Study Guide for Exam 2
Anth 4234: Genes, Health, and Human History

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1 Introduction

The exam will have the same format as the 1st exam. When the study guide asks a question, you are expected to figure out the answer, using your lecture notes and the online lecture slides. The study guide covers only the lectures.

Each section heading below corresponds to one lecture topic.

2 Agriculture: Origins

The following argument has a long history in anthropology. To build an elaborate temple or a pyramid, you need to support a large work crew. This requires a supply of stored food. You also need a hierarchy of managers to organize the work and the flow of food and building materials. In all likelihood, you need an army to collect taxes, enforce order, and compel labor. In short, you need an agricultural economy and the apparatus of a state.

Human populations can double in a generation—about 25 years. At that rate, starting with 1000 people, how many people would there be after 4 generations, i.e. about a century? After 40 generations (1000 years).

What was "Old Europe?" What happened to it?

3 The Neolithic

During the Neolithic, people of the Middle East and Europe switched from a diet of wild plants and animals to a diet of domesticated ones. They became more sedentary, built substantial houses, and learned to make ceramic pots.

When did the Neolithic appear in the Middle East? In Turkey? In Crete? In northern Europe?

Wild foods are not ideal for babies. In foraging societies, women nurse children for 3 years. With farming—and especially with pots—it becomes easier to make babyfood, and women don't need to nurse babies so long.

Farming plus pots → porridge → jaw doesn't grow as much → overbite, impacted wisdom teeth.

High-starch diet → tooth decay.

See review paper by Clark Larsen.

In Neolithic, skeletons became frail, people got 5 inches shorter, anemias became common.

Old Europe is the term that Marija Gimbutas coined to refer to the early European Neolithic, from roughly 7000 BC until the incursion of the Corded Ware people, about 3000 BC. In Old Europe, houses and farms were dispersed, with no fortifications. They made beautiful pots, worked copper and gold, and produced sculpture.

We know a lot about one Neolithic man. Ötzi, the "Ice Man," was found frozen in the Alps, on the border between Austria and Italy. Died 3300 BC, 45 y old, 5 feet 5 inches tall, 110 lbs.

Ötzi's stomach contents: chamois, red deer, eikorn wheat bran, berries, nuts. He was lactose intolerant. Carried a copper axe. Hair was full of copper and arsenic, suggesting that he was a metal smith. In the modern world, Ötzi's closest genetic relatives live high in hills of Corsica and Sardinia. He died from an arrow in the back—his was not a peaceful world.

4 Genetics and the European Neolithic

In the 1920s, V. Gordon Childe proposed that the European Neolithic was an invasion of Middle-Eastern Farmers into Europe—a movement of people. In the 1960s, Grahame Clark argued otherwise. In his view, the Neolithic moved through Europe as foraging populations adopted the agricultural economy of their neighbors. It now appears that neither argument is completely correct. Neolithic European farmers lived in proximity to foragers for thousands of years, gradually exchanging genes.

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At the Blätterhöle site in Germany, there are human burials that range in age from the Mesolithic through the Neolithic. Isotopic data tell us about the diet of these individuals, and mitochondrial DNA (mtDNA) tell us about their genetics. What does this site tell us about the issue raised by Childe and Clark (see preceding paragraph)?

The Y chromosome haplogroup R1b1b2 is most common in NW Europe and Iceland. It declines in frequency toward the SE. Originally, this pattern suggested that R1b1b2 is a relic of the earlier Mesolithic inhabitants of Europe, which was largely replaced in regions near the origin of agriculture, but was not replaced in other regions. More recent research has used microsatellites to date the arrival of R1b1b2 in different parts of Europe. This research tells a different story. (1) how do microsatellites allow us to date the arrival of a Y-chromosome haplogroup, and (2) what do these data tell us about the history of R1b1b2 in Europe?

Skoglund et al (2012) analyzed nuclear DNA from 4 ancient Swedes: 3 Mesolithic foragers and 1 Neolithic farmer. The foragers were genetically similar to modern Finns, whereas the farmers were similar to modern Sardinians.

The study of Lipson et al (2017) shows that foragers and farmers coexisted for thousands of years after the arrival of agriculture in Europe. They must have been partially but not totally isolated, because the fraction of forager DNA within the farmer population increases very gradually over a period of 4000 years.

The study of Brace et al (2018) documents a very different story. What is that story? What evidence supports it?

