Historical and Geographical Genetic Variation: Europe

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Two Major Questions

- Who are the ancestors of modern Europeans?
- From where and when did they arrive in Europe?

Genetic Tools

- Nuclear markers
  - classical markers and DNA variants
- Uniparental markers
  - mtDNA and Y chromosome
Advantage of Uniparental Markers

- Y chromosome
- mtDNA
- Autosomes

Ancestor of Y chromosome
Ancestor of mtDNA

First Question
Who Are the Ancestors of Modern Europeans?
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Neanderthals Are Not Our Ancestors

(Krings et al., 1997 Cell 90: 19-30)

Homo neanderthalensis

- 1856 Discovery of a skull and a number of other bones from a limestone cave deposit in the small Neander River Valley
- 1864 They were given the name "Neanderthal man" by William King. He named them after the Neander Valley (or thal, in German)

www.antropos.galeon.comimag220402neandertal1

H. neanderthalensis H. sapiens

- "Following at least 200,000 years of successful adaptation to the glacial climates of the northwestern Eurasia, they disappeared abruptly between 30,000 and 40,000 years ago" (Mellars 2004 Nature 432: 461-465)
- "Data based on high-resolution record of human occupation from Gorham’s Cave, Gibraltar, establish the survival of a population of Neanderthals to 28,000 years ago" (Finlayson et al., 2006 Nature 443: 850-853)

Location of Neanderthal Remains

[Diagram of Neanderthal remains location]

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Homo neanderthalensis: Questions

- Direct ancestor of modern Europeans?
- Contributed some genes to modern Europeans?
- Was completely replaced by modern humans without contributing any gene?

Human Mitochondrial DNA (mtDNA)

- Extra-nuclear circular genome of 16,569 base pairs (bp)

Human mtDNA Genome

- Encodes 37 genes
  - 22 tRNAs
  - 2 rRNAs
  - 13 proteins (for energy metabolism)
- Control region (modern)
  - HVS-I
  - HVS-II

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Location of Neanderthal Skeletal Remains
First Analyzed for mtDNA Variation

Schematic Phylogenetic Trees Including Neanderthal mtDNA Sequences

The Recent African Genesis of Humans

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**Origin of Modern Humans**

- First traces of modern humans in Europe go back to ~ 46,000 ya
- Aurignacian industry

_Neanderthals are not our ancestors, and neither partially contributed to the gene pool of modern Europeans_

**So When Did Modern Humans Arrive in Europe?**

_Homo Sapiens_ Paleanthropological Data

- First traces of modern humans in Europe go back to ~ 46,000 ya
- Aurignacian industry

(Wilson, Cann 1992 Sci. Am 266: 68-73)

(Mellars 2004 Nature 432: 461-465)
A New Radiocarbon Revolution and the Dispersal of Modern Humans in Eurasia

"The speed of colonization of Europe by modern human populations was more rapid than previously believed."

- Dispersal routes of modern human populations across Europe
- The ages (ky) are based on a rate of dispersal of ~ 0.4 km/y


What About the Genetic Evidence?

- A lot of information from uniparental markers in particular from mtDNA

mtDNA Genetics

- Numerous copies
- High evolution rate
  - 10-20 higher than nDNA
Maternal Inheritance and Lack of Recombination

Therefore, the differentiation of mtDNA has been generated only by the sequential accumulation of new mutations along radiating maternal lineages.

Over the course of time, this process of molecular divergence has given rise to the monophyletic units that are now called haplogroups.

What Is a mtDNA Haplogroup?

A group of mtDNAs which are defined by a unique set of variants acquired from the same common ancient (female) ancestor.

The mtDNA Process of Molecular Differentiation

It is fast and occurred mainly during and after the recent process of human colonization and diffusion into different regions and continents, thus the different subsets of mtDNA variation tend to be restricted to different geographic areas and population groups.
The Most Recent Molecular Approach to Determine mtDNA Variation

Sequencing of numerous entire mtDNA genomes selected on the basis of preliminary molecular data

Worldwide mtDNA Phylogeny and Distribution of Major Haplogroups

The "out of Africa" exit

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Paleoenvironmental Evidence

"Paleoenvironmental evidence is crucial to this argument, suggesting that an earlier migration toward the north >50 kya would have been impossible given the climate of the time, with desert extending from North Africa to Central Asia."

(Olivieri et al., 2006. Science 314: 1767-70)

Temperature Change Over the Last 150 Ky


Out of Africa and Back Again?

