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Biology 1 Mod ¾
Project Rough Draft

How the Human Leukocyte Antigen Haplotype of an Individual Affects Organ Donation and Transplantation

HLA Haplotype

The Human Leukocyte Antigen (HLA) system is the name of the major histocompatibility complex (*MHC*: molecules on the surface of leukocytes that dictate their interactions with pathogens and other cells) in humans. The super locus (a gene or DNA sequence's location/position on a chromosome) holds a large amount of genes related to the human immune system functions, which reside in human chromosome #6. They encode cell surface antigen-presenting proteins which have many different functions. HLA is basically the human versions of the MHC genes found in most vertebrate. Proteins encoded by some genes are known as antigens. As a result of a historic discovery these antigens are a factor in organ transplants. The major HLA antigens are absolutely necessary for immune functions. But different classes have different functions.

"Fingerprint"

In a way HLA could be a genetic "fingerprint". HLA genes are passed on from the Mother and Father. Haplotypes could be used to trace migrations in the human population. They are like a fingerprint because of an event in evolution. An example of this is the Super-B8 haplotypes which is thriving in Western Irish region and gradually declines as you get farther away from the region.

How HLA Works

The proteins encoded by HLA on the outer part of the body cells that are unique to that person. The immune system then uses the HLA to differentiate like cells from unlike cells. Any cell with that person's HLA type belongs to that person and the immune system recognize them as not an invader but if they do not match they attack. When a foreign pathogen enters the body the APCs engulf the pathogen through the process of phagocytosis.

Basically the immune system surveys the body for unlike cells (Cells with non-similar HLA). Then the Helper T Cells promote the invaders information. Then they attack that invading cell.

How HLA Affects Organ Donation

Since every human has a unique Haplotype it can be difficult to find an organ donor because there always a risk your body may think it's an invader and destroys the organ because it doesn't recognize the corresponding Haplotype. In order for an organ to be donated to an individual you must have at least a 75% match of Haplotypes. If not your immune system will destroy it. After surgery the individual takes immunosuppression drugs to lower the chances of rejection. There is a 25% chance a sibling can donate an organ.

Data and Analysis

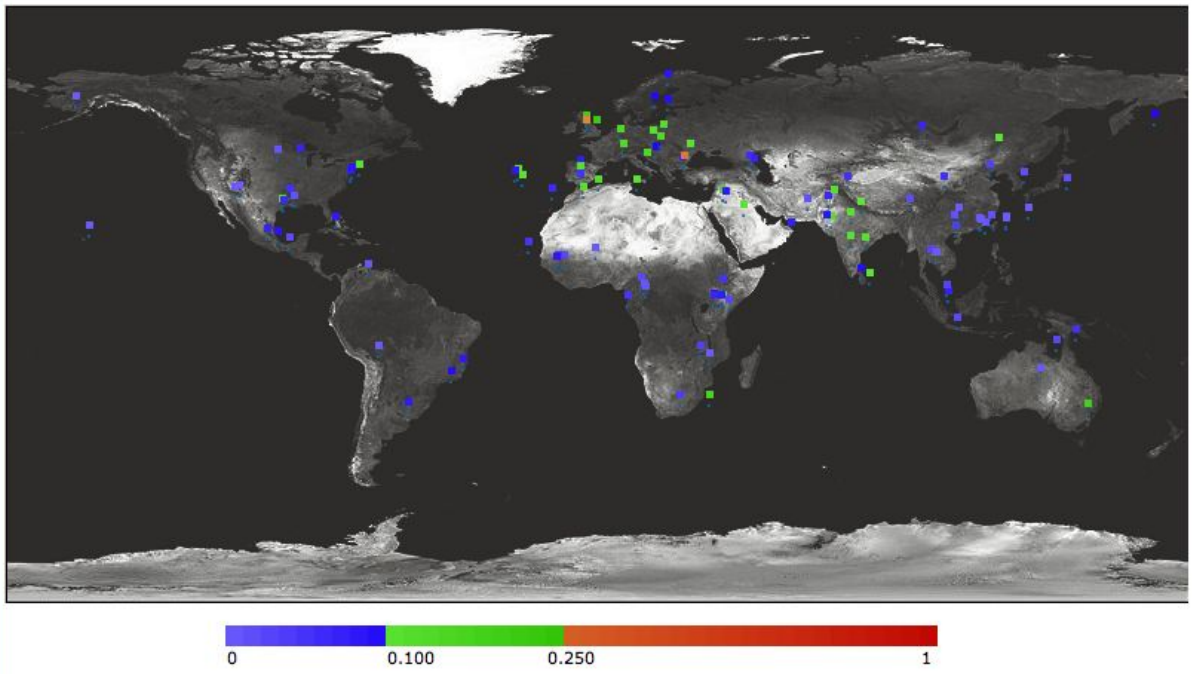
In order to ensure organ donation is successful, doctors and scientists must collect large amounts of data, not only featuring the patient and donor's haplotype, but the frequencies of certain haplotypes as well. Some variations of the trait may be more common than others, but there's still a voluminous array of them. It's one of the fastest, most frequently mutating traits of the human species. Even though the human species underwent an evolutionary constriction several thousand years ago, the variability of the HLA loci (plural of *locus*) survived. In fact, the variability of MHC loci in mammals is one of the highest in general.