This lecture also presented results from my own research, which used linkage disequilibrium (LD) to estimate the history of population size in Europe. We won't ask about this on the exam.

5 Hemochromatosis

Hemochromatosis is a genetic disease whose carriers absorb too much iron from the food they eat. It is a serious disease in homozygotes and can be lethal if untreated. Nonetheless, the disease allele has a frequency of 14% in some European populations. Why would a deleterious allele be so common?

Hemochromatosis is caused by a mutation in the HFE gene, which occurred about 5,000 years ago. Most common in N Europe, in populations with high levels of lactase persistence.

What evidence suggests that anemia was more prevalent during the European Neolithic than the preceeding Mesolithic? (Hint: what effects does anemia have on the human skeleton?)

John McCullough and Kathleen Heath have suggested a hypothesis to explain this increase in anemia. Be prepared to summarize their hypothesis.

What are phytates? What foods are they found in? How do they affect iron metabolism?

Milk became an important food during the Neolithic. How would this have affected the supply of dietary iron?

The only way to get rid of excess iron is to bleed. This may explain why the allele causing hemochromatosis is most common near coasts. Coastal populations get fish tapeworms, which cause bleeding, thus reducing iron and protecting against the deleterious effects of hemochromatosis.

Heterozygous HFE carriers are taller than other people.

6 Digesting starch

Glucose is a sugar, and starch is a chain of glucose molecules. The enzyme *amylase* chops this chain up, turning it into molecules of easily-absorbed glucose. Amylase is found both in saliva (salivary amylase) and in the stomach (pancreatic amylase). Perry et al (2007) studies AMY1, the gene that encodes human salivary amylase.

How did the Neolithic change human diets?

Some individuals carry several copies of AMY1. How does this affect the amount of amylase in their saliva?

Some populations eat a lot of starch; others eat only a little. How do these populations differ in the number of copies of AMY1 per individual?

7 Crohn's disease

Crohn's disease causes inflammation of the bowel. It is common in northern Europe and among Ashkenazi Jews. There is no cure, and it causes tens of thousands of deaths every year. Siblings of affected individuals are 30× as likely to have the disease.

Although many genes affect this condition, we focused in class on a single region of the genome—the IBD5 haplotype—which includes 5 genes spread over 250 kb of chromosome. This haplotype is associated with Crohn's disease and reaches a frequency of 40% in Europe. Why would a deleterious allele be so common? This lecture discusses the hypothesis of Huff et al (2012).

Their hypothesis involves an antioxidant called *ergothionine*, which is synthesized by fungi and is present in most plants and animals. The gene OCTN1, within the IBD5 haplotype, encodes a protein that transports ergothionine. It is associated with Crohn's disease, but there is no obvious reason why it should be.

Huff et al point out that although ergothionine is common in wild foods, it would have been rare in Neolithic diets. Which foods have abundant ergothionine? Which foods have little?

The function of ergothionine is poorly understood. Huff et al argue that it must be important, because its transporter (OCTN1) is highly conserved (by stabilizing selection) in vertebrates. It is an antioxidant and protects against neurotoxins. None of this is entirely convincing, but let us assume that Huff et al are right—that ergothionine is an important nutrient, which Neolithic Europeans got very little of.

Crohn's disease is associated with the 503F allele of the IBD5 haplotype. In what part of the world is this allele most common?

What evidence suggests that the 503F allele has been favored by selection (in spite of its association with Crohn's disease)? What is the best estimate of the time since this selection began?

8 Harpending's 2015 lecture on infectious disease

These are notes on a lecture that Henry Harpending delivered to Anth 4234 in 2015. I've left it in this study guide, because it is interesting.

When an infectious disease enters a population, people get sick. When they get better, they are immune. If everyone becomes immune, the disease will die out. But there is also a steady supply of new susceptible individuals—children—entering the population. If this supply is large enough, the disease can stay in the population permanently. In this case, the disease is said to be *endemic*. If the disease comes and goes, it is *epidemic*.

In small populations, the supply of susceptibles is small, so most infectious diseases are epidemic. Only in large populations do diseases become endemic. As humans adopted agriculture, their populations grew, and many diseases must have become endemic.

In small populations, a new epidemic cannot start until a substantial crop of susceptibles has accumulated. The smaller the population, the longer this takes. Consequently, epidemics come rarely in very small populations. The larger the population, the smaller the interval between epidemics. When the population size exceeds a million, measles becomes permanent. Among foragers, measles would die out.

