Faith & Genetics

Genetics of Race and Genetics for Guiding Therapy

Genetic Racial Distinctions

What is the genetic basis of race? Are Africans genetically different from Asians? Are there race-specific genes? The more closely researchers examine the human genome the more most of them are convinced that the standard labels used to distinguish people by race have little biological meaning. They say that while it may seem easy to tell at a glance whether a person is Caucasian, African or Asian, the ease dissolves when one probes beneath surface characteristics and scans the genome for DNA hallmarks of race. Humans have spread out over the world in a relatively short time. Therefore there has simply not been enough time for the human species to divide itself into separate biological groups in any genetically significant way.

Of the small amount of total human variation, 85% exists within any local population, be they Italians, Kurds, Koreans or Inuit. About 94% can be found within any continent. That means two random Koreans may be as genetically different as a Korean and an Italian. About 75% of all the genes come in only one form and are identical in everybody. That is, about 75% of genes are have no allelic variation and are considered monoallelic. For example, if there was only one blood allele, say the A allele, then everyone would have the AA genotype and only have blood type A.

The way we measure human variation genetically is to look and find all the different variations of a gene and then see what percentage of the population has each form or that gene. Let's use blood type as an example. The distribution of blood types among Philippinos is nearly identical to the distribution of blood types among the Chinese population. There is genetic variation within each population but not much variation between the two populations. Alternatively, 100% of Peruvian Indians have blood type O, while among Blackfoot Indians, 82% of individuals have blood type A and 18% have blood type O. Within these two populations, there is little or no genetic variation, but there is a great deal of variation between the two populations.

Therefore, to characterize genetic differences between two populations, you examine the percentages of the different forms in different populations and you ask: If I take a sample from one population, are proportions of the different forms similar whether it's an African population or an Asian population or a European population?

If so, there's no difference between populations, and all the difference is found within populations. The measured amount of genetic variation in the human population is extremely small; genetically we really aren't very different from each other. Most of that genetic variability can be found within populations. For example, about 93% of all of the genetic variability that exits on this planet occurs within Sub-Saharan Africans. So, if there were a catastrophe that destroyed the rest of the world's population, 93% of the genetic variability in the world would still be present in Sub-Saharan Africans.

Medical Implications of Racial and Geographically-distinct Human Groupings

Are there genetic differences between human groups that are medically important? If race has any bearing on health at all, it is likely simply a marker for the geographic origins of certain populations. In the Eastern Hemisphere, where humans have lived for at least 2 million years, differences that developed in skin color were closely correlated with latitude and, thus, exposure to sunlight. The same pattern is not apparent in the Western Hemisphere, to where anthropologists suggest humans migrated only about 35,000 years ago.

Sickle cell anemia is often found in African and Mediterranean peoples but also among immigrants or ancestors of immigrants to North America from these regions. This prevalence in these peoples is thought to be due to the advantage of its presence in battling the malaria endemic to those areas because malaria parasites do not survive as well in sickled cells. Sickle cell anemia is rarely seen in descendants of people from northern Europe, where malaria is rare or absent. As mentioned previously, sickle cell is a disease caused by a single mutation of the hemoglobin molecule, causing it to carry oxygen poorly compared to normal hemoglobin and resulting in the curved or sickled appearance of red blood cells. So the genetic link here is clear-cut. But for the major diseases that cause or contribute to most deaths and disabilities, the genetic contribution is harder to pinpoint. For these diseases, such as heart disease, high blood pressure and cancer, multiple genetic mutations are thought to increase the susceptibility of some individuals, but environmental factors, such as diet and lifestyle, also play an essential role in development of these diseases.

It's much harder to make the case that high blood pressure is a bigger burden in some ethnic groups because of their genetic makeup. For example, high blood pressure more severely affects people of African descent in the Canada compared to those of European descent . African-Canadians are also much more likely to die of stroke than Canadians of European descent. Some have speculated that African slaves who were better able to retain salt were more likely to have survived the deprivations of the Middle Passage on their way to North America and that the same genetic makeup, passed on by the survivors, has put later generations of black Americans at risk for developing high blood pressure. But there are also a number of societal and cultural factors that might predispose African-Canadians to hypertension including the stress of living in a prejudiced society, lack of access to health care, poor diet, etc. Complicating matters is that no one really knows which combination of genes is responsible for susceptibility to hypertension. It's likely that a large number of mutated genes may contribute to high blood pressure, but that not all patients may have all those mutations.

Genetic Testing for Improving Therapy and for Reducing Treatment-Related Toxicity

Genetic testing can be very helpful in cancer therapy. Testing the genetic composition of tumours can help to determine what tumours are more effectively destroyed by certain therapies than other tumours and thus which patients may benefit more from such therapies. Genetic testing of cancer patients themselves can also be helpful in determining which therapies are predictably more or less toxic based on the presence of different alleles on the patient’s chromosomes.

Identifying Patients Most Likely To Benefit from Treatment

The increasing knowledge of genetic mutations linked to the development of cancer has led to new therapies directed specifically against such genetic changes in cancer cells. These targeted therapies are significantly changing cancer therapy. Whereas many conventional chemotherapy drugs attack many types of dividing cancer cells as well as dividing normal cells of the body, many newer targeted drugs appear to attack only cancer cells that possess such specific genetic changes.

Such improved therapeutic discrimination between cancer and normal cells has led to less treatment-related toxicity compared to conventional chemotherapy. In addition, newer targeted agents can be used more efficiently by identifying patients who are most likely to respond to therapy because their tumours possess the mutations against which the treatment was designed to attack. Similarly, patients whose tumours do not have the specific mutations will be spared the risks of treatment since they will not likely benefit. Treatment guidelines are beginning to recommend pretreatment genetic testing for tumour samples to identify patients most likely to benefit.

For example, tumour samples of patients with breast cancer can now be tested for a specific mutation associated with tumour development. Testing for one such mutation, know as the HER2/neu, is being used to identify patients most likely to benefit from a targeted treatment known as trastuzumab (the easier to pronounce trade name is Herceptin). Herceptin is a manufactured antibody which blocks the receptor protein product of the mutated gene that contributes to uncontrolled growth of the tumour. About 20 to 25% of breast cancers have this mutation which is associated with more aggressively growing and more treatment-resistant tumours. It is clearly not effective in patients whose tumours do not have the mutation but very effective in those who do. In addition, it is generally well tolerated, in large part because it affects only cancer cells and not normal cells of the body.

Identifying Patients with Increased Risk of Therapy-related Toxicity

Genetic information is now being used to identify patients who may be more or less tolerant to standard doses of chemotherapy. For example, patients with colorectal cancer are often treated with a combination of chemotherapy agents that include the drug known as irinotecan. Initially, safe doses of the drug were determined on the basis of the demonstration of a specified level of effectiveness and an acceptable level of toxic effects. However, it is now know that patents who are homozygous for a certain genetic allele (i.e., possess the allele known as UGT 1A1 *28 on both sets of chromosomes as opposed to just one set) are predisposed to an increased risk of infection due to extremely low white blood cell counts experienced one to two weeks after the drug is administered. This appears to be a consequence of reduced metabolic processing and disposal of irinotecan associated with the presence of the allele on both chromosomes.

As a consequence of this genetic information, patients can now be identified who are at less risk for infection using conventional doses of irinotecan (i.e., those who are only heterozygous for the allele or who do not carry the allele at all). Perhaps more important for future patients with colorectal cancer, patients who are not homozygous for the allele may benefit more from higher doses of irinotecan than can be tolerated by those who are homozygous. Clinical studies testing the safety and efficacy of cancer therapies in such genetically-selected patients are underway.