The following data presents two main sets of information, one showing the distribution of three different HLA haplotypes around the world, and another exhibiting the frequency of those same haplotypes among four different ethnicities. So, in effect, the influence that both region and ethnicity play on an individual's haplotype are both communicated.

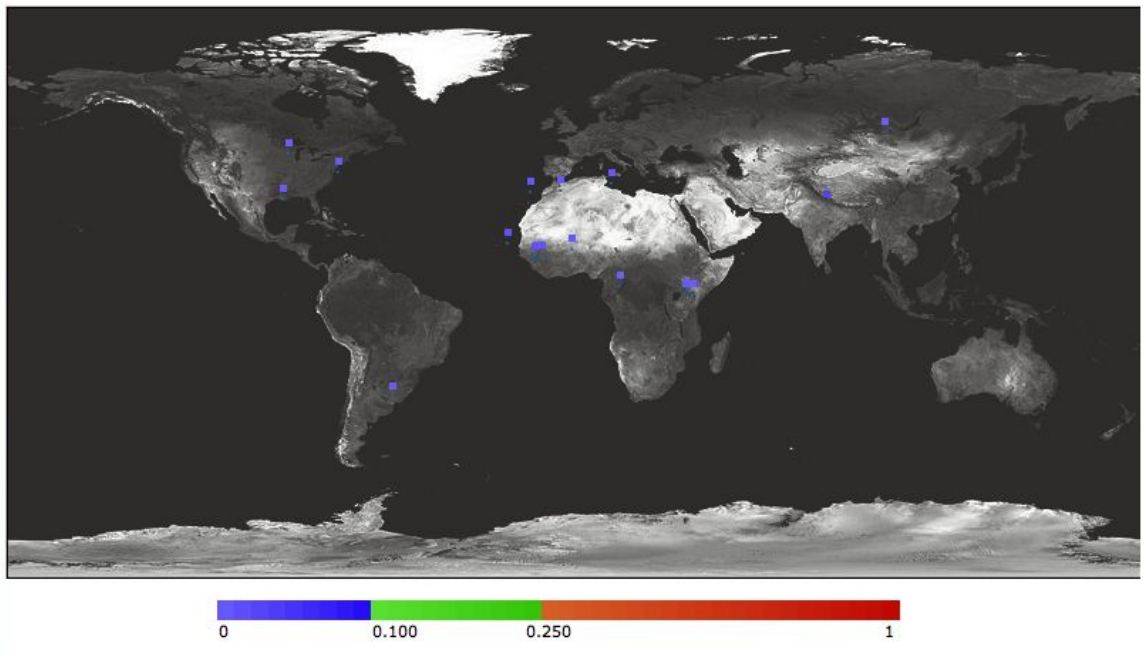
*HLA Haplotypes A*01:01, A*01:02, and A*01:03 Worldwide Distribution* *(courtesy of allelefrequencies.net)*

