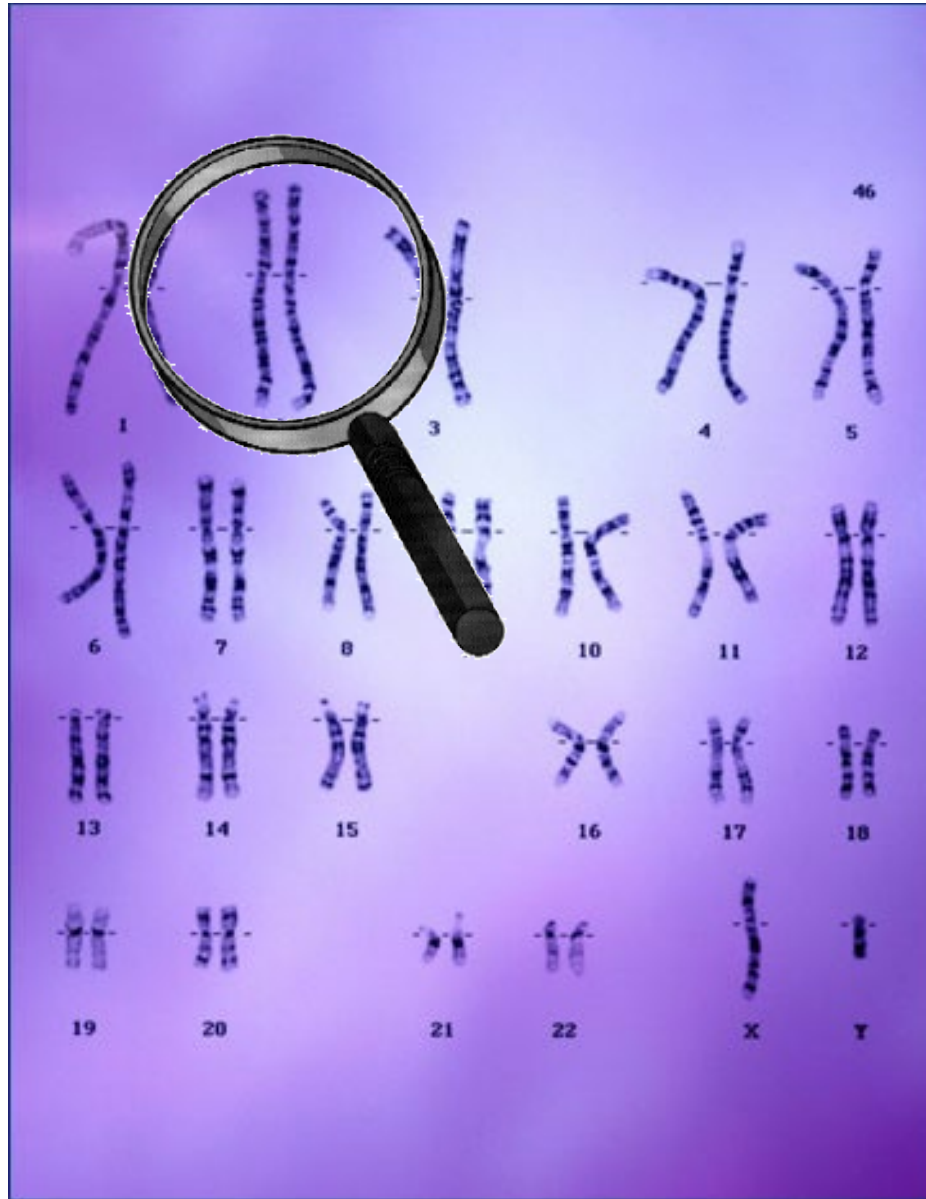
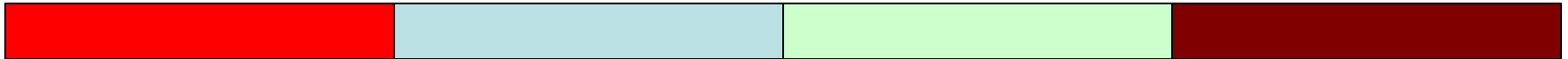


