GENETICS FOR GENEALOGY

Getting to Know Your DNA Relatives

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University of Iowa

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Coralville, IA
October 5, 2016
COURSE GOALS

• Encourage understanding of the biological basis of DNA test results
• Foster proficiency navigating the web interface and interpreting DNA test results
Course Schedule

Today
  • The Language of DNA (tests)
  • Ancestry Composition

Tomorrow
  • DNA Identity Between Close Relatives
  • Connecting Genetics with Genealogy
OBJECTIVES

• Conceptualize the organization of the human genome and properties that contribute to its variability among individuals
• Build proficiency in the data, methods and interpretation of test results of human ancestry and biological relationships
LANGUAGE OF DNA (TESTS)
THE ACCOUNT INTERFACE

Take control of your account(s)!
Major SNP Testing Options:

- **AncestryDNA** – ($99) Includes Ancestry Estimate and DNA Matching. Integrated with Ancestry.com family tree for an extra subscription fee.

- **Family Tree DNA** – Family Finder Test ($99) Includes Ancestry Estimate and DNA Matching. Accepts AncestryDNA data transfer ($39).

AncestryDNA

• Primary application is family history research through DNA matches, but includes an ancestry composition estimate.
• **Largest database of tested customers.**
• **AncestryDNA test can be linked with family tree in Ancestry.com for fully integrated research.**
• Sophisticated DNA matching algorithm that reduces the number of false-positive matches of close relationship.
• Automated family clustering in DNA circles.
• Ability to manage DNA kits of multiple family members in a single account, and share results between accounts.
Bryant McAllister

This test is shown to matches as bmcallis86

Linked to Bryant Fulton McAllister
Family Tree DNA

- Primary application is family history research through DNA matches.
- **Broad set of tests and tools for working with DNA matches for family history research**, but their utility and integration in the website is not intuitive.
- Relatively small database, but participants are mostly engaged and knowledgeable about family history research.
- Each DNA sample is registered in an account, and different tests on that sample are managed in a single account.
- Participate and/or administer projects that include multiple participants.
- **Accepts raw DNA data from AncestryDNA**, The Genographic Project, and older 23andMe tests.
Welcome to myFTDNA

Your Account

Profile
Name: Bryant McAllister
Email: bmcallis@mchsi.com
Address: 1530 Buresh Avenue
City/State/Zip: Iowa City, IA 52245
Phone: 319-338-0420
Last sign in: Today
Manage Personal Information Change Password

Order History
Product Ordered

Family Tree

Family Finder Results Completed: 3/9/2016

Matches Chromosome Browser Known Relationships

myOrigins

Matrix Advanced Matches Download Raw Data Learn More
23andMe

- Primary application is self-exploration through DNA.
- Broadest set of interpretations from a DNA test including maternal line, paternal line for males, ancestry composition, Neanderthal composition, DNA relatives, and traits.
- Choice to maintain privacy or not.
- Interface for browsing raw DNA data.
- Multiple kits can be managed in a single account, and some results can be shared between accounts.
Answer the next Research question.

Answer questions, earn insights, and make an impact with 23andMe Research.

Get started

Learn about Ethnicity and Your Reports.

Learn how your ethnicity affects our interpretation of your genetic health.

View tutorial

Learn about Wellness Reports.

Our Wellness Reports make connections between your DNA and traits that may relate to healthy living.

View tutorial

Learn about Traits Reports.

Our Traits Reports are a fun way to help you understand how your DNA makes you unique.
Account Settings:

- **AncestryDNA** – DNA linked to profile in Ancestry.com tree; privacy of the DNA tester; notifications; sharing of DNA results; research participation. Multiple DNA test results accessible from single account – tests can be added and shared.

- **Family Tree DNA** – Privacy settings; surnames; notifications. Single account for each individual – different tests and upgrades requested on previous DNA kit.