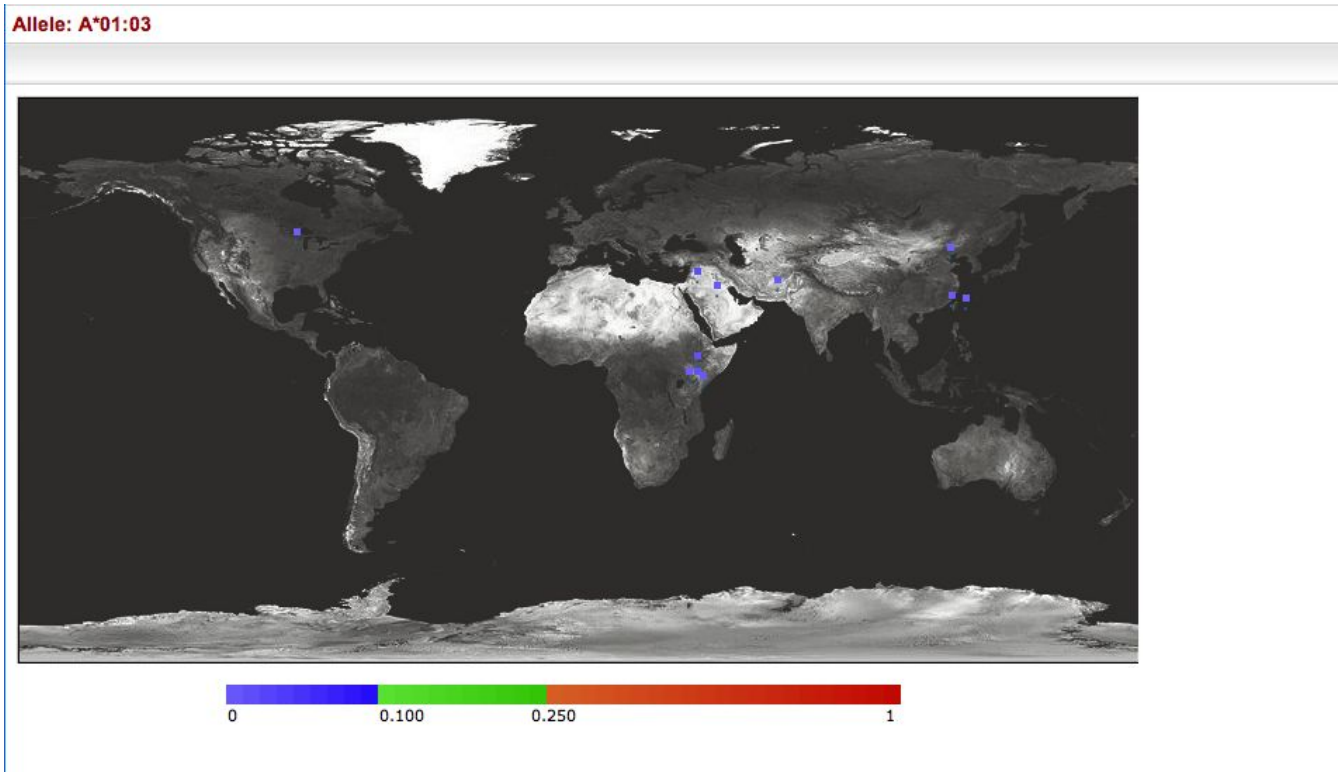
*Note, for simplicity, only three alleles are used. Also, for identical reasons, the allele communicated on the images are part of a homozygous, not heterozygous, haplotype. Also, the bar at the bottom of each map represents how similar individuals are to the presented haplotype (how much of a difference there is in decimal places).

