to judge the preFlood atmosphere O_2 concentration based on analysis of air bubbles trapped in amber. Amber is unlikely to form a seal impervious to gas molecules, and bubbles add to the pressure in any case. Whereas the tracheal tube comparisons could conceivably tell us about the oxygen content in the atmosphere in which the insect actually grew to maturity.

If such future studies suggest that oxygen levels pre-Flood were higher, this may be because the pre-Flood world carried more oxygen-producing vegetation, possibly due to greater land area and 'floating forests', much of it buried during the Flood.[7]

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The height of genome-wide association studies and what they tell us

Jean K. Lightner

Recently, a news release was carried by several science media outlets regarding a large study that was a 'giant' step forward in explaining the genetics behind differences in height in humans.[1] This highlighted the findings of the GIANT (Genetic Investigation of ANthropometric Traits) Consortium which were published in *Nature*.[2] Based on genome-wide association (GWA) studies, they reported that adult height in humans is influenced by hundreds of genetic variants found in at least 180 different spots in the genome (loci).

Height in humans is highly heritable, but is also considered a classic example of a polygenic trait, meaning it is influenced by many genes. In the end, this study was able to explain about 10% of the variation in human height, though estimates suggest that genetics should account for closer to 80% of the variation. GWA studies provide valuable information for future research, as well as important reminders about the complexity of the genome.

Recent rise in GWA studies

In GWA studies, genetic markers are rapidly scanned across the genomes of many individuals to see which areas of the genome vary in association with a particular trait or disease. These studies have increased dramatically in the past five years with the increased use of high-throughput genotyping technologies. Many loci have been identified which are associated with particular diseases or traits. This methodology should continue to play a valuable role in genetic research. As with any statistically based study, there are important assumptions, advantages, and disadvantages associated with GWA studies.[3]

It is important to recognize that an association of one particular genetic marker, usually a single nucleotide polymorphism (SNP), with a particular trait does not necessarily mean it is the cause of that trait. However, the SNP is often near or within genes that play a role in determining a trait or are a risk factor for a particular disease. GWA studies are susceptible to false positives, so it is used as a screening tool. Once loci are identified, further research is done to determine what role, if any, particular genes have in producing a trait or disease.

One gene with a large effect

When Gregor Mendel studied peas, he chose obvious traits, like color, that varied discretely. These studies formed the basis of what is called Mendelian genetics. Essentially, one gene has two or more alleles, each producing a different form of the trait (e.g. yellow or green colored peas). One allele may be dominant over another, but the appearance of the trait is easily explained by understanding basic laws about inheritance. This would be an example where one gene has a large or very noticeable effect on a particular trait.

GWA studies occasionally identify these types of genes. For example, a GWA study on dogs, followed by further investigation identified a dominant mutation in one gene (RSPO2) responsible for furnishings (mustache and eyebrows) in wire-haired dogs; a recessive mutation in another gene (FGF5) responsible for long hair in the majority of dogs carrying that trait; and a mutation in a third gene (KRT71) responsible for curly hair.[4]

These types of examples are helpful in understanding some of the basics about genetics. It is interesting to note that a very small change in a gene will sometimes make a very big difference in the animal or person. Mendelian genetics is relatively simple and has proved useful. Despite the importance of these concepts, they are a drop in

the bucket compared to all that goes on in genetics.

Many loci with smaller effects

Most common traits in humans have a polygenic pattern of inheritance. In other words, there are many loci which influence that trait. GWA studies have identified many hundreds of variants that influence traits. These loci are not just randomly scattered throughout the genome, but often are connected in biological pathways that play an important role in the development of the trait.

This brings up an important subject that evolutionary 'just so' stories tend to neglect. Genes do not work in isolation. In order to accomplish something biologically, many genes must work together in an organized fashion. There are pathways, or a series of steps involved in producing various traits. Life depends on having the right molecules present in the right place at the right time and in the right concentration. Some degree of variation is tolerable in certain circumstances. For example, many of the variants that influence height still allow for development of a healthy adult. However, there are limitations to how much change can occur before things break down biologically.