- **23andMe** – Participation in DNA Relatives; sharing options; notifications; research participation. Multiple DNA test results accessible from single account – tests can be added and limited results shared.
ACTIVITY

• Verify settings on the user account
GENOME-WIDE SNP DATA

A common technological platform is used to survey an individual’s unique genetic profile
Chromosomes:
23 pairs of linear DNA molecules inherited from both parents; 22 pairs of autosomes, and a single pair of sex chromosomes

Gametes (egg or sperm) contain only 1 member of each pair
DNA is the Cellular Recipe for Life

- A **Genome** is the entire set of **DNA** molecules present in a cell.
- Each DNA molecule contains a string of A=T pairs and G=C pairs as a **DNA sequence**.
- Cells of an individual contain the same genome sequence, but different from any other individual.
SNP Analysis
Single Nucleotide Polymorphism

My mum’s hair colour is grey.
My mom’s hair color is gray.
Each company uses a common testing technology that assesses about 600,000 different known variable sites (SNPs) in the DNA of your genome (including mtDNA in some cases). Most of the same sites are used in the tests of different companies.
Activity: Relate These Terms

- chromosome
- DNA
- genome
- gene
- SNP
- basepair
- sequence
- genotype
Activity: Relate These Terms

- chromosome
- DNA
- genome
- gene
- SNP
- basepair
- sequence
- genotype

- packaged into
- contains
Activity: Relate These Terms

- **DNA**
- **SNP**
- **chromosome**
- **genome**
- **basepair**
- **sequence**
- **genotype**
- **gene**

- genome contains many SNP site within reference produces differences
- SNP represents order within internal structure of instructions for functional region within
- sequence contains many gene
- basepair contains functional region within gene
- chromosome packaged into contains all genome contains all information in DNA
- genotype comprises product of basepair contains many gene
- formed through inheritance of chromosome representation of each genotype
Each company uses a common testing technology that assesses about 600,000 different known variable sites (SNPs) in the DNA of your genome (including mtDNA in some cases). Most of the same sites are used in the tests of different companies.
### Genome-Wide SNP Analysis

<table>
<thead>
<tr>
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<th>chromosome</th>
<th>position</th>
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<td>AA</td>
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<td>GG</td>
</tr>
<tr>
<td>rs2272756</td>
<td>1</td>
<td>882033</td>
<td>GG</td>
</tr>
</tbody>
</table>
ACTIVITY

• Download raw data file and browse
Test Settings for Bryant McAllister

Email Settings for Bryant McAllister
Receive emails about new findings in your DNA results

- Weekly
- Off

Privacy

Your Display Name
You will be identified to your DNA matches as bmcallis86.  

Edit

Ethnicity Preference
Show your complete ethnicity profile to DNA matches

Family Tree Linking
Connecting your DNA to your tree helps determine how you are related to your matches.

This test is linked to:

Bryant Fulton McAllister
in the Bryant Fulton McAllister family tree

Your Information  Edit

Actions

Download Expired DNA Matches
Download a subset of your previous matching results (available for a limited time).

Download Expired Matches

Download Raw DNA data
Complete security steps to protect your information and download your data.

What is Raw DNA data?

Download Raw DNA Data

Delete test results from AncestryDNA
Prior to deleting the DNA test results, we will ask you to enter your password.

Delete Test Results
Download Raw Data

Search for specific genes and markers (SNPs) of interest.* You can view or download your data at anytime in its raw, uninterpreted format (your A’s, T’s, G’s, and C’s).

File Information

• The text file consists of lines of your genotype call data (your A’s, T’s, C’s and G’s).

• The download is a zipped text file 5 MB to 30 MB in size.

• It can be opened in a text editor like WordPad or Excel.

Utility

Keep in mind that having your data in hand may be of limited practical usefulness, depending on how much information you can extract from the data beyond what the 23andMe site already gives you.
Lactose Intolerance

Dairy products like milk, yogurt, and cheese contain the sugar lactose. An enzyme called lactase breaks down this sugar. If you don’t produce enough lactase, gut bacteria can convert lactose into gas, causing indigestion.

Bryant, you likely produce the lactase enzyme.

Likely not lactose intolerant
Bryant, you likely produce the lactase enzyme.

