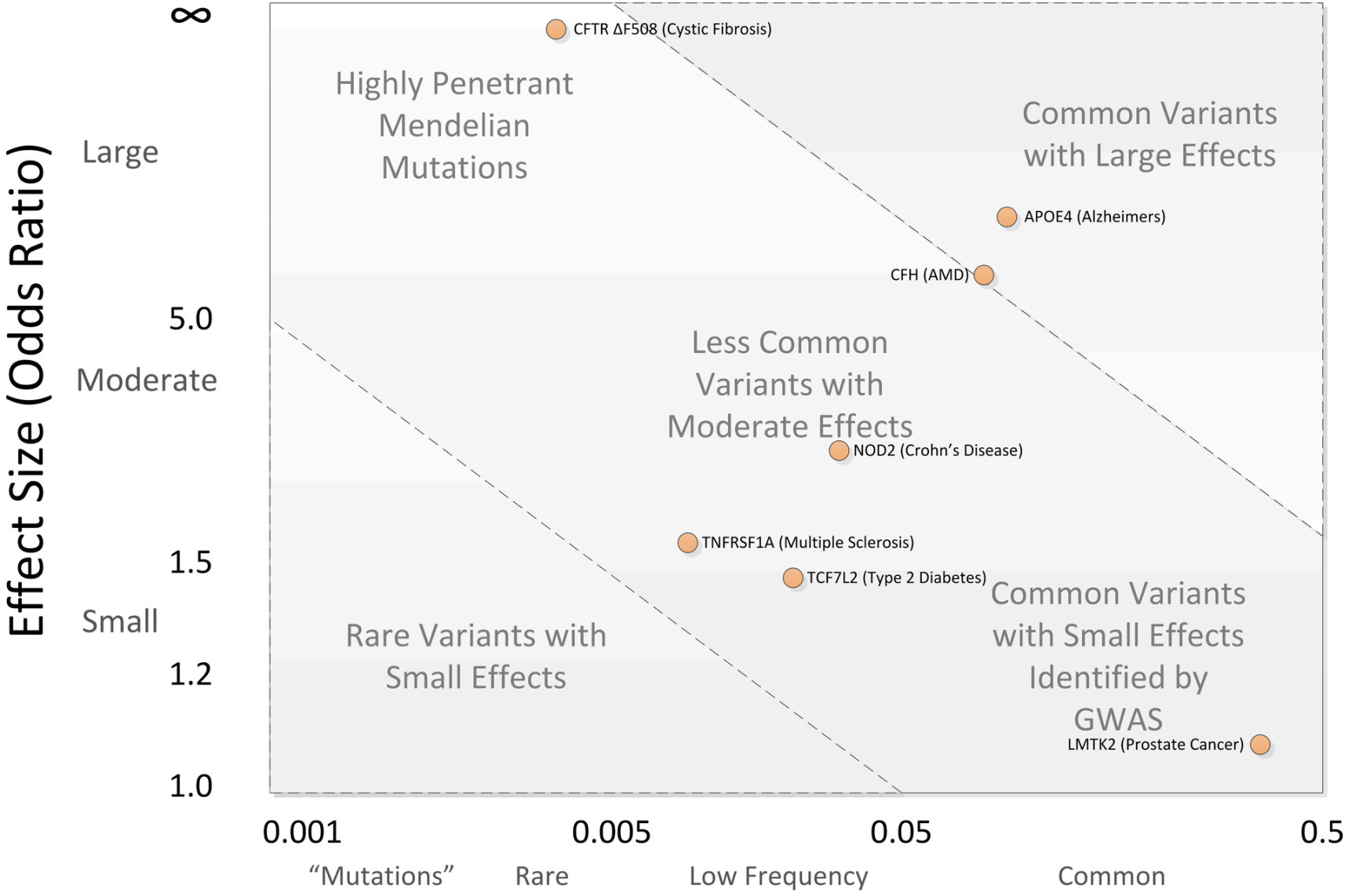
This pedigree chart of the English Royal Family gives us a picture of the inheritance of this X-linked disorder.



