LAB1915 Introduction to Chromosome Mapping

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Overview:

Through the comparison of autosomal DNA tests between several family members, specific segments of DNA can often be assigned to common ancestors. Though chromosome mapping has typically focused on segments shared in common, segments not shared in common can also be useful. Although chromosome mapping can be very helpful, there are some situations where caution should be used in applying these techniques - particularly for small segments, endogamous populations, and pile-up regions. In this hands-on lab, participants will use a public dataset and third-party chromosome mapping tools to create a chromosome map. They will be guided through all steps of downloading segment data, preparing a .csv file, and running the mapping tool. Participants will learn about considerations for hierarchical versus collateral relationships and will create maps for both. Though participants are welcome to use their own datasets, we strongly encourage use of the public dataset while participants are learning.

Review of DNA Inheritance:

There are four types of DNA with unique inheritance patterns: mitochondrial DNA, Y-DNA, Autosomal DNA and X-DNA. **Mitochondrial DNA** is passed intact from generation to generation along the direct maternal line. Each individual inherits mitochondrial DNA, but only females pass it on to their children. **The Y-chromosome (Y-DNA)** is inherited intact from generation to generation along the direct paternal line of ancestry. Therefore, Y-DNA follows an inheritance pattern that mirrors the inheritance of surnames in many Western cultures**. Autosomal DNA** is composed of 22 pairs of nuclear chromosomes which are inherited from many ancestors across all lines of ancestry. A process called recombination results in a shuffling of autosomal DNA before it is passed on to the next generation. Each individual inherits exactly 50% of their autosomal DNA from each parent. Due to recombination, the amount of DNA inherited from more distant generations can only be approximated. Most individuals inherit about 25% of their autosomal DNA from each grandparent, about 12.5% from each great grandparent and about half of the previous amount for each previous generation. Eventually there will be some ancestors from whom an individual inherits no autosomal DNA**. The X chromosome (X-DNA)** is a sex chromosome inherited by men and women. Men have one and females have two. Men inherit their X-chromosome from their mother whereas females inherit one X-chromosome from their mother and one from their father.

Introduction to Chromosome Mapping

Chromosome mapping is the process of assigning the origin of DNA segments to specific ancestors. These chromosome maps can be used to support or refute genealogical hypotheses, guide research and correspondence with genetic cousins and provide deeper insight regarding specific ancestors. Assignment of an ancestral origin to specific segments of DNA requires testing of additional relatives. Because the Y-chromosome and mitochondrial DNA are inherited intact, they can be easily mapped to direct line paternal and maternal ancestors. These assignments, which assume no cases of misattributed parentage, can be confirmed by testing additional relatives. Chromosome mapping is most commonly applied to investigation of autosomal and X-DNA.

Chromosome mapping has typically focused on the segments of DNA shared in common with relatives in order to assign ancestral origin. However, identification of segments of DNA not shared in common can also be an

important element of chromosome mapping. For example if a comparison is possible between a subject and their maternal grandmother, then the remaining maternally inherited segments not shared in common can be assigned by process of elimination to the maternal grandfather.

Components of a Chromosome Map

A chromosome map is a representation of the origin of segments of DNA and includes several components:

- Chromosomes
  - Each individual has 22 pairs of homologous chromosomes and one pair of sex chromosomes.
- Paternal vs. Maternal copies
  - Each individual inherits one set of 23 chromosomes from each parent.
    - 22 autosomes and 1 sex chromosome
    - For every maternally inherited autosomal chromosome there is a paternally inherited autosomal chromosome of the same shape, size, and distribution of genetic loci. They are homologous, but not identical since mutations distinguish one copy from the other.
    - Chromosome maps should indicate whether a segment is a maternally or paternally inherited segment
- Location on the chromosome
  - Chromosomes are composed of millions of base pairs
  - The location of an overlapping segment is defined by a range of base pairs on a chromosome
- Centimorgans
  - A measure of the likelihood of recombination. 1 cM is equal to a 1% chance that a genetic loci will be separated from another genetic loci on the same chromosome due to recombination in a single generation.
- Number of SNPs
  - Overlapping segments of DNA between two individuals are identified by sampling Single Nucleotide Polymorphisms (SNPs) along the length of a chromosome. Not all loci in a segment are analyzed.
  - When two individuals share the same SNP values over a long section of DNA, it is assumed that the majority of the non-tested loci in between the tested sites are shared in common as well.
- Generational levels
  - Each genetic loci is inherited from several different generations of ancestry. Therefore a chromosome map should indicate what generational level the segment pertains to – grandparents, great grandparents, etc.