• What about haplogroups M3 and U6?
• Why are they in Africa?
• Same event of gene flow?

(Olivieri et al., 2006. Science 314: 1767-70)
Spatial Frequency Map of M1

(Olivieri et al., 2006 Science 314: 1767-70)

Spatial Frequency Map of U6

(Olivieri et al., 2006 Science 314: 1767-70)

The mtDNA Legacy of the Levantine Early Upper Palaeolithic in Africa

(Olivieri et al., 2006 Science 314: 1767-70)
Phylogeny of M1

51 complete mtDNA sequences

Phylogeny of U6

30 complete mtDNA sequences

Conclusions

- A migration event from West Asia to Africa (about 40-45 ka) affected both haplogroups
- M1 and U6 did not follow the southern coastal route that was used in the "out of Africa" exit
- The arrival of M1 and U6 to Africa 40-45 ka would temporally overlap with the event(s) that led to the peopling of Europe by modern humans
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What Is U5?

Haplogroup U in the Worldwide mtDNA Phylogeny

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Into Europe...

"Classical" Genetic Markers

- 94 alleles at 34 loci (distributed among 16 different chromosomes) used in Principal Component Analysis (PCA) of European populations:
  - blood groups
  - human lymphocyte antigens (HLA)
  - immunoglobulins
  - other proteins

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Principal Component Analysis

- PCA is a dimension-reduction method that seeks to explain the variance of multivariate data by a smaller number of variables (the principal components, PCs), which are linear functions of the original variables.

- Cavalli-Sforza and colleagues presented synthetic geographical maps of the individual PCs.
  - The maps have hills and valleys that are interchangeable.
  - A hill and a valley indicate local populations with extreme allele frequencies (frequency peaks) and opposite characteristics.

First PC (28% of the Variance)

Interpreted as supporting the Neolithic demic diffusion hypothesis.

Second PC (22% of the Variance)

Genetic adaptation to climate or due to migrations of Uralic populations from north-western Asia.
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Third PC (11% of the Variance)

MtDNA Data Support
Some of the Scenarios Suggested by Classical Markers
But in the Case of the Second PC Provide an Alternative Explanation

PCA of mtDNA Haplogroup Profiles in Europe and the Near East

(Cavalli-Sforza et al., Eds 1994 The history and geography of human genes Princeton University Press, Princeton. It has been attributed to the expansion of Kurgan people or other Steppe populations)

(Richards et al., 2002 Am J Hum Genet 76: 853-66)
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Haplogroup H in the Worldwide mtDNA Phylogeny

The Molecular Dissection of mtDNA Haplogroup H Confirms That the Franco-Cantabrian Glacial Refuge Was a Major Source for the European Gene Pool


Phylogeny of H (and Sister Clades)
62 complete mtDNA sequences

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Spatial Frequency Maps

Haplogroup H

(Achilli et al., 2004 Am J Hum Genet 75: 910-18)

A Signal, from Human mtDNA, of Postglacial Recolonization in Europe

Spatial frequency map of V

(Torroni et al., 2001 Am J Hum Genet 69: 544-52)

Haplogroup V in the Worldwide mtDNA Phylogeny
### Coalescence Ages of H1, H3 and V

<table>
<thead>
<tr>
<th>Haplogroup</th>
<th>Source of data</th>
<th>No. of mtDNAs</th>
<th>$\rho$</th>
<th>$\sigma$</th>
<th>$T (\pm \Delta T)$ (ky)</th>
</tr>
</thead>
<tbody>
<tr>
<td>H1</td>
<td>Total</td>
<td>134</td>
<td>2.118</td>
<td>0.218</td>
<td>10.8 (± 1.1)</td>
</tr>
<tr>
<td>H2</td>
<td>Total</td>
<td>50</td>
<td>2.140</td>
<td>0.279</td>
<td>11.0 (± 1.4)</td>
</tr>
<tr>
<td>V</td>
<td>Total</td>
<td>66</td>
<td>2.409</td>
<td>0.463</td>
<td>12.4 (± 2.0)</td>
</tr>
</tbody>
</table>

$T_{medium} = 11,300 \ (\pm 900) \ years$

(Achilli et al., 2004. Am J Hum Genet 75: 910-38)

### Temperature Change Over the Last 150 Ky


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### Conclusion

These studies have highlighted the role of the Franco-Cantabrian refuge area as a major source of the hunter-gatherer populations that gradually repopulated much of central and northern Europe when climatic conditions improved from around 13,000 years ago.

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