Understanding Us

A. Early *Homo sapiens* evolution and interaction with Neanderthals
   - Lecture from Mon and activity linking CH2 in Racism not Race to images that were on the walls.

B. Evolutionary adaptions to different environments
   - Ex. Lactase Persistence (We did this one)
   - Lots more from "Recent Human Evol" Reading (Qs in Groups)
   - **Ex. Skin Pigmentation (Vit D-Folate Hypothesis)**
   - **Ex. Sickle Cell (Here and see pps listed on handout)**

C. Exploring apparent relationships between Health and Race
   - **Handout on Sickle cell and Hypertension**

A. Early *Homo sapiens* evolution and interaction with Neanderthals

B. Evolutionary adaption to different environments

We will focus on evolutionary or genetic differences (and similarities) between populations of humans on the earth.

But remember there are **cultural, historical differences and peoples live in very different environments all of which also generate variation.**

These factors interact in complicated ways.

B. Evolutionary adaptions to different environments

- Ex. Lactase Persistence (We did this one)
- **Ex. Skin Pigmentation (Vit D-Folate Hypothesis)**

Two important nutrients!
Problem: Folate breaks down under UV radiation
BUT can protect skin by having darker skin!
That leads to a second problem: Vit D is made in the skin as a result of UV radiation.
So when skin is dark might not get enough Vit D!
Ex. as darker skinned humans settled areas in the far north..they were getting less UV and thus less vit D.

This probably selected for lighter skin color.
Skin color may be a balance between these two selection pressures.

Nutrients. 2018 Apr 30;10(5):554. doi: 10.3390/nu10050554

The Vitamin D–Folate Hypothesis as an Evolutionary Model for Skin Pigmentation: An Update and Integration of Current Ideas

Patrice Jones [1], Mark Lucock [1,*], Martin Veysey [2], Emma Beckett [1,3]

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PMCID: PMC5986434 PMID: 29710859

2. The Vitamin D–Folate Hypothesis

The vitamin D–folate hypothesis is one of the main theories potentially explaining the evolution of human skin pigmentation. It is apparent that human skin tones arose as an adaptation to our UVR climate, with individuals of the darkest pigmentation having an origin in high-UVR areas near to the equator and lighter-skinned populations arising in low-UVR regions closer to the poles. This pattern arose as a result of two clines in skin pigmentation, whereby our early human ancestors firstly evolved to have darker skin pigmentation while residing in Africa but then evolved to lose their pigmentation when out-of-Africa migrations occurred [25]. The vitamin D–folate hypothesis proposes that these two clines of skin pigmentation evolved as a balancing mechanism to maintain levels of two vitamins: vitamin D and folate [16].

Vitamin D and folate are linked by their disparate sensitivities to UVR. UVR, on the one hand, stimulates the production of vitamin D in the skin, but, on the other hand, it may cause folate degradation through the absorption of UVR by folates or the oxidation of folates via free radicals following UVR exposure [1,17,18,19,20,21]. The vitamin D–folate hypothesis proposes that the original cline for increased pigmentation in high-UVR environments was driven by a need to protect folate levels against UVR-driven degradation. In turn, the second cline for depigmentation is suggested to have occurred to facilitate adequate vitamin D production in areas of lower UVR [16].

This hypothesis is plausible, given that in maintaining levels of vitamin D and folate via skin pigmentation processes, the widespread action of these nutrients in maintaining reproductive success would have been preserved [26,27]. The vitamin D status influences the reproductive health of both men and women and is associated with adverse pregnancy outcomes, semen quality, and the production of sex hormones [26]. Since the relatively recent discovery of VDRs in reproductive tissues of both sexes, studies on VDR-null mice link vitamin D inadequacy to a decline in sperm counts and motility, and aberrations in the testis, gonads, ovary, and uterus [26,28,29,30]. A link between the folate status and adverse pregnancy outcomes is well established, particularly with respect to the influence of this vitamin on the occurrence of neural tube defects [31]. Folate has importance in processes of DNA synthesis, repair, and methylation, and disruption to these processes can significantly impact on maternal and embryonic physiology [27] and affect paternal fertility by reducing sperm counts and motility [32]. The potential impacts of a deficiency of these nutrients on natural selection is an ongoing debate and is a common argument raised against the vitamin D–folate hypothesis. However, these arguments often do not consider that the benefits of an adequate vitamin D and folate status on reproductive success extend far beyond their roles in maintaining reproductive health. Vitamin D and folate regulate many mechanisms that offer immediate protection from potential lethal environmental stresses at life stages before reproduction. The following sections provide key examples of such mechanisms, which relate to other prominent theories for the evolution of skin pigmentation.