# The Human Chromosomes



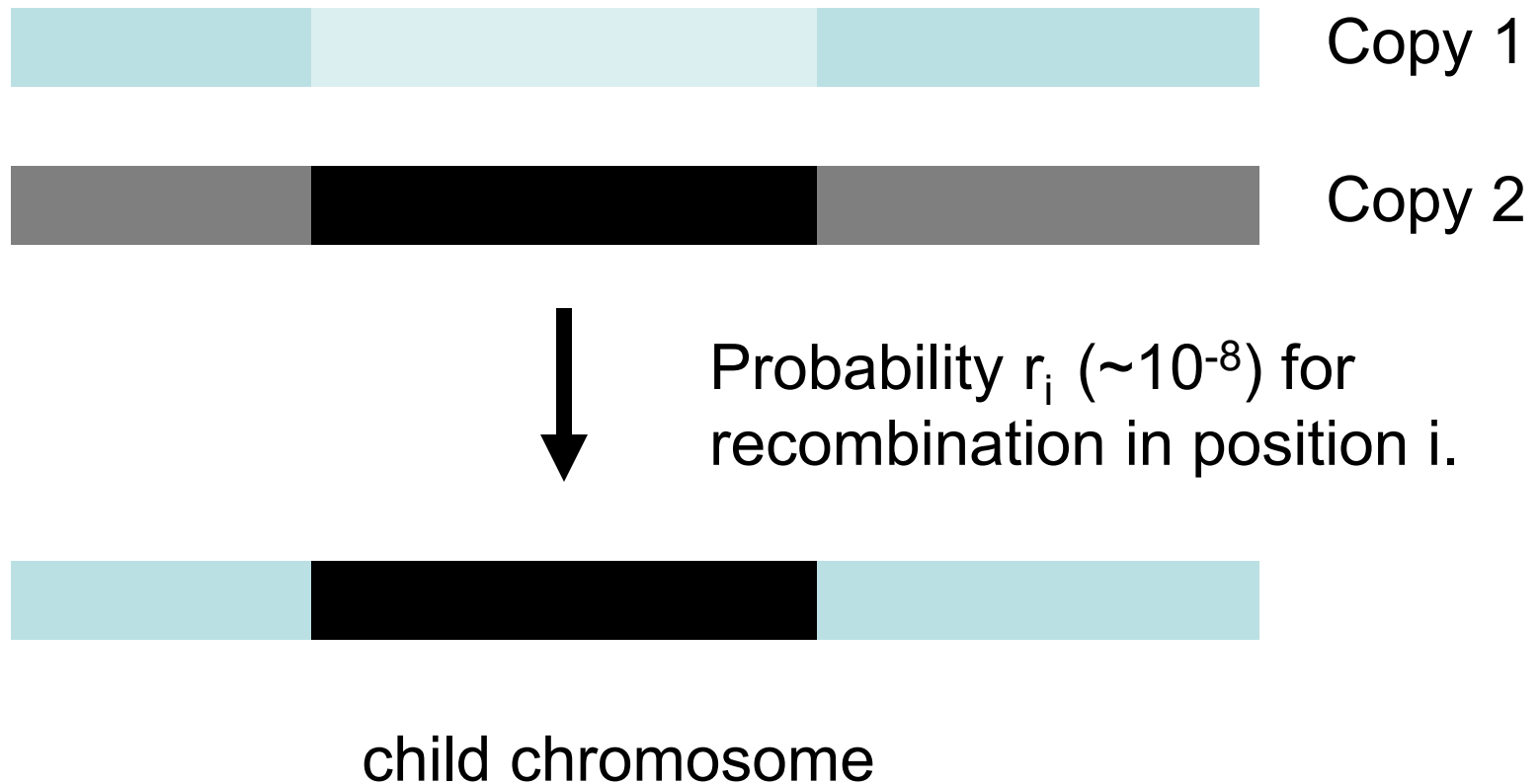
# Other Structural Variants

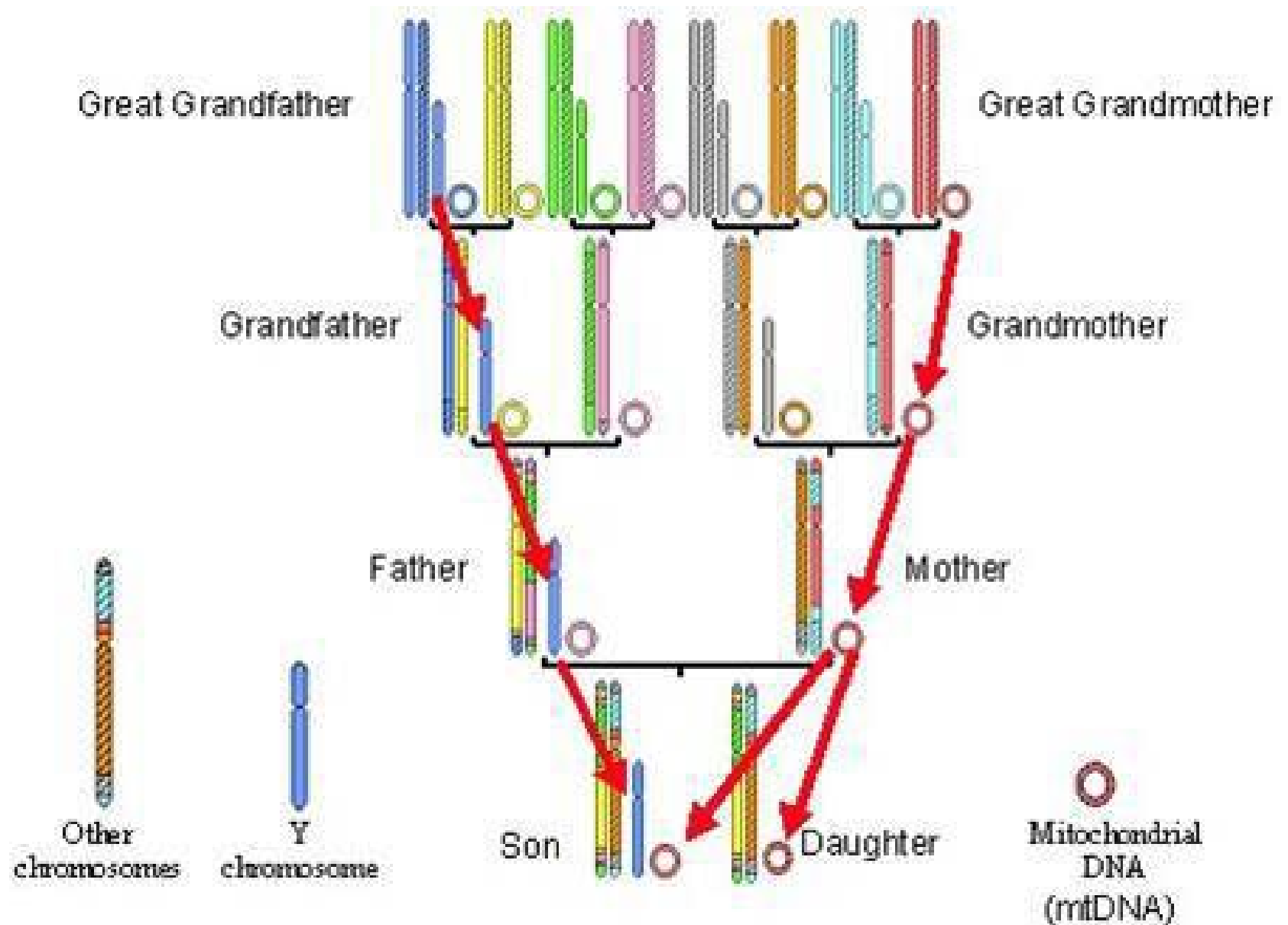


**Deletion**  
**Duplication**  
**Number variant**

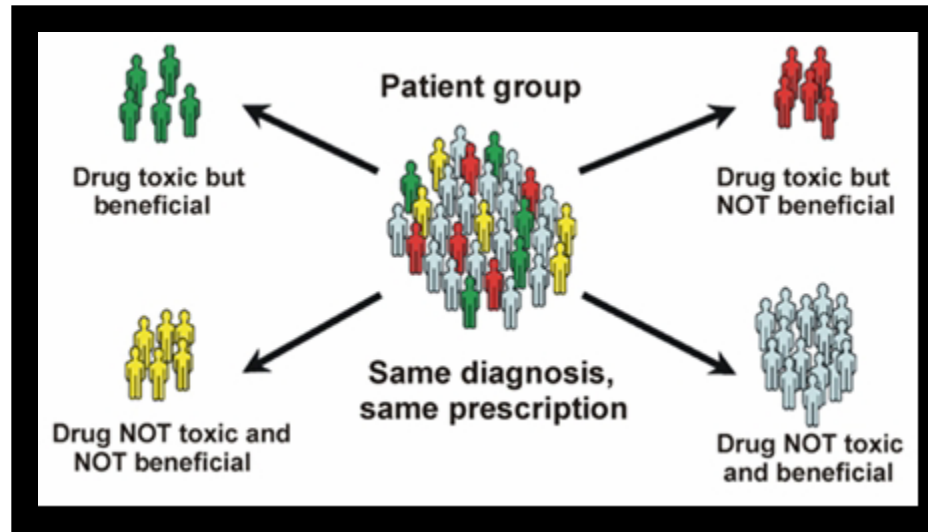