When epidemics are recurrent like this, only the children get sick, because the adults are immune. Even if many of the children die, there are still healthy people around to keep the economy going and care for the sick. Things are *much* worse when a fatal disease strikes a population in which no one is immune.

In the 14th century, bubonic plague was such an epidemic. It began in 1347. Within a few years, it had killed half the population of Europe. Paradoxically, life was good for the survivors. With half the population gone, it was easy to find land to farm, and Europeans became prosperous.

Rural Africans have plague outbreaks in wet years, but few people die. The most lethal form of plague is pneunomic—spread by aerosol—and this doesn't seem to happen in Africa.

Historically, smallpox was a real killer. Highly infectious, with a death rate of 20-60%.

Plagues like these would never have happened before farming. Wouldn't last in a population of Bushmen. Diseases that are directly transmitted have to be post-agricultural.

In foraging populations, people get other sorts of infections. For example, tapeworms, toxoplasmosis, and malaria. These diseases don't require large human populations, because they also live in other animals.

In Europe, the mortality rates of many diseases—TB, smallpox, scarlet fever—have declined since 1850. Other diseases—pertussis and measles—have declined in severity since 1900. These declines have been gradual and steady. There is little evidence of any large effect from improvements in public health or medicine.

Harpending proposes an alternative hypothesis. Populations increased with agriculture and again with the industrial revolution. In these larger populations, infections became endemic, and there was strong selection in humans for enhanced immune function. The gradual decline in mortality reflects genetic evolution for enhanced human immune function.

Devastating epidemics afflicted Amerindian populations shortly after Columbus arrived. The epidemics started 3–4 years later, because this was when Spanish children showed up. A huge fraction of Amerindian populations died. In the 1540s, De Soto reported abandoned villages in what is now the southeastern US.

9 Infectious disease

Diseases that rapidly make you very sick are said to be *virulent*. They are often fatal. Why does virulence evolve? Shouldn't evolution select against virulence in order to prevent pathogens from killing their host? Why are vector-borne and water-borne pathogens usually more virulent than those transmitted directly from person to person.

Be able to name a few temperate diseases and a few tropical ones. How do temperate diseases (in general) differ from tropical ones in *(1)* mode of transmission, *(2)* duration of infection, *(3)* immunity among survivors, and *(4)* origin (wild vs. domestic animals)? In lecture, we related these characteristics to the difference in population size that distinguish foragers from agriculturalists. How does this argument work?

How does the prevalence of pathogens vary with latitude, with temperature, and with rainfall? Which pathogens are prevalent where it is very dry, and why is this so? Are pathogens more prevalent in mobile human populations or in sedentary ones? On islands or on continents?

10 Indo-Europeans

Indo-European (IE) is a family of languages spoken in most of Europe, Russia, Iran, Afghanistan, Pakistan, and India. During the age of European colonization, it spread to North America, Australia, and New Zealand.

The languages in this family share similar forms of many words. For example, words for numbers, body parts, oak, beech, wolf, bear, salmon, snow. These shared words suggest that IE originated somewhere cold. IE languages do *not* share words for olive, grape, or wine, further reinforcing the idea that the IE homeland was cold. This much was known by 1800.

By the 1930s, scholars thought that the IE homeland was in the steppes of Russia and Ukraine. At some point, IE speakers migrated into what is now Europe.

Late 20th century, this view fell from favor. Rather than mass movements and invasions, scholars envisioned a peaceful diffusion of language into and through an existing population.

The ancestral Indo-European language is called *proto-Indo-European* (PIE). The vocabulary of PIE can be inferred by comparing words in widely separated IE languages. Words that are shared by Celtic and Sanskrit, for example, were probably inherited from PIE. The vocabulary of PIE tells us something about the culture and the ecology of PIE-speakers.

The PIE vocabulary contains *(1)* milk words; *(2)* horses, sheep, cattle, pigs, goats; *(3)* grain; *(4)* copper, maybe bronze, not iron; *(5)* carts, weaving, mead; *(6)* patrilineal clans, raiding, war, revenge; *(7)* young male warriors; *(8)* wolf totem; *(9)* three classes: warriors,clergy, farmers; *(10)* the same Gods: Deus, Zeus, Jupiter (Zeu Pater) etc. The PIE were herders at the same time that (far to the south) Sumerians had a civilization. Yamnaya, who lived on the Pontic steppes, may have spoken PIE.