B. Evolutionary adaptions to different environments

- Ex. Lactase Persistence (We did this one)
- Ex. Skin Pigmentation
- **Ex. Sickle Cell** (CH 6 p207, Racism not Race p88 and I will go over now)

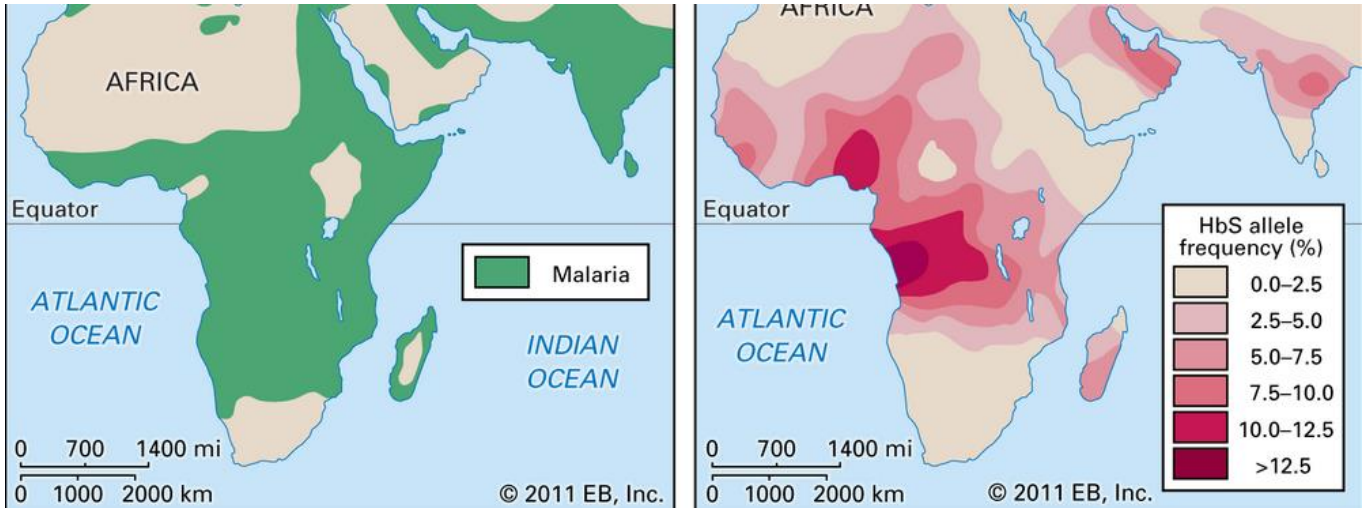
FYI….Covered in the "Selecting for Diversity" section CH6 which highlights how selection can maintain two alleles at a single locus in a population, when the heterozygote has a higher fitness than either of the homozygotes.

Heterozygote advantage

A very serious condition and huge numbers of people globally are affected.

Sickle Cell Disease

An example of human adaptation to different environments.
Selection has worked in different ways in different populations!
But…Is it a condition only found in people with a particular skin color?



HbS=S

FYI Malaria is caused by a protist pathogen!!