Allele: A*01:01



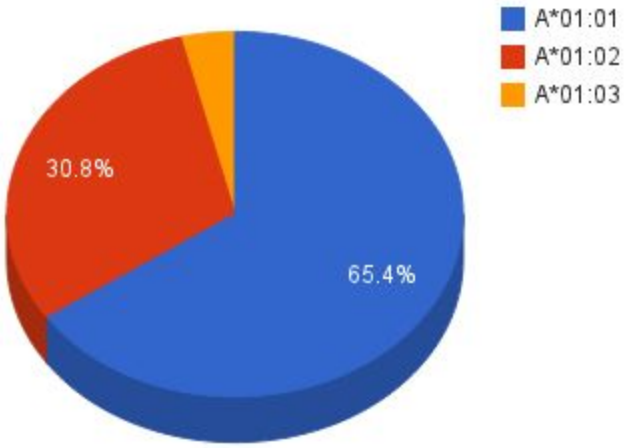
Allele: A*01:02



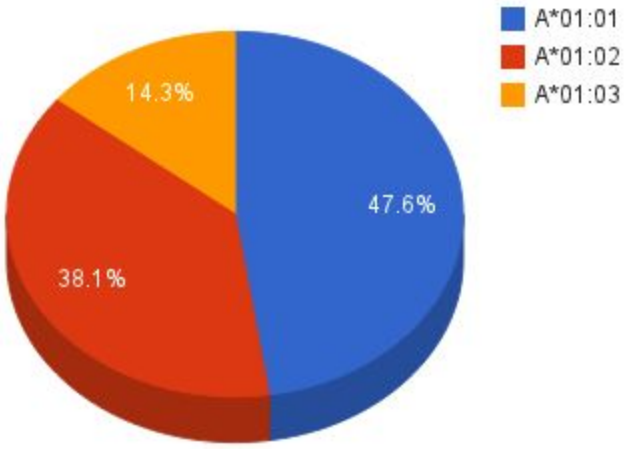


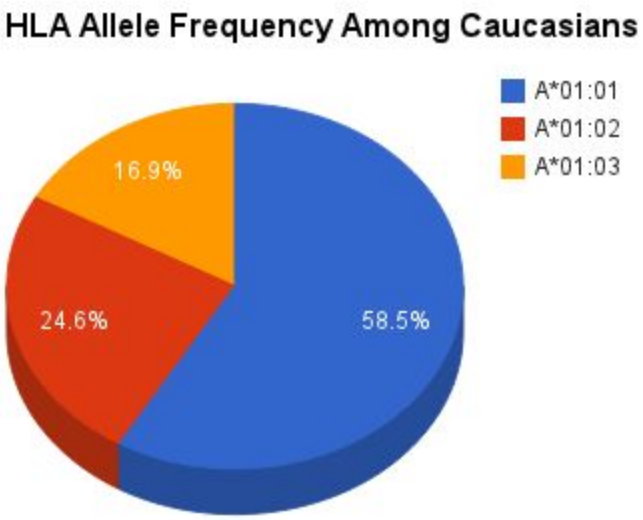
*Relative Frequencies of Haplotypes A*01:01, A*01:02, and A*01:03 Among Various Ethnicities*

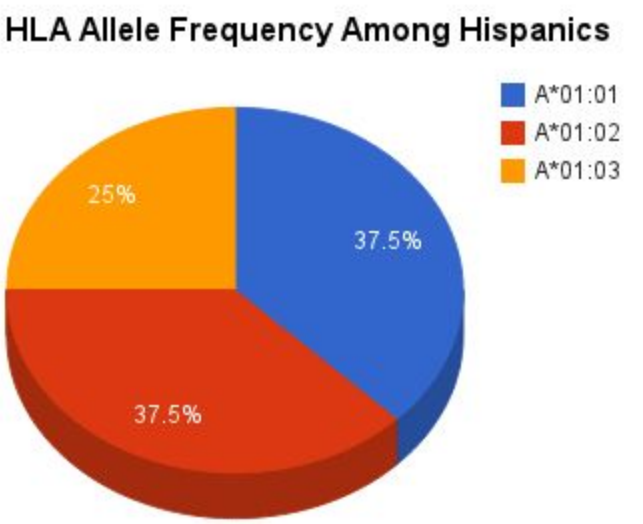
HLA Allele Frequency Among Asians



HLA Allele Frequency Among Blacks







As the images communicate, the distribution of haplotypes varies from haplotype to haplotype. Some are more conjugated in an area of Europe, while others are more common if