What are the Pontic steppes? Where is the Caspian sea in relation to the Black sea?

Who were the Tocharians? Who are their descendants today? What color were they?

Name 5 Indo-European languages.

Who were the Yamnaya, and where did they live?

The Corded Ware culture appears in northern and eastern Europe ∼4.5 kya. Haak et al (2015) studied dozens of ancient genomes from Europe and Central Asia. They found that 75% of the DNA in Corded Ware burials derives from the Yamnaya. Use this to evaluate the following two hypotheses:

The Anatolian hypothesis of Colin Renfrew. Indo-European languages originated in Anatolia (modern Turkey). It spread north into Europe about 7 kya, carried by the earliest European farmers.

The Kurgan hypothesis of Marija Gimbutas. The word "kurgan" refers to the burial mounds found on the Pontic Steppe, north of the Black Sea in Ukraine and Russia. Gimbutas argued that Proto-Indo-European originated here, in the Yamnaya Culture. It then spread west into Europe during the Bronze Age

What evidence supports each of these hypotheses?

Just after the Yamnaya invasion of Europe, 75% of European DNA derived from the Yamnaya. What happened to this fraction during the centuries that followed? Did it increase, decrease, or stay the same? What does this imply about the the population of Bronze-age Europe?

11 Milk in the Kalahari and Europe

Milk contains a sugar called *lactose*. We digest that sugar with an enzyme called *lactase*. Nearly all mammals (including most humans) stop producing lactase at the age when they are weaned. After this, they are *lactose intolerant*. If they drink fresh milk, they cannot digest the sugar. The bacteria in their guts

digest it instead, and this causes cramps, flatulence, and diarrhea.

Some human populations, mainly in Europe and Africa, have evolved the ability to digest milk sugar throughout life. They continue producing lactase and can therefore digest lactose. This condition is called *lactase persistence*.

When we turn cow's milk into cheese or yoghurt, we lose the lactose. What fraction of the energy in the milk does this waste?

Bantu languages expanded through Africa in a manner analogous to that of Indo-Europeans in Europe. Harpending worked with the Herero, a Bantu-speaking population in southern Africa. Although the Herero make extensive use of milk, they don't have lactase persistence.

In Eurasia, the first evidence of dairying—milk residues on pottery—was found along the sea of Marmara, near Istanbul, at 6000 BC. By 4000 BC, we find it in the Funnel Beaker culture, in Germany and Scandanavia. By 3300 BC, dairying reaches the Yamnaya horizon in southern Russia.

The Funnel Beaker culture of northern Europe occupied a region of heavy clay soils, which were marginal for agriculture before the advent of metal plows. Perhaps for this reason, they relied heavily on dairying and achieved 10× the population density of the pre-dairy LBK culture in the same region.

The European lactase persistence allele first appears in an ancient genome dated to 4300 BP, from the central European Bell Beaker Culture. Don't confuse the Bell Beaker Culture with its predecessor, the Funnel Beaker Culture.

12 Lactase persistence in Africa

Lactase persistence (LP) alleles are also present in Africa. As in Europe, they are most common in dairying populations. But something different happened in Africa. Whereas Europe has only one LP allele, Africa has five. Several of these show evidence of a recent selective sweep; others do not. There was strong selection on the C14010 allele of East Africa and on the European LP allele (T13910) among the Fulani, but not at the other 3 African LP alleles.

What is the difference between "hard" and "soft" selective sweeps, and how might this distinction explain the pattern of LP alleles in Africa?

13 The D4 dopamine receptor (DRD4)

Neurons are cells of the nervous system. Neurons are connected together to form the "wiring" of the nervous system. The connection between a pair of neurons is called a *synapse*. To communicate with each other, neurons use molecules called *neurotransmitters*, which are produced in one neuron, travel across the synapse, and are absorbed by receptors on the other neuron. *Dopamine* is one type of neurotransmitter. It can bind to any of several receptors, one of which is the D4 dopamine receptor, or DRD4.

DRD4 is encoded by a gene on chromosome 11. Genetic variation at this locus affects positive reinforcement, risk assessment, hunger satisfaction, time preference, and ADHD.

In human populations, there is little genetic variation in most parts of the DRD4 gene. One part, however, is quite variable. There is a 48-base-pair sequence which is repeated several times. One allele has 2 copies of the repeated segment and is called the "2r allele." The most common allele in most populations is the 4r allele, which has 4 copies of the repeat. The 7r allele is common in the Americas, approaching 80% in some Amerindian populations. The 4r allele is the ancestral state in humans. The 7r allele is derived.