Sickle Cell Disease

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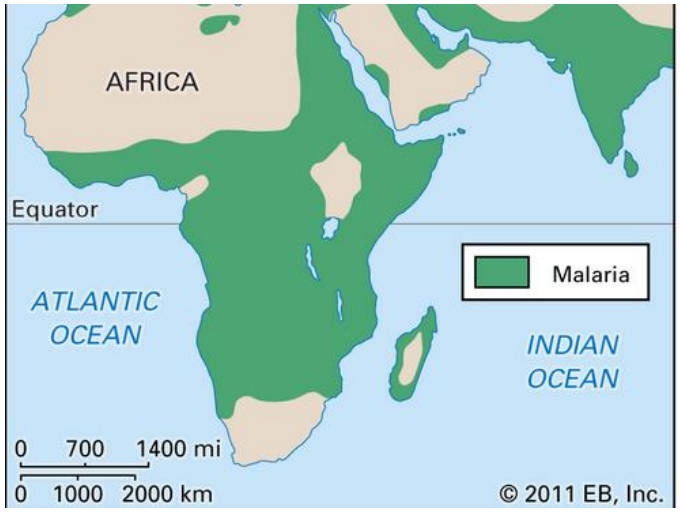
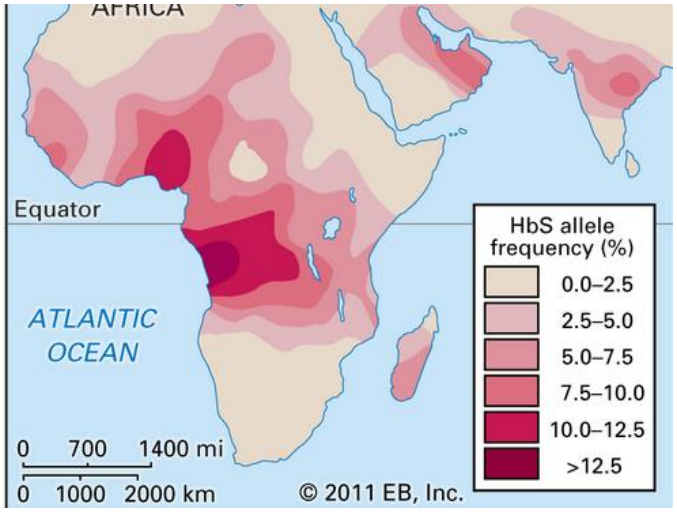




HbS=S

FYI Malaria is caused by a protist pathogen!!

AA	*AS*	*SS*
Normal	Normal	Anemic
But	And	But
Susceptible	Resistant	Resistant

Heterozygote advantage!

SS=Lots of cells sickle or collapse and block arteries when you are SS making you anemic

AS= That happens to some cells but you have enough normal cells so you do not haver symptoms and are not anemic.

Sickle Cell Disease

Is there a genetic basis?

Single locus trait!!!
"In the malaria belt regions of Africa, the Middle East, southern Europe and South Asia, this gene variant flourished because the benefits of malaria resistance outweighed the negative impact of sickle cell disease."

Why does sickle cell seem to occur in those with darker skin (there is a correlation)?
"Sickle cell is found more frequently in persons of Middle Eastern, Indian, Mediterranean and African heritage because those geographic regions are most prone to malaria. The gene variant for sickle cell disease is related to malaria, not skin color."
Physicians have missed this condition because they assumed it was always related to race!

More about hemoglobin

This is from our Transcription and Translation material

What are these changes made to the polypeptide after it is made ("Post Translational Modifications")

It will coil and fold due to its primary structure (its amino acid sequence)

- Groups are **added** (sugars, lipids, phosphate groups)
- Parts might be **removed** (e.g. amino acids from leading end or middle EX. Insulin is formed after a chunk of a.a. are taken out of its middle.)
- Several polypeptides may be joined together to become subunits of a big protein like hemoglobin

More about hemoglobin

Adult hemoglobin consists of four protein "subunits" that are combined to make a big functioning hemoglobin protein.