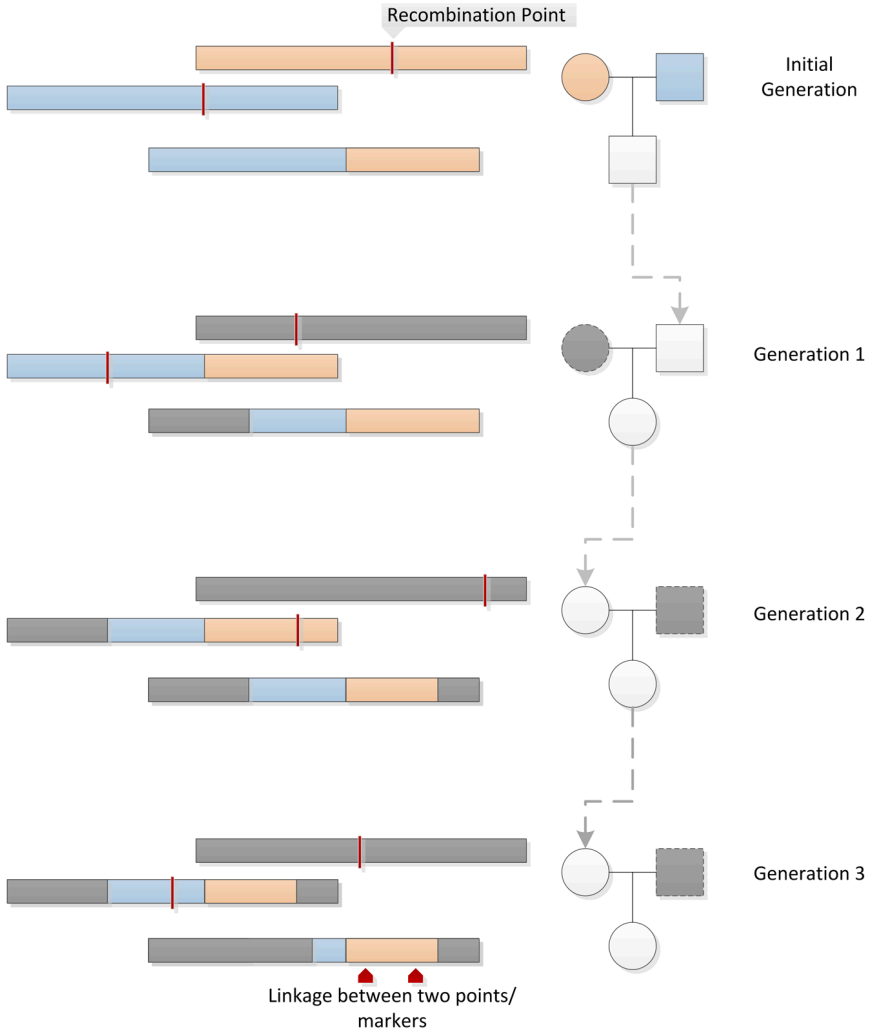
Royal Family Pedigree Chart from:
http://www.sciencecases.org/hemo/hemo.asp