# Other mutations - recombination



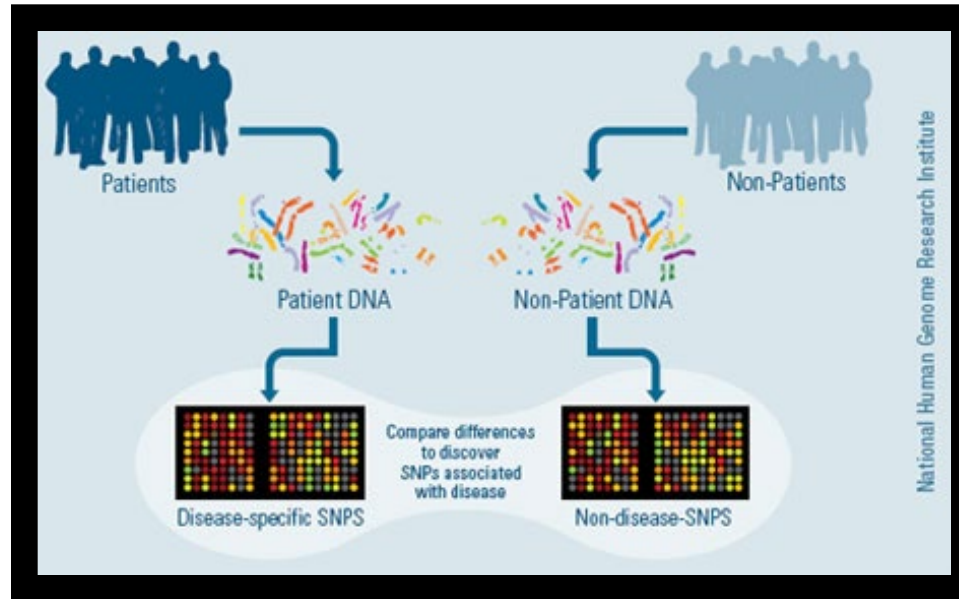


# The Vision of Personalized Medicine



**Genetic and epigenetic variants +  
measurable environmental/behavioral factors would  
be used for a personalized treatment and diagnosis**

# Association Studies



Genetic variants such as Single Nucleotide Polymorphisms (**SNPs**), Copy Number Variants (**CNVs**) are tested for association with the trait.