Likely not lactose intolerant

- **C/T-13910**
  - **Gene:** Near LCT
  - **Marker:** rs4988235
  - **Your Genotype:** A
  - **Your Other Parent:** A
  - **Additional Information:**
    - Biological explanation
    - Typical vs. variant DNA sequence(s)
    - Percent of 23andMe customers with variant
    - References [1, 3, 6] | ClinVar
Lactose intolerance, 
*LCT* gene

Infantile expression of lactase, with a cessation of production in adulthood – **lactose intolerance**

**rs182549**  
C or T

Infantile expression of lactase, with continued expression into adulthood

**rs4988235**  
G or A
Lactose intolerance, *LCT* gene

Infantile expression of lactase, with a cessation of production in adulthood – lactose intolerance

Infantile expression of lactase, with continued expression into adulthood

Lactose intolerant

Lactose

-22,018  -13,910

G≡C  C≡G

A=T  T=A

rs182549  rs4988235

C or T  G or A
rs182549

Or browse by chromosome:

<table>
<thead>
<tr>
<th>Genes</th>
<th>Marker (SNP)</th>
<th>Genomic Position</th>
<th>Variants</th>
<th>Your Genotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>MCM6</td>
<td>rs182549</td>
<td>136616754</td>
<td>C or T</td>
<td>T / T</td>
</tr>
</tbody>
</table>
Promethease

The easiest way to make a report is to visit promethease.com

This takes about 10 minutes and costs $5 (all major currencies and credit cards accepted).

How-to videos

- Making a Promethease report
- Reading a Promethease report

An example report based on either

- 23andMe v1 (2008)
- 23andMe v3 (2011)
- 23andMe v4 (2014)

What is Promethease?  [edit]

Promethease is a literature retrieval system that builds a personal DNA report based on the scientific literature cited in SNPedia and a file of genotype (DNA) data. Customers of DNA testing services (23andMe, FamilyTreeDNA, Ancestry.com, Complete Genomics, ...) can use it to retrieve published data about their DNA completely independent of whichever company produced the data.

Read about the features of Promethease.
USING DATA FILE IN OTHER PLATFORMS
User Registration

First & Last Name: Please enter your real name here. Your name is needed by administrators for verification purposes. It may also be displayed in some applications that are not associated with individual results. If you do not want your real name shown in those cases, you may also specify a 'screen name' in the 'alias' field to the left.

Optional Alias:

Email Address: You must be able to receive a confirmation email at this address. If possible, it should match the email address used for uploads prior to the registration requirement on this site.
Enter email address again:

Password: Case sensitive. At least 6 characters. Include at least one number or symbol.
Enter Password Again:

Register
File Uploads

Raw DNA file Uploads

- FTDNA concatenated DNA file
- WeGene upload BETA
  NOTE: WeGene file must be zipped before uploading
- 23andMe (Old method)
- 23andMe fast & easy
- AncestryDNA.Com
- GENETIC!Concept NEW, BETA
  Do NOT open or un-zip raw DNA data files before uploading.

Genealogy - Family Trees

- GEDCOM
  genealogy Upload
- GEDCOM
- genealogy Upload
  Fast Beta version
**Analyze Your Data**

**DNA raw data**
- 'One-to-many' matches
- 'One-to-one' compare
- X 'One-to-one'
- Admixture (heritage)
- Admixture/Oracle with Population Search
- Phasing
- People who match one or both of 2 kits Updated
- Predict Eye Color
- Are your parents related?
- 3D Chromosome Browser
- Archaic DNA matches
- Multiple Kit Analysis NEW
- DNA File Diagnostic Utility
  Analyze DNA file upload for potential problems.

**Genealogy**
- 1 GEDCOM to all
- 2 GEDCOMs
  - Search all GEDCOMs
  - Revised
- GEDCOM + DNA matches
Interpretome

Explore your genome
- Load your genome file (upper-right corner) and choose some of the analyses above. Currently, only raw data files from 23andme and Lumigenix (unzipped) are supported.
- Sample genotype files (and a description of the individuals) can be found here.
- A detailed description of the website design and some of the modules can be found in our PSB paper as well as in blog posts here and here.