One example of biological breakdown is evident in a recessive mutation in a gene (STAT5B) which results in an insensitivity to growth hormone.[5] Not surprisingly, children homozygous (carrying two copies) for this mutation are extremely short. Their bodies produce high levels of growth hormone, but they are unable to respond to it and thus they are unable to grow normally.[5] In addition, these children have significant immune dysfunction, often associated with chronic lung disease.[6]

Biological research continues to uncover details within the many biological pathways and provide insight into the ways in which different pathways are interconnected. There is already a mind-boggling degree of complexity known for many pathways, and this is only a fraction of the even greater number of pathways and interactions that exist. This complexity is entirely inconsistent with the idea that life could have arisen by chance, random processes. In fact, life has the hallmarks of excellent design by an ingenious designer. GWA studies have helped identify genes in *different* pathways that play a role in producing a single trait. For example, in one analysis the most strongly connected genes for human height come from three pathways (Hedgehog, TGF-β, and growth hormone). A second analysis revealed other pathways as well.[8]

Raising the level of significance

One challenge faced by GWA studies is getting a large enough sample size to find the many genes which have small effects on the trait or disease of interest. The study on human height used information from nearly 184,000 people, yet only found genes explaining 10% of the variation in human height. They estimated that a sample size of 500,000 would detect over 99% of the genes that had a comparable effect on height. Still, there would likely be other genes with smaller effects that would be missed in a study this size. If all genes with comparable effect could be identified, they estimate this would still explain less than 20% of the variation in human height. As mentioned above, this is quite low, given that genetic factors are believed to account for 80% of the variation in height.

The authors suggest one possible reason for the low heritability could be allelic heterogeneity. In other words, there are multiple independent variants that influence the trait at the same locus. If this is the case, further research should uncover multiple alleles in particular genes influencing height. There are already several examples in humans where 50 to 60 alleles exist for a given gene influencing pigmentation.[9] Genes in the major histocompatibility complex also have many alleles represented in the population. This highlights the fact that there are some genes where considerable variability is well tolerated. In fact, it has been suggested that they were designed to vary and that some mutations in these genes may be from designed mechanisms created to induce such changes.[10]

At one time it was predicted that GWA studies, in finding genes associated with disease, would allow for personalized genomic medicine. In other words, a person could have their genome sequenced and know what diseases they were susceptible to. Then personalized recommendations and preventive measures could be taken to help them avoid these diseases. This idea seems to have been seriously overly optimistic and has led to some sharp criticism of GWA studies. In most cases, gene variants associated with susceptibility to disease are only weakly predictive.[11] For this reason, GWA studies have been more valuable in providing biological insights than in supplying predictive power.

Other factors

In many traits, such as height, as well as with many diseases, there are non-genetic factors which contribute to their formation. Environmental

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Genome-wide association studies have identified genetic variation in at least 180 different locations in the genome that are associated with adult height in humans, yet this only explains about 10% of the variation that exists.

factors, such as nutrition or exposure to certain toxic substances, play an important role in the final outcome. Additionally, epigenetic changes, such as DNA methylation, can be inherited and can influence the outcome. In neither case is a change in the DNA sequence involved. Therefore, environmental and epigenetic factors are not detectable by GWA studies. It is possible they are more of a factor than initially believed. This may be another reason the heritability accounted for by genes identified through GWA studies is so low.

Conclusion

Scientific studies, including GWA studies, have been valuable in providing information about genes that influence various traits or diseases. They are helpful in adding to our understanding and directing future research. They can lead to diverse practical applications. One important application I'd like to highlight here is that they should naturally lead to a deeper sense of awe for our Creator.

The more we learn about the genetics, the astounding programming involved and the complex, interconnected biological networks in living things, the more apparent it is how much we have left to learn. Life is far more complex and wonderfully designed than we could have anticipated, and we have just scratched the surface in our knowledge of how things work. While we might be tempted to magnify the importance of certain biological studies, it quickly becomes apparent that, although they may be useful, they are very limited in the answers they can provide. Science is a wonderful tool that should naturally point us to our awesome Creator who created and sustains life.[12z]

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Lizards moving from eggs to live birth: evolution in action?

Shaun Doyle

Lizards reproduce in an amazing variety of ways. Some lay eggs (oviparity) and some bear live young (viviparity). Most species rely primarily on egg yolk for nutrition during embryonic development; a few have next to no yolk and rely completely on a placental connection to the mother. Some lizard placentas even compare with the complexity of mammalian placentas. Some species can vary the timing of birth. There are a rare few species that even have variety in their reproductive mode.

Viviparity in lizards has many modes, but one thing they all have in common is that they give birth to live young. Moreover, despite the variety in placental morphology, there is no such thing as *aplacental* viviparity among squamates either. Blackburn comments:

> "The skeptical reader should note that no known squamate—*not one*—exhibits either matrotrophic oviparity (the ancestral pattern for mammals) or aplacental viviparity, the ancestral pattern traditionally assumed for viviparous squamates [emphasis original]."[1]

This is no help for evolution because it shows there's no evidence for the traditionally assumed ancestral condition for viviparous squamates. Even evolutionary critics of this model, such as Blackburn, have to postulate unlikely punctuational 'jumps' to avoid it, where both viviparity and placentation evolved together.[1]

National Geographic recently reported on one of the rare few species that have differing reproductive modes between populations—one of only three in the world—the yellow-bellied three-toed skink *Saiphos equalis*.[2,3]