# Usually SNPs are biallelic

## When we should have a polymorphism

### Cases:

|       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|-------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| AGAGC | A | G | T | C | G | A | C | A | G | G | T | A | T | A | G | C | T | A | C | A | T | G | A | G | A | T | C | G | A | C | A | T | G | A | G | A | T | C | G | T | A | G | A | G | C | C |   |   |   |
| AGAGC | C | G | T | C | G | A | C | A | T | G | T | A | T | A | G | T | C | T | A | C | A | T | G | A | G | A | T | C | G | T | A | G | A | G | C | A | T | G | A | T | C | G | T | A | G | A | G | C |   |
| AGAGC | A | G | T | C | G | A | C | A | G | G | T | A | T | A | G | T | C | T | A | C | A | T | G | A | G | A | T | C | G | T | A | G | A | G | C | A | T | G | A | T | C | G | T | A | G | A | G | C |   |
| AGAGC | A | G | T | C | G | A | C | A | G | G | T | A | T | A | G | C | T | A | C | A | T | G | A | G | A | T | C | A | A | C | A | T | G | A | G | A | T | C | G | T | A | G | A | G | C | C |   |   |   |
| AGAGC | C | G | T | C | G | A | C | A | T | G | T | A | T | A | G | C | T | A | C | A | T | G | A | G | A | T | C | G | T | A | G | A | G | C | A | T | G | A | T | C | A | A | C | A | T | G | A | T | C |
| AGAGC | C | G | T | C | G | A | C | A | T | G | T | A | T | A | G | C | T | A | C | A | T | G | A | G | A | T | C | G | T | A | G | A | G | C | A | T | G | A | T | C | A | A | C | A | T | G | A | T | C |
| AGAGC | C | G | T | C | G | A | C | A | G | G | T | A | T | A | G | C | T | A | C | A | T | G | A | G | A | T | C | G | T | A | G | A | G | C | A | T | G | A | T | C | A | A | C | A | T | G | A | T | C |
| AGAGC | A | G | T | C | G | A | C | A | G | G | T | A | T | A | G | C | T | A | C | A | T | G | A | G | A | T | C | T | T | A | G | A | G | C | A | T | G | A | T | C | G | T | A | G | A | G | C |   |   |

### Controls:

|       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|-------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| AGAGC | A | G | T | C | G | A | C | A | T | G | T | A | T | A | G | T | C | T | A | C | A | T | G | A | G | A | T | C | G | T | A | G | A | G | C | A | T | G | A | T | C | A | A | C | A | T | G | A | T | C | C |
| AGAGC | A | G | T | C | G | A | C | A | T | G | T | A | T | A | G | T | C | T | A | C | A | T | G | A | G | A | T | C | A | A | C | A | T | G | A | T | C | T | T | A | G | A | G | C | C |   |   |   |   |   |   |
| AGAGC | A | G | T | C | G | A | C | A | T | G | T | A | T | A | G | C | T | A | C | A | T | G | A | G | A | T | C | T | T | A | G | A | G | C | A | T | G | A | T | C | A | A | C | A | T | G | A | T | C |   |   |
| AGAGC | C | G | T | C | G | A | C | A | G | G | T | A | T | A | G | C | T | A | C | A | T | G | A | G | A | T | C | T | T | A | G | A | G | C | A | T | G | A | T | C | A | A | C | A | T | G | A | T | C |   |   |
| AGAGC | C | G | T | C | G | A | C | A | G | G | T | A | T | A | G | T | C | T | A | C | A | T | G | A | G | A | T | C | T | T | A | G | A | G | C | A | T | G | A | T | C | A | A | C | A | T | G | A | T | C |   |
| AGAGC | A | G | T | C | G | A | C | A | G | G | T | A | T | A | G | T | C | T | A | C | A | T | G | A | G | A | T | C | T | T | A | G | A | G | C | A | T | G | A | T | C | A | A | C | A | T | G | A | T | C |   |
| AGAGC | C | G | T | C | G | A | C | A | G | G | T | A | T | A | G | C | T | A | C | A | T | G | A | G | A | T | C | T | T | A | G | A | G | C | A | T | G | A | T | C | A | A | C | A | T | G | A | T | C |   |   |
| AGAGC | C | G | T | C | G | A | C | A | G | G | T | A | T | A | G | T | C | T | A | C | A | T | G | A | G | A | T | C | T | T | A | G | A | G | C | A | T | G | A | T | C | A | A | C | A | T | G | A | T | C |   |