Interpretome is intended for educational and research purposes only.
No information should be considered diagnostic and as with any genetic testing service, the interpretation is not regulated by the FDA. We assume no responsibility for any injury or damage to persons or property arising out of or related to any use of interpretome annotations or for any errors or omissions: consult your physician with any medical concerns. We retain copyright to the materials herein. By using this website, you agree that you accept these terms and are aware of the risks and benefits of genome interpretation. For more information, please read the full Terms and Conditions.

How are my data kept private?
Your genome will not be sent to any server, it remains on your computer. This website will make requests to a database that only contain "rsid" (without genotypes) and "population" (self-reported in the top-right) information. At no point will any genotypes be sent across the wires (all computation will be done in the browser). Some exercises may have an option to submit personal information, including genotypes or results of analyses, which will be anonymously stored on a secure server.

Compatibility
This website requires an HTML5 compatible browser, including current versions of:
- Google Chrome (≥ 6.0), the preferred browser
ANCESTRY ESTIMATES
UNI-PARENTAL INHERITANCE
Mitochondrial DNA
Uni-Parental Haplogroups

Maternal haplogroup

Haplogroup H Migration

Origin: H originated in the Near East, but expanded into isolated pockets of Europe. After the Ice Age, this haplogroup spread across Europe where it is the most prevalent haplogroup today. It is present in about half of the Scandinavian population and is also common along the continent’s Atlantic coast.

Highlight: Mitochondrial DNA extracted from the remains of St. Luke belong to haplogroup H.

Example Populations: Basques, Scandinavians
Y Chromosomes

Y chromosome
Uni-Parental Haplogroups

Maternal haplogroup

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**Origin:** H originated in the Near East, but expanded into isolated pockets of Europe. After the Ice Age, this haplogroup spread across Europe where it is the most prevalent haplogroup today. It is present in about half of the Scandinavian population and is also common along the continent’s Atlantic coast.

**Highlight:** Mitochondrial DNA extracted from the remains of St. Luke belong to haplogroup H.

**Example Populations:** Basques, Scandinavians

Paternal haplogroup

Haplogroup R1b1b2 Migration

**Origin:** R1b1b2 is the most common haplogroup in western Europe, where its branches are clustered in various national populations. R1b1b2a1a2b is characteristic of the Basque, while R1b1b2a1a2f2 reaches its peak in Ireland and R1b1b2a1a1 is most commonly found on the fringes of the North Sea.

**Highlight:** R1b1b2 is found in more than 50% of men in western Europe.

**Example Populations:** Irish, Basques, British, French
ANCESTRY COMPOSITION
Autosomal Inheritance
1:1 segregation each generation

Numbers of ancestors in each generation
Expected autosomal contribution of each ancestor

~ expectation ~
From One Genome to 1000 and Beyond in 25 years

We celebrate the 25th anniversary of the launch of the Human Genome Project (HGP) with recognition for human genomics resources, from one genome to over one thousand genomes and beyond.

The 1000 Genomes Project began in 2007 with the goal of developing a comprehensive resource of human genetic variation across worldwide populations. Eight years later, we publish in this issue the final phase reports from this project, representing the most comprehensive assessment of human genetic variation across global populations to date. The already established datasets have, since their launch, provided a foundational open resource that has enabled a wealth of robust genetic associations to disease as well as many key insights into population history and evolution.

The final phase 1000 Genomes Project publications represent not only the completion of this project, but also the culmination of a series of international collaborations stemming from the HGP, including the International HapMap Project, all focused on establishing open reference catalogues of genetic variation as a resource to the community.

We are pleased to present this Nature Collection of all the primary publications and related news and commentary on the International HapMap and 1000 Genomes Projects.