Carriers of the 7r allele tend to *(1)* like novelty; *(2)* take risks; *(3)* have low time preference when associated with low childhood SES; *(4)* respond more positively to good parenting, more negatively to bad parenting; *(5)* have more sexual partners; *(6)* are predisposed to alcoholism; *(7)* be healthier in nomadic groups, not as healthy in non-nomadic pastoral groups; *(8)* be predisposed to "disorganized attachment disorder;" *(9)* exhibit attention-deficit hyperactivity disorder, or ADHD (maybe: results mixed, possibly because of poor diagnosis. Pattern clearest in severe ADHD.)

7r is common in populations far from origin of their language family. Some authors suggest that 7r carriers may be predisposed to emigrate.

DRD4 repeat polymorphism is shared throughout primates. Variants affect personality in vervet monkeys. Carriers of the 6r allele are more fearful of novel objects than are carriers of 5r.

14 Males and females

People vary in reproductive success. Some have many children, others only a few. These differences affect genetic evolution. If 10% of the people produce 90%

of the children, then the population will evolve as though it were much smaller than it really is. There will be less genetic variation, and selection will be less effective at removing deleterious alleles. Such populations are said to have a small *effective size* even though their *census size* may be much larger. In human populations, the effective population size is often 1/5 to 1/3 of the census size.

In some populations, a small number of males is able to monopolize most of the females. Consequently, the effective size of the male population may be smaller than that of the female population. We can study these effects by comparing genetic variation in mitochondrial DNA (which is transmitted only by females) to that in Y-chromosome DNA (transmitted only by males).

This lecture begins with background on Genghis Khan. Be prepared for a question about him. When and where did he live? What did he do?

Then we covered a 2003 paper by Zerjal et al: "The genetic legacy of the Mongols." What is the "star cluster?" Where is it found? How old is it? How many men carry it? What evidence suggests it was Genghis Khan's Y chromosome?

Next, we covered a 2005 paper by Xue et al on the "Manchu haplotype." Same questions as in preceding paragraph, except we're concerned here with the genetic legacy of Giocangga rather than Genghis.

These examples make the following point: a few men have had a profound effect on genetic variation in the human Y chromosome. Nothing comparable exists in mitochondrial DNA. And these reproductively-successful males had several things in common: they lived in stratified societies, and they had armies. It is unlikely that anything of the sort could have happened among foragers.

Finally, this lecture covered the 2015 study of Karmin et al, who examined both mtDNA and yDNA in a worldwide sample. These authors argue that, during the Neolithic in many parts of the world, a few males did most of the reproducing. Be prepared to summarize the evidence that underlies this conclusion.

I am somewhat skeptical of this conclusion, both because the effect isn't apparent in autosomal DNA and also because in the European case, it appears that mitochondrial and Y DNA came largely from different populations. Be prepared to summarize this argument.

15 Ashkenazi evolution

The Jewish population includes two major subdivisions: the *Ashkenazi Jews* (plural *Ashkenazim*) and the *Sephardic Jews* (plural *Sephardim*). Broadly speaking, the Ashkenazim lived north of the Alps and the Pyrenees and the Sephardim lived farther south. The Ashkenazim originated with a diaspora following Roman genocide against Middle Eastern Jews around 100 AD. After this, they disappear from history for 700 y. The Sephardim originated as Babylonian Jews and came to Europe with the Arabs. Genetics suggest that Ashkenazi are about half Middle Eastern and half Italian. The Italian contribution is old—presumably Roman.

Several hereditary diseases are common among Ashkenazi Jews. Disease alleles arise as new mutations and are thus initially rare. The question is, why did so many of them become common in Ashkenazi Jews?

One possibility is genetic drift. When a population becomes small for a while, it is said to have "passed through a bottleneck." During the bottleneck, genetic drift is stronger, so disease alleles may increase in frequency. This seems to explain the genetic diseases of another population, the Amish.

It is also possible that these disease alleles represent a *balanced polymorphism*—that one copy of the allele is helpful, whereas two are harmful. Cochran, Hardy, and Harpending (2005) argue that this underlies the genetic diseases common in Ashkenazi Jews.