Problems with Linkage Studies

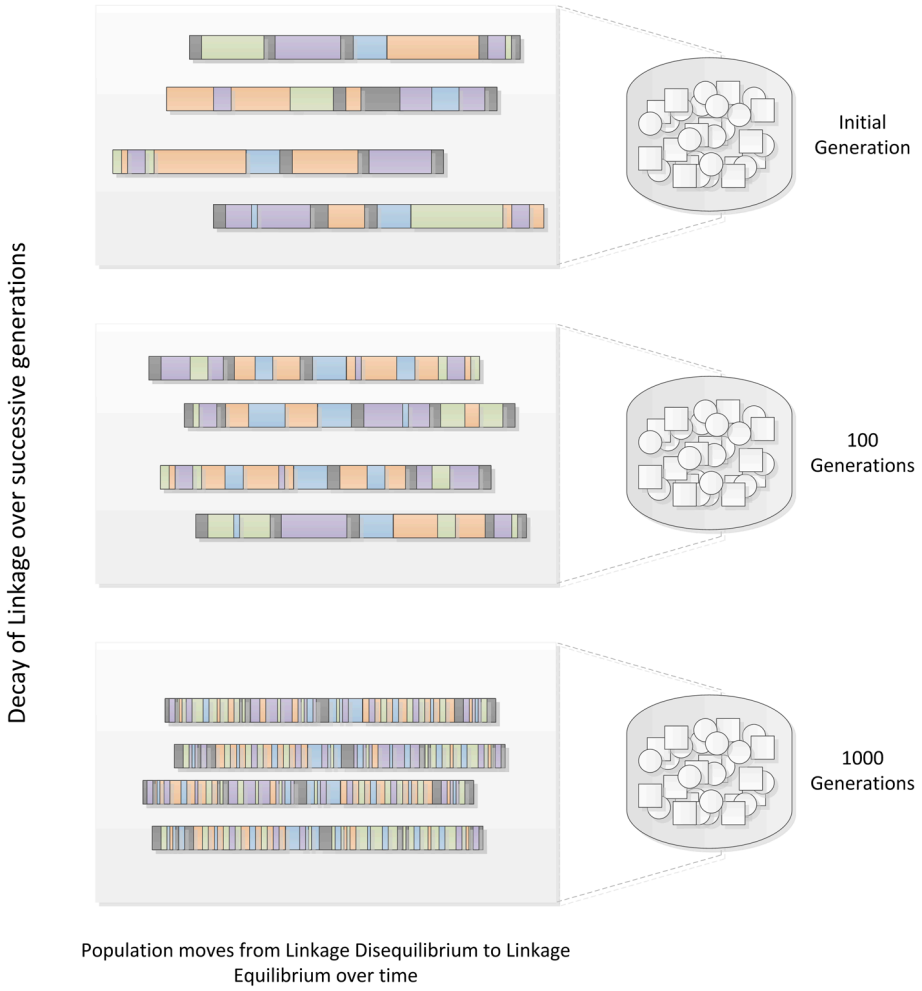
- Sample size is almost always too small
- Might only pick up one type of correlated variant


Effect Size (Odds Ratio)
∞
Large
5.0
Moderate
1.5
Small
1.2
1.0
CFTR ΔF508 (Cystic Fibrosis)
Highly Penetrant Mendelian Mutations
Common Variants with Large Effects
APOE4 (Alzheimers)
CFH (AMD)
Less Common Variants with Moderate Effects
NOD2 (Crohn's Disease)
TNFRSF1A (Multiple Sclerosis)
TCF7L2 (Type 2 Diabetes)
Common Variants with Small Effects Identified by GWAS
Rare Variants with Small Effects
LMTK2 (Prostate Cancer)
0.001
0.005
0.05
0.5
"Mutations"
Rare
Low Frequency
Common
Allele Frequency

Linkage Within A Family



Linkage Disequilibrium Within A Population



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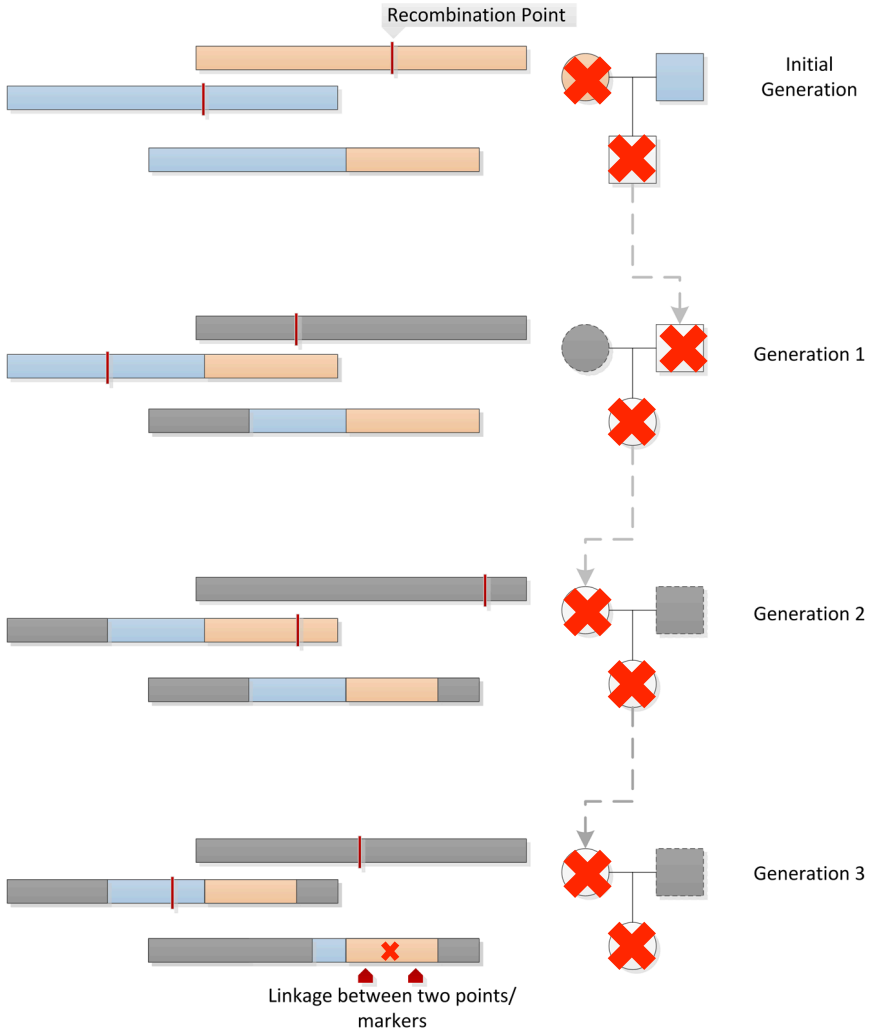