- 2 alpha-globins
- 2 beta-globins

Each globin is made by a different gene or region of genome

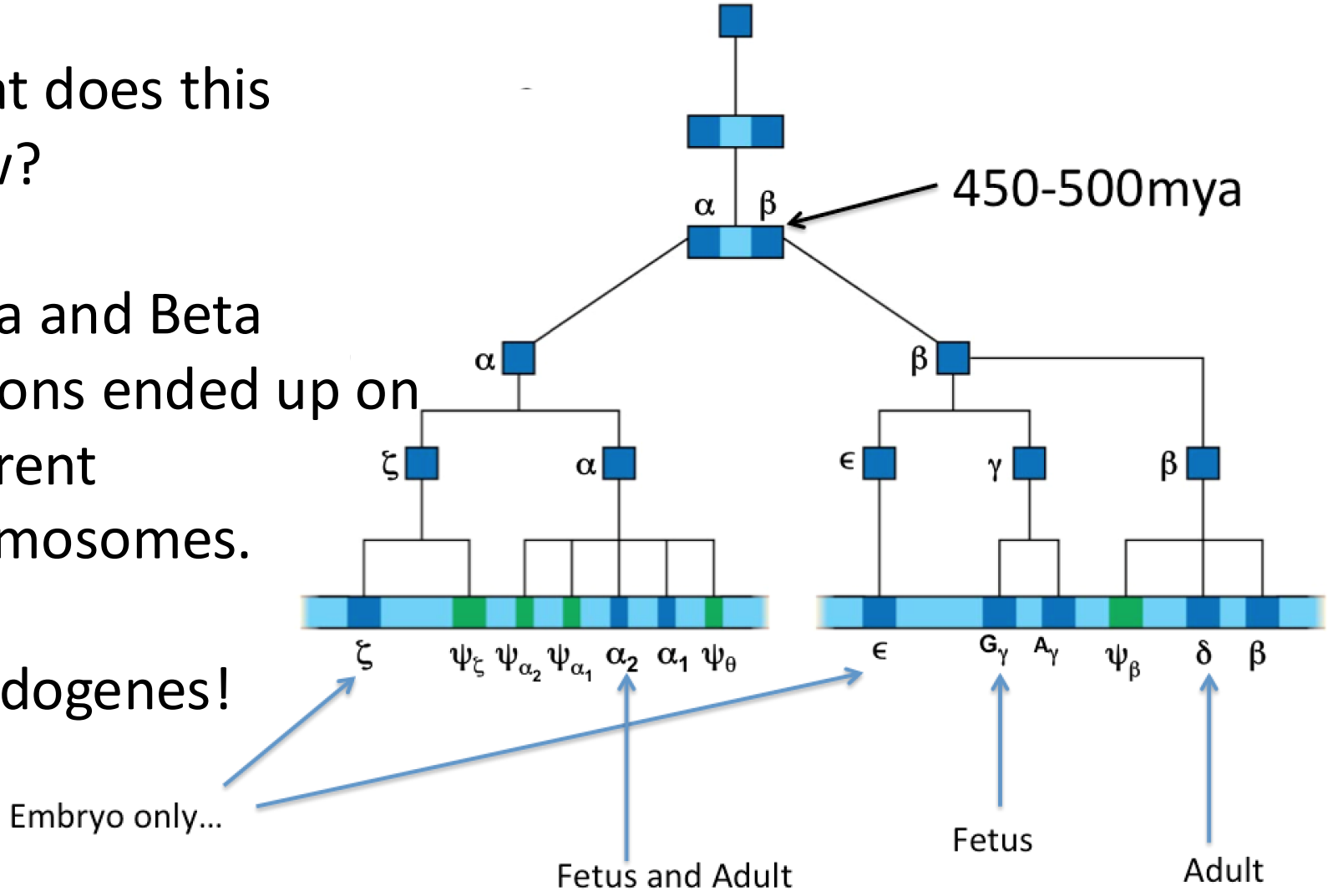
A mutation in one of the **beta-globin genes** causes sickle cell disease.

Hemoglobin is a big **family** of genes due to many duplication events.

What does this show?

Alpha and Beta versions ended up on different chromosomes.

Psuedogenes!



Note I do not have all the adult active ones pointed out!

Even relatives with the same HBB alleles can be affected differently. Some need medical treatment while others remain symptom-free for life.

Some of these differences are due to variations in other genes. For example, genes that code for fetal globins are usually switched off soon after birth. But some people keep making fetal hemoglobin until later in childhood or even into adulthood. As a result, they make more healthy red blood cells, and their symptoms are milder. Other genetic differences affect the amount or type of alpha-globin protein a person makes. This can affect how beta-globin interacts to form hemoglobin, making symptoms better or worse. Still other gene variations affect how well we absorb iron from food. In people with beta-thalassemia, these variations can increase or decrease the risk of iron overload.

Environmental factors also affect the symptoms of hemoglobin disorders. Good nutrition can help the body make and break down red blood cells more quickly. Infections can stress the body and make symptoms worse. Some women experience anemia only during pregnancy, when they need to make more blood to support their growing baby. People tend to do better when they have access to good medical care, and when they closely follow the advice of their caregivers.