- Orli Bahcall, Senior Editor, Nature
Human Migration

- **Kennewick**: 12,000 years ago
- **Spirit Cave**: 12,000 years ago
- **Meadowcroft**: 14,000 years ago
- **Clovis**: 14,000 years ago
- **Yana River**: 30,000 years ago
- **Peeters cu Oase**: 30,000 years ago
- **Qafzeh**: 100,000 years ago
- **Nile River**: 40,000–50,000 years ago
- **Omo Kibish**: Oldest modern human, 200,000 years ago
- **Klasies River Mouth**: 200,000 years ago
- **Lake Mungo**: 40,000 years ago
- **Minatogawa**: 10,000 years ago
- **Niah Cave**: 30,000 years ago
- **Malakunanja**: 50,000 years ago
- **Monte Verde**: 12,000 years ago

**Sources:**
- Susan Antolin, New York University
- Alison Brooks, George Washington University
- Peter Andrews, University of Cambridge
- James A. G. Abdullah, University of Utah
- Stephen Oppenheimer, Oxford University
- Spencer Wells, National Geographic Society
- Ofer Bar-Yosef, Harvard University

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Genetic Structure of Human Populations

A global reference for human genetic variation
The 1000 Genomes Project Consortium

Nature 526, 68–74 (01 October 2015) | doi:10.1038/nature15393

- Each vertical line represents an individual
- Samples of individuals organized by continent
- Eight ancestry groups identified by color
- Ancestry composition of each individual represented proportionally by each color
### Genome-Wide SNP Analysis

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<th>chromosome</th>
<th>position</th>
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<tr>
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<td>1</td>
<td>882033</td>
<td>GG</td>
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</tbody>
</table>
Prediction of Ancestry Composition

Given an individual with this genotype, which group is the individual most likely from?
Genome-Wide SNP Analysis

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<td>1</td>
<td>752721</td>
<td>CC</td>
</tr>
</tbody>
</table>

![Genome-Wide SNP Analysis diagram]
<table>
<thead>
<tr>
<th>REGION</th>
<th>APPROXIMATE AMOUNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa</td>
<td>2%</td>
</tr>
<tr>
<td>Trace Regions</td>
<td>2%</td>
</tr>
<tr>
<td>Europe</td>
<td>97%</td>
</tr>
<tr>
<td>Great Britain</td>
<td>41%</td>
</tr>
<tr>
<td>Ireland</td>
<td>39%</td>
</tr>
<tr>
<td>Europe West</td>
<td>8%</td>
</tr>
<tr>
<td>Scandinavia</td>
<td>6%</td>
</tr>
<tr>
<td>Trace Regions</td>
<td>3%</td>
</tr>
<tr>
<td>West Asia</td>
<td>&lt; 1%</td>
</tr>
</tbody>
</table>

**European**
- British Isles: 54%
- Western and Central Europe: 20%
- Scandinavia: 14%
- Eastern Europe: 9%

**Middle Eastern**
- North Africa: 3%
ACTIVITY

• Compare ancestry estimate with ethnicity of grandparents
Autosomal Inheritance
1:1 segregation each generation

Numbers of ancestors in each generation
Expected autosomal contribution of each ancestor
**Father**

- European: 49.9%
  - Northwestern European: 32.5%
  - French & German: 14.2%
  - Scandinavian: 9.3%
  - British & Irish: 1.3%
  - Broadly Northwestern European: 7.7%
  - Eastern European: 5.7%

**Mother**

- European: 49.7%
  - Northwestern European: 39.9%
  - French & German: 20.0%
  - Scandinavian: 0.3%
  - British & Irish: 1.2%
  - Broadly Northwestern European: 18.3%
  - Eastern European: 3.9%
<table>
<thead>
<tr>
<th>Populations</th>
<th>Child</th>
<th>Father</th>
<th>Mother</th>
</tr>
</thead>
<tbody>
<tr>
<td>European</td>
<td>99.6%</td>
<td>100%</td>
<td>98.5%</td>
</tr>
<tr>
<td>Northwestern European</td>
<td>72.3%</td>
<td>73.6%</td>
<td>70.1%</td>
</tr>
<tr>
<td>French &amp; German</td>
<td>34.2%</td>
<td>21.7%</td>
<td>26.7%</td>
</tr>
<tr>
<td>Scandinavian</td>
<td>9.6%</td>
<td>12.8%</td>
<td>4.6%</td>
</tr>
<tr>
<td>British &amp; Irish</td>
<td>2.5%</td>
<td>10.5%</td>
<td>5.6%</td>
</tr>
<tr>
<td>Broadly Northwestern European</td>
<td>26.0%</td>
<td>28.6%</td>
<td>33.2%</td>
</tr>
<tr>
<td>Eastern European</td>
<td>9.6%</td>
<td>9.1%</td>
<td>7.0%</td>
</tr>
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### Dad