Sub-Saharan Africa. The same applies to the HLA haplotype frequencies considering race, each has a different frequency of each one within the ethnicity, no matter how insignificant it may appear.

However, there are major downsides to this data, the predominant one being the lack of data itself. The entire human race hasn't been sequenced to determine every individual's haplotype. As a result, serious holes are left in the data, which can ultimately alter conclusions drawn from them. Due to this, other seemingly unimportant factors come into play, such as the fact of whether, even if they wanted to, certain individuals could receive a transplant due to poverty or unstable conditions. This in turn feeds into the lack of data: HLA haplotypes are usually sequenced as a result of organ implantation. For example, little, if any, information on the HLA distribution of the Congo region of Africa is presented at all, which can be attributed to the lack of resources and money. Unless several haplotypes from this area are sequenced, they cannot be included in, and thus alter, the frequencies and distribution presented.

It's also important to note that region isn't always the best indicator of haplotype influence. For example, the United States is shown with a large number of individuals with the haplotypes of A*01 homozygous. However, most of these individuals were Caucasian, and don't account for the numerous other ethnicities that live in America. The argument could be made that individuals living in near each other are more likely to interbreed, however, that only adds to the confusion in a melting pot like the United States. The fact of the matter still remains: ethnicity is linked more directly to genetic makeup, and so has a greater influence on haplotype distribution than an individual's location in relation to other individuals.

Conclusion

The human leukocyte antigen is one of the most influential factors of making organ donation possible, and the better it's understood, the more possibilities open up for the field in the future. Patterns need to be found and frequencies established if it's to be of any use. Without these patterns, it will be difficult to find and locate appropriate donors. However, since it is one the mammalian traits of greatest variability, meaning there's a wide variety of alleles that code for it, this can be a difficult task.

Based on the information and data collected, it is evident that ethnicity and race have more of a direct influence on HLA haplotype frequencies, although that doesn't totally discard region's effect. By looking at the region distribution maps, it is easy to see that certain haplotypes tend to be more frequent in different areas. For example, the haplotype for A*01:03 homozygous is frequent in western central Africa and western China, but A*01:02 isn't found in western China at all. There are most likely a great number of holes in the data, not to mention anomalies and misinterpretations that distort the reality of the situation. Nevertheless, patterns still can be discerned; and even though places like the United States contain various ethnic groups that can further complicate the perception of the role region and proximity play, ethnicities CAN blend (like Hispanics for example), but that still leads back to the more

prominent role of ethnicity.

Ethnicity and race are more directly influential and genotype, and therefore appear to be more consistent with haplotype frequency. As shown in the charts, different ethnicities possess different frequencies of each haplotype. This is important to note as doctors and scientists continue to improve organ donation. The closer the haplotype matches, the more likely it is that the implantation will be successful.

Organ donation is a relatively new technology and saves countless lives all the time, changing the way we perceive life in general and opening countless doors for the future. Perhaps people will have an organ bank where organs are grown from their own DNA. Maybe this will help increase the human life expectancy beyond what we can now comprehend. However, there are obstacles to this revolutionary procedure. Millions around the world don't have access to basic human needs, much less this technology and doctors with the expertise to execute it (as is made evident by the maps showing allele distribution), and there are moral issues that come up as well as the science progresses. However, there is no doubt, it will improve in the future, and how we use it and apply can dictate the future of the human race.

Sources

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