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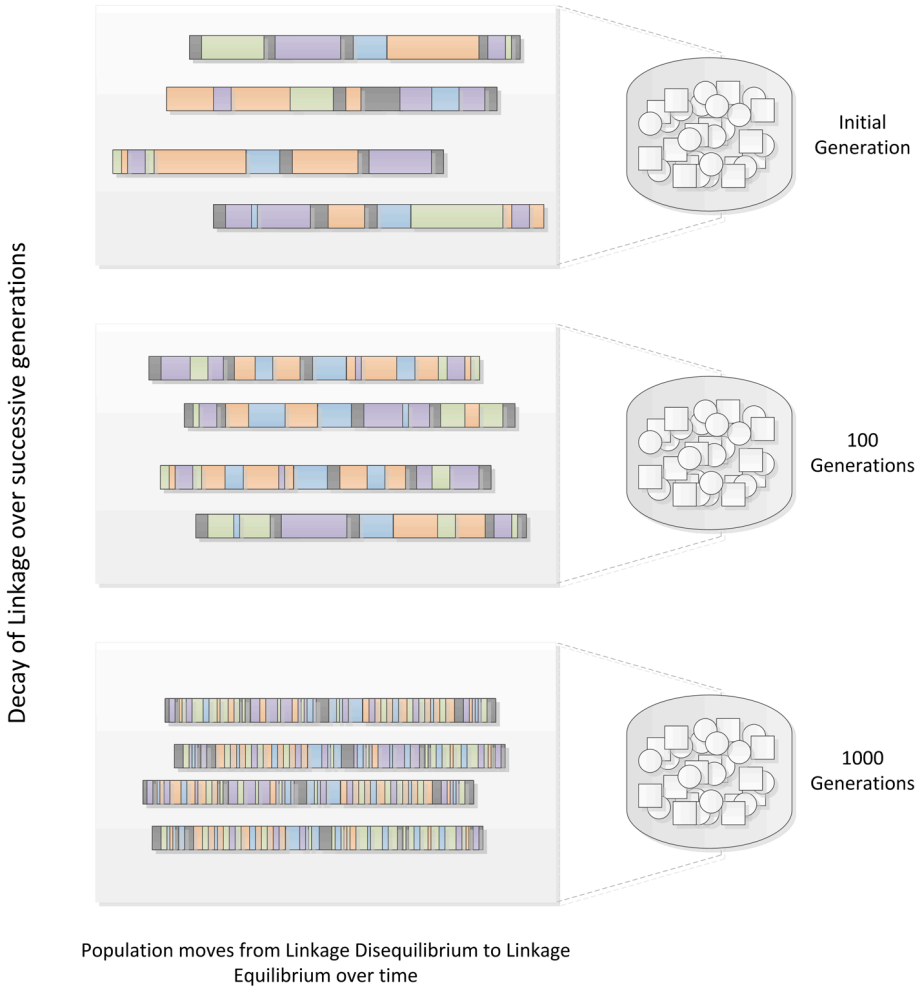

Indirect Association