Limitations on Chromosome Mapping

Though chromosome mapping can be very useful in genealogical investigation, there are some situations that require added caution in application of chromosome mapping:

- Small segments
  - Chromosome mapping of small segments may result in erroneous conclusions since some small segments are simply identical by state rather than identical by descent.
  - It is typically best to only map segments larger than 5 cMs and larger than 500 SNPs.
- Distant relationships
  - Mapping ancestral DNA based on distant relationships can be difficult and must confirm that there are no other possible relationships between the test subject and the match.

- Endogamous Populations
    - In endogamous populations, be cautious assigning shared segments to specific ancestors beyond the level of 2nd – 3rd cousins
- Pile-up regions
    - Some regions of DNA are persistent in populations and may be held by a large number of people who have no detectable genealogical relationship. Identify pile-up regions, by strict base pair range boundaries and many people matching on the same segment of DNA.

Creating a Chromosome Map

In order to create a chromosome map, it is necessary to have access to the shared segment data for an individual and their known relatives. This information can be obtained from autosomal DNA tests at Family Tree DNA and 23 and Me. This information can also be obtained by upload and comparison at Gedmatch.com. This information is not available for AncestryDNA test results unless the results are transferred to Gedmatch.com.

For chromosome mapping we recommend the following 5 steps

1. Identify known relatives who have tested
2. Compile their segment data into a spreadsheet
3. Map the information
4. Evaluate the map for any discrepancies or anomalies
5. Repeat process for additional known family members

It is best to start with individuals who are closer relatives and then build upon the foundational map to include more distant relatives. All known family members can be included in the same file, but this increases the chances of making an incorrect segment assignment.

Demonstration and Lab Activity

In this presentation we will apply the general principles above to a dataset developed for this course from overlapping segments found at Family Tree DNA, 23andMe and Gedmatch.com. These segments are for the presenter's own family, but names and initials have been changed to preserve privacy. Also for privacy reasons, detailed instructions for each part of the lab will only be provided in class. We will use Kitty Cooper's Ancestor Chromosome Mapper

1. Identify known relatives who have tested:
    a. The test subject has tested several of his own family members and has several known cousins at each of the DNA testing companies.
2. Compile the segment data into a spreadsheet
    a. For this activity, spreadsheets will be provided, follow the instructions in the materials provided in class.
    b. Spreadsheets can be prepared by creating a .csv file and entering information by hand or by downloading segment data from 23andMe, Family Tree DNA, or Gedmatch.com and adjusting the headings
    c. After downloading a .csv file from one of the companies, sort the segments by size and delete all cM values lower than 5.
    d. The input .csv file for Kitty Cooper's tool requires very specific column headings.

i. side: This column is optional, select which side (warm or cool colors) the segment appears on. To use it put the letter M or P or any words starting with those letters to indicate maternal or paternal side of your tree.
ii. MRCA: Most Recent Common Ancestor(s) – this is the name to use in the chromosome map picture.
iii. chr: Chromosome number 1-22 or X
iv. Start: The starting number for the segment location.
v. End: The ending number for the segment
vi. cMs: The number of centimorgans in the segment, used for display purposes only.
vii. Color: This column is optional, you can let the tool pick the colors; but if you want different colors then put any color name from this list: http://www.html-color-names.com/color-chart.php

e. Save your file as a .csv file.

3. Map the information
   a. Upload your file to https://ns2193.hostgator.com/~kitty/dna/ChromosomeMapper.php
4. Evaluate the map for any discrepancies or anomalies
5. Repeat the process to include additional known family members.

Conclusion

Chromosome mapping is a valuable tool for genetic genealogy research and can assist in breaking through brick walls in family history research. It also provides a unique opportunity to document your own ancestry through investigation of your genetic material – Information that can be very useful for future generations of descendants.

Additional Resources

- Kitty Cooper, *Ancestor Chromosome Mapper,* http://blog.kittycooper.com/tools/my-graphing-or-mapping-tools/chromosome-mapper/, accessed January 2015.
- Kitty Cooper, *Overlapping Segment Mapper,* http://blog.kittycooper.com/tools/my-graphing-or-mapping-tools/segment-mapper/, accessed January 2016.
- "Chromosome Mapping," International Society of Genetic Genealogy Wiki, isogg.org/wiki/Chromosome_mapping, accessed January 2016.
  - Presentation materials by Tim Janzen from RootsTech 2014 and SCGS Jamboree DNA Day June 2013.

Acknowledgements

Special thanks to Kitty Cooper for allowing us to use the Ancestor Chromosome Mapper and the Overlapping Segment Mapper as part of this hands-on learning lab and for her work in developing these wonderful tools. We encourage participants and readers who benefit from these tools to offer donations at her website for her wonderful work.