<table>
<thead>
<tr>
<th>Region</th>
<th>Approximate Amount</th>
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</thead>
<tbody>
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<td>Africa</td>
<td>2%</td>
</tr>
<tr>
<td>Europe</td>
<td>97%</td>
</tr>
<tr>
<td>Great Britain</td>
<td>41%</td>
</tr>
<tr>
<td>Ireland</td>
<td>39%</td>
</tr>
<tr>
<td>Europe West</td>
<td>8%</td>
</tr>
<tr>
<td>Scandinavia</td>
<td>6%</td>
</tr>
</tbody>
</table>

### Son

<table>
<thead>
<tr>
<th>Region</th>
<th>Approximate Amount</th>
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<tbody>
<tr>
<td>Africa</td>
<td>&lt; 1%</td>
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<tr>
<td>America</td>
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<tr>
<td>Europe</td>
<td>98%</td>
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<tr>
<td>Great Britain</td>
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</tr>
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<td>Ireland</td>
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<tr>
<td>Europe West</td>
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<tr>
<td>Scandinavia</td>
<td>5%</td>
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### Mom

<table>
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<tr>
<th>Region</th>
<th>Approximate Amount</th>
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<tbody>
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<tr>
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<tr>
<td>Pacific Islander</td>
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[Source: Ancestry](https://www.ancestry.com)
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<td></td>
<td>Trace Regions</td>
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Analyze Your Data

DNA raw data
- 'One-to-many' matches
- 'One-to-one' compare
- X 'One-to-one'
- Admixture (heritage)
- **Admixture/Oracle with Population Search**
- Phasing
- People who match one or both of 2 kits **Updated**
- Predict Eye Color
- Are your parents related?
- 3D Chromosome Browser
- Archaic DNA matches
- Multiple Kit Analysis **NEW**
- DNA File Diagnostic Utility
  Analyze DNA file upload for potential problems.

Genealogy

- 1 GEDCOM to all
- 2 GEDCOMs
- Search all GEDCOMs
- **Revised**
- GEDCOM + DNA matches
Eurogenes K13 Admixture Proportions

This utility uses the Eurogenes K13 model (rev 21 Nov 2013), created by Davidski (Polako). Questions and comments about this model should be directed to him at his Project Blog.

Kit Number: M092221  Elapsed Time: 22.79 seconds

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Single Population Sharing:

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Well-designed sampling strategies empowered by genome-wide SNP data reveal geographic patterns in genetic variation established through historical events.

The fine-scale genetic structure of the British population
Find out where you really come from

Living DNA is a personal DNA service, designed to help people understand more about themselves and where they came from in unparalleled detail.

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But that is only the beginning, as new discoveries are made we update your results offering you ongoing insights over time.

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Includes Free Delivery - Limited Availability - Shipping Mid Oct 2016

Find out more  Order now
Ancestry Composition

• *It’s an estimate!!!*
  • Each analysis is based on a set of computer algorithms for handling data from a broad diversity of individuals.
  • The set of reference samples used in the analysis, and how the analysis is (or isn’t) tailored to self-reported ancestry, differs between companies.

• Current political boundaries have little relevance
  • Broadest categories captures genetic similarities present among peoples in different countries.

• Small contributions can represent a variety of things
  • Application of an admixture model using many reference populations over-emphasizes effect of rare variants.