Other genes play a role and the condition is not as simple as we first thought! Symptoms vary from person to person.

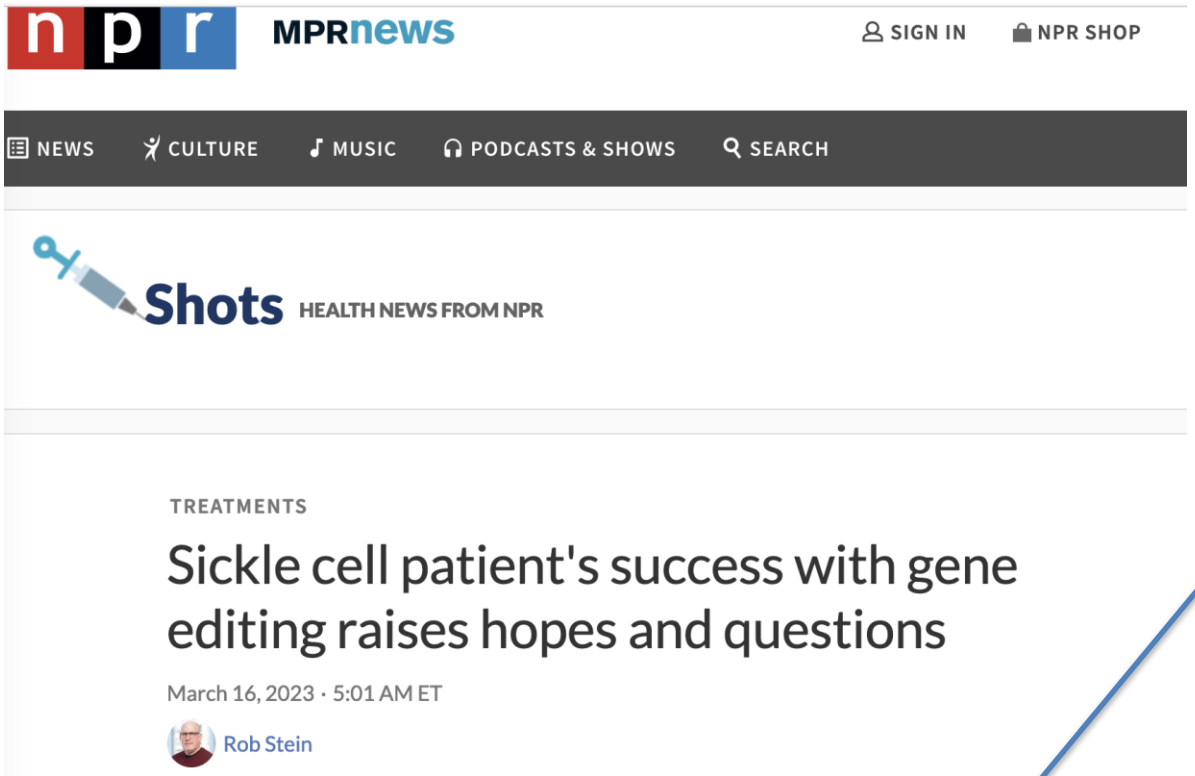
This is because…

Some people with the mutation keep making a form of the fetal hemoglobin until later in childhood or even into adulthood.

Does that pattern sound familiar??

https://learn.genetics.utah.edu/content/genetics/hemoglobin/

https://www.npr.org/sections/health-shots/2023/03/16/1163104822/crispr-gene-editing-sickle-cell-success-cost-ethics



Look fetal hemoglobin!

But then she received the treatment on July 2, 2019. Doctors removed some of her bone marrow cells, genetically modified them with CRISPR and infused billions of the modified cells back into her body. The genetic modification was designed to make the cells produce fetal hemoglobin, in the hopes the cells would compensate for the defective hemoglobin that causes the disease.

Review Hemoglobin Story

- What is a gene family?
- When genes duplicate one copy can keep doing the original "job" and the new copies can take on new tasks.
- Green on previous slide indicates pseudogenes.
- What is significant about the date 450-500mya?
- Note that in this gene family, some genes "turn on" at different times-affinity for oxygen is different for each.
- In some people (and in llamas living at high altitude) their fetal hemoglobin is active in adults.
- Sound familiar?
- Notice the importance of changes in gene regulation!