Associated SNP

# Genome-Wide Association Studies

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nature

BRIEF COMMUNICATIONS

## ARTICLES

nature

### Genome-wide association study identifies novel breast cancer susceptibility loci

Douglas F. Easton<sup>1</sup>, Karen A. Pooley<sup>2</sup>, Alison M. Dunning<sup>2</sup>, Paul D. P. Pharoah<sup>2</sup>, Deborah Thompson<sup>1</sup>, Dennis G. Ballinger<sup>3</sup>, Jeffery P. Struwing<sup>4</sup>, Jonathan Morrison<sup>2</sup>, Helen Field<sup>2</sup>, Robert Luben<sup>5</sup>, Nicholas Wareham<sup>5</sup>, Shahana Ahmed<sup>2</sup>, Catherine S. Healey<sup>2</sup>, Richard Bowman<sup>6</sup>, the SEARCH collaborators<sup>2\*</sup>, Kerstin B. Meyer<sup>7</sup>, Christopher A. Haiman<sup>8</sup>, Laurence K. Kolonel<sup>9</sup>, Brian E. Henderson<sup>8</sup>, Loic Le Marchand<sup>9</sup>, Paul Brennan<sup>10</sup>, Suleeporn Sangrajrang<sup>11</sup>, Valerie Gabor Hui-Chun Wang<sup>12</sup>, Diana Eccles<sup>13</sup>, D. C. Sheila Seal<sup>17</sup>, Michael R. Stratton<sup>17,18</sup>, I. Berge G. Nordestgaard<sup>20</sup>, Christen K. A. Jolanta Lissowska<sup>24</sup>, Beata Peplonska<sup>2</sup>, Daehee Kang<sup>28</sup>, Keun-Young Yoo<sup>28,29</sup>, Susan E. Hankinson<sup>32</sup>, David G. Cox<sup>31</sup>, Natalia Bogdanova<sup>35,36</sup>, Peter Schürma Peter Devilee<sup>39</sup>, Jan G. M. Klijn<sup>40</sup>, Alice Angela Cox<sup>43</sup>, Ian W. Brock<sup>43</sup>, Gordon Janet E. Olson<sup>45</sup>, Hanne Meijers-Heijboer Fernando Rivadeneira<sup>48</sup>, Roger L. Milne Margaret McCredie<sup>51</sup>, Melissa Southey Hiltrud Brauch<sup>54</sup>, Ute Hamann<sup>55</sup>, Yon-I kConFab<sup>57\*</sup>, AOCs Management Group Jaana Hartikainen<sup>58,59</sup>, Nicholas E. Day

Breast cancer exhibits familial aggregation; susceptibility genes account for less than 10% of cases.

Vol 447 | 7 June 2007 | doi:10.1038/nature05911

nature

## ARTICLES

### Genome-wide association study identifies novel type 2 diabetes susceptibility loci

Jiang Shen<sup>1</sup>, David Serre<sup>1</sup>,

## ARTICLES

### Genome-wide association study of 14,000 cases of seven common diseases and 3,000 shared controls

The Wellcome Trust Case Control Consortium\*

There is increasing evidence that genome-wide association (GWA) studies represent a powerful approach to the

# Two minute genetic primer

- Recombining DNA:
  - Chromosome we get from each parent is mixture of both their copies
  - Every base pair can have different inheritance history
- Non-recombining DNA:
  - Mitochondrial (mtDNA) maternally inherited
  - Most Y chromosome (NRY) in men paternally inherited

Non-recombining DNA has unique inheritance history. In particular, there is a unique mtDNA family tree and a unique NRY family tree on which we all sit:

NRY-Adam lived about 60K years ago in Africa – [Y chromosome tree](#)  
mtDNA-Eve lived about 150K years ago in Africa

Phylogenetic tree showing the relationships between various populations. The tree is rooted at the top left with a star symbol. The populations are grouped into four main clusters: L0-L4 (orange), L3 (yellow), M (purple), and N (cyan). The M cluster includes M8, M9, C, Z, E, G, Q, and D. The N cluster includes N1, N2, N9, N\*, I, W, Y, A, S, and X. The R cluster (green) includes R0, HV, HV0, H, J, T, R9, F, B, P, U, U\*, and K. The L3 cluster is further divided into L3\* and L3. The L0-L4 cluster is the most diverse, with L0 being the most basal and L4 being the most derived.

# Example of conclusion: my story

- **My background:** Ashkenazi Jewish on all sides
  - **My family name:** Rosset, Western-European non-Jewish sounding
  - **Question:** which is my paternal heritage story?
  - **Answer:** I belong to Y-haplogroup J2, which is very common among Jews, very rare in Western Europe
- ⇒ Confirms family story, family name still a mystery

# Example of conclusion: Genghis Khan's Y?

Investigating populations throughout East and Central Asia, investigators discovered 8% of men had VERY closely related Y chromosome

Suggests common ancestor within 1000 years

Obvious candidate: Genghis Khan and his male progeny

Verifying conclusion:

1. This lineage had greatest diversity in Mongolia (indicates origin)
2. Had higher prevalence among Hazara in Pakistan, who have oral tradition of being Genghis Khan's descendents