The argument has several pieces. First, if the Ashkenazim had passed through a bottleneck, it would have reduced their heterozygosity. But heterozygosity among Ashkenazi Jews is as high as that of other European populations. This is inconsistent with the bottleneck hypothesis.

Second, Ashkenazi genetic diseases fall into several clusters. Diseases within any given cluster affect a single biochemical pathway. This suggests that selection has been at work. Absent selection, there is no reason to expect genetic diseases to be clustered. In other populations, such as those of Finland and Quebec, genetic diseases are not clustered in this fashion.

Cochran, Hardy, and Harpending propose that these disease alleles were favored by selection because they have a beneficial effect on IQ. To make this case, let us begin with the data on IQ.

Ashkenazi Jews have the highest IQ in world. Mean is 112–115. This is 0.75–1.00 standard deviations above the European mean. This does not seem to be an artifact of testing: although they are only 3% of the US population, they have received 27% of US Nobel prizes, 25% of US Turing awards, and 28%

of Fields medals. Sephardic Jews, on the other hand, show no elevation in IQ scores.

Although Jews were farmers in classical times, the Ashkenazim entered a new niche as cities were restored following the fall of the Roman empire. The Christian church forbade "usury" (lending money at interest), but this prohibition did not apply to Jews. Furthermore, they were literate. They first became money lenders, then managers and tax collectors. They were welcomed into Poland in the 13th and 14th centuries to replace the middle managers, whose ranks had been decimated by the Mongol invasions. In the Polish-Lithuanian Commonwealth, they were the managerial class: no farmers and few artisans.

In these jobs, success required managerial and accounting abilities, that is, IQ. The smarter you were, the better you were likely to do at the jobs available to Ashkenazi Jews. And in this society, the wealthy outreproduced the poor. Jewish communities had welfare for poor people, but poor people weren't allowed to marry. This suggests that selection would have favored higher IQ.

This would not have mattered much, if there had been free interbreeding between the Ashkenazi and their gentile neighbors. But the Jewish population remained isolated by food taboos and restrictions on inter-marriage. After Ashkenazi communities were founded, there was almost no gene flow into the population. In such circumstances, if IQ is heritable, it should respond to selection.

Cochran, Hardy, and Harpending argue that selection for IQ produced—as a side effect—the genetic diseases that are common in Ashkenazi Jews. This makes sense only if there is a plausible link between these diseases and neural function. Is there?

There are several forms of evidence suggesting such a link. For example, several Ashkenazi diseases promote the growth of nerve cells. One disease, congenital adrenal hyperplasia, seems to be associated with high IQ. In Israel, there is one clinic that treats all cases of Gaucher's disease in that country. Among the patients, there are as many theoretical physicists as laborers—far different than the ratio in the general population. The same clinic also has several justices of the Supreme Court, prominent rabbis, and an assortment of physicians and scientists. This suggests that Gaucher's disease is also associated with high IQ.

Canavan's disease is caused by a defective enzyme that degrades a chemical called N-Acetylaspartate (NAA). High levels of NAA are associated with high IQ. Although it is lethal in homozygotes, it seems to boost the IQ of heterozygote carriers.

Tortion dystonia is another Ashkenazi disease that is linked to IQ. People with disease have IQs 10 points higher than average.

These data suggest that at least some of the Ashkenazi diseases are associated with IQ, as predicted by the hypothesis of Cochran, Hardy, and Harpending.

16 Genetics, language, and the prehistory the Americas

Greenberg (1987) classified all Native American languages into three families: Amerind, Na-Dene, and Eskimo-Aleut. He argued that these represented three waves of migration into the New World. Where are the Na-Dene and Eskimo-Aleut families found today? Which language family (according to Greenberg) is thought to have arrived first? Which second? Which last?

Most linguists would argue that Greenberg's method is flawed: that it isn't possible to reconstruct linguistic history so far back in the past. Accordingly, they don't recognize Greenberg's three major groupings but instead recognize 150–180 independent language families.

Raghavan et al (2015) describe the genomes of several ancient Amerindians and compare them with modern Amerindians. The earliest archaic genomes from N America are around 10 ky old. Their DNA is most similar to modern Amerindians who live far to the South. This suggests that that the earliest N American populations were replaced by immigrants from the N.

Early S American genomes (3.5–5.5 ky old) are similar to modern Amerindians scattered throughout S America and Mexico. They are not especially similar to modern Amerindians of their own regions of S America. This suggests that the regional differences of modern S Americans had not evolved by 5.5 kya.

By 500 ya, we begin to see ancient genomes that closely resemble modern Amerindians of their own region. Thus, it appears that the geographic structure of Amerindian DNA evolved fairly recently.

Genomes from each of Greenberg's three groups cluster with each other genetically. This suggests that there may be some reality to Greenberg's groupings.

However, Greenberg's hypothesis implies that the Amerinds separated from Asians earlier than the Athabascans did. The genetic data refutes this part of Greenberg's hypothesis. It appears that Amerinds and the Athabascans both separate from Asians at about the same time: $\sim$20 kya.

Goldberg et al (2016) use radiocarbon dates to estimate the early growth human populations in South America. What do they find?

17 Skin color in human evolution

Where are the Cape Verde Islands? What makes them ideal for a study of the genetic basis of the skin-color difference between Africans and Europeans?

What does GWAS stand for?

The Cape Verde GWAS identified several genetic loci with important effects on the European-African difference in skin color and eye color. You should be generally familiar with the study and what it found.

The GWAS identified 4 loci that affect skin color. Taking these together, what fraction do they explain of the total heritability of skin color?

Several of these loci were genotyped in the La Braña skeleton, a 7000-year-old Mesolithic European. What do they imply about the color of this individual's skin and eyes?

Berg and Coop (2014) used the 4 skin-color loci from the Cape Verde GWAS to define a "genetic skin color." As expected, genetic skin color predicts dark skin in Africans and light skin in Europeans. However, it predicts dark, African-like skin in East Asians. What does this imply?

Mathieson et al (2015) study change across time in the frequencies of European alleles for skin color (SLC24A5 and SLC45A2) and eye color (HERC2). Be prepared to describe the history of the European allele at each of these loci. When did the major changes occur? What do these suggeste about the history of skin color and eye color in Europe?

18 Geographic population structure

Genetic differences between populations are shaped by several evolutionary forces. Selection plays a role. It may increase population differences by favoring different traits in different populations, or it may reduce difference by favoring the same thing everywhere. We talked about these effects in the lecture on skin color. Here, we focus on two other evolutionary forces.

First, there is genetic drift, which perturbs allele frequencies randomly each generation. If this were the only process at work, each allele frequency would eventually drift either to 0 or to 1, and all variation would be lost. Although its effect is unpredictable at a given locus in a given generation, it tends on average to reduce genetic variation within populations and to increase genetic differences between them. The effect of drift is largest in small populations, so we expect to see little variation within such populations and big differences between them.

Migration (also called gene flow) refers to the movement of individuals from one population to another. Its effect opposes that of genetic drift. It increases variation within populations and reduces differences between them. Migration tends to be strong between neighboring populations and weak between populations that are far apart. For this reason, genetic differences often mimic geographic distances. The map of genetic similarities often resembles a geographic map.

The era of genomic data has added a new dimension to this subject. It is now possible to recognize segments of chromosome that two individuals have inherited from a common ancestor. These are called *identity by descent* blocks, or IBD blocks. If the common ancestor was recent, these blocks will tend to be large—perhaps even entire chromosomes. But if that ancestor was ancient, recombination will have whittled down the sizes of these blocks. Thus, IBD blocks allow us to study genetic relatedness at different scales of time.

Ralph and Coop (2013) studied IBD blocks in European populations. Among Italians, individuals who share a lot of ancestry with the French-speaking Swiss also share a lot with the British. This suggests that the immigrants who introduced this DNA into Italy, came from a population that was ancestral both to the Swiss and to the British.

Among the British, on the other hand, individuals who share a lot of ancestry with Germans share very little with the Irish, and vice versa. This confirms history, which tells us that the British are a mixture of Celts and Germans, whereas the Irish are mainly Celtic.

It is also possible to compare IBD blocks of different lengths. Long IBD blocks tend to be recent, whereas short ones tend to be older. Using this yardstick, Ralph and Coop show that the descendants of recent ancestors tend to be local, whereas those of ancient ancestors are spread far and wide.

The study of Leslie et al (2015) uses similar ideas to construct a fine-scale genetic map of the British population. Each region within Britain is a mixture of immigrants from various parts of Europe. The modern distribution of genetic similarity reflects the political map of Britain in about 600 AD. The earlier invasions of the Angles, Saxons, and Jutes obliterated earlier relationships, as they must have existed in Roman Britain. But the later invasions, first of the Danes and then of the Normans, had no appreciable effect.