Positive Selection In Human Evolution

Human Evolution has become a very prevalent topic of conversation over the past number of decades, with various ideas of how humans came to be who we are today. From a time where it was once thought that humans were a very close-knit evolutionary group, to now understanding that we do in fact, derive from apes. It is now believed that our closest ancestors are those of the African apes, the chimpanzee and the gorilla. Evidence from Charles Darwin and many other evolutionary scientists have contributed to the topic of human evolution in the such beneficial ways.

Positive Selection

Positive selection refers to changes or mutations in a gene that harvest benefits in the individual bearing the mutation. Throughout evolution, positive selection has allowed the human species to adapt to changed environments to allow for their continues survival. Several examples of positive selection have been discovered. Previous human ancestors would have lived very differently to how humans live today and overtime certain deletions in the human genome have taken place, thus removing certain unesesscary characteristics/ functions. The MYH16 gene is a myosin heavy chain gene which is inactivated in humans by a frame shift mutation. It is possible that because the myosin isoform encoded by MYH16 is expressed in muscles that are involved in chewing, that this may have contributed to or resulted in the consequent reduction in the masticatory apparatus in the ancestors of the human species. A systemic search was conducted to identify deletions in the human genome and 510 deletions were discovered. In one of these deletions it was found that an enhancer was removed from a gene involved in the development of penile spines- a trait which is lost in humans. Another deletion involved the removal of an enhancer near the gene GADD45G that in the subventricular zone, may have limited cell division during cerebral cortex development. This deletion may be therefore associated with the expansion in the size of the human brain. Human accelerated regions (HAR's) are molecules that first of all, in the developing human cortex, encode an RNA expressed in a subclass of neurons and secondly encodes an enhancer which in its human form can drive expression of a reporter gene in mouse limbs, which however in the ancestral sequence version carried by apes is not able to do so. Another example of positive selection is glycosylation. On the surface of their cells, humans lack the hydroxylated form of sialic acid, referred to as N-glycoylneuraminic acid. The 92 bp deletion in the gene encoding the enzyme (CMAH) CMP-N-acetylneuraminic acid hydroxylase is responsible for this absence.

A recombination between two Alu elements is responsible for this deletion and occurred approximately two million years ago. Experiments were conducted with mice that were engineered to lack the gene encoding CMAH, which meant, just as in humans, lack endogenous Neu5Gc. These mice were found to have T cells that proliferate at a much faster rate than wild type T cells and induce greater T cell responses to a virus. This same mutation found in humans could mean that humans have a significantly more active T-cell response than in apes.

As a result of incomplete duplications and deletions genes can gain functional differences. The SRGAP2 gene is a gene that is present in humans three times and only once in apes. This

gene, when expressed in neuronal precursor cells in mice, the truncated protein variant leads to an increased density of longer neuronal spines, a feature which may be typical of human neurons. Another gene, FOXP2, is one that has been subject to changes needed for human evolution. The inactivation of a single copy of FOXP2 subsequently results in severe speech and language problems. It has been hypothesised that SRGAP2 and FOXP2 are the first identified members of a postulated set of genes that around three million years ago changed function. This is in conjunction with human ancestors growing larger brains and their beginning in using these larger brains to complete complex tasks. The basis of this idea resides in an experiment where SRGAP2 and FOXP2 are introduced into mice.

The resulting effects are identified as neurons in the striatum increasing their synaptic plasticity and growing longer dendrites. Cortico- basal ganglia circuits which are important for motor learning, appear to be involved in these changes. This led to the conclusion of their involvement in brain development and complexity. Roughly 2,000 genes & 10% of the human genome are affected by positive selection. There have been variants of immunity genes which have been positively selected affecting genes involved in both innate and adaptive immunity. The gene CCR5 is affected by positive selection. CCR5 encodes the C-C chemokine receptor 5, which is required for the human immunodeficiency virus (HIV)-1 entry into T lymphocytes. Deletion of a 32bp in CCR5 confers protection from HIV infection- this presents an example of positive selection in population where HIV-1 occurs. (paablo article) (human heredity) one of the strongest signals of positive selection in Europeans is the genomic region containing the lactase (LCT) gene. Lactase is an enzyme that has a role in carrying out lactose digestion. In 68% of all living adult humans, its expression generally decreases. However, there are some humans, in particular those with a history of dairying, which have lactase persistence which refers to lactase being expressed through adulthood and is associated with a single mutation (13910 T) in those of European ancestry. The strong selection signals are associated with a single nucleotide polymorphism (rs4988235, C > T) of which allele – 13910T) located at 13910 nucleotides upstream of the transcription start of LCT, is casual of LP [1214]. Dairying dates back as far as the Neolithic period, with dairying presenting the cultural trait of drinking milk and consequently a potential selection pressure, which predates the occurrence of 13910T the advantageous allele in these populations. Selection ‘on a de novo mutation’ is a type of selection that depends on both the timing of the mutation and the population size considered. The larger number of variants that can remain in that population, a selection from standing variation is more likely.

The evolution of EP would have also been affected by environmental factors. During the Holocene, (period of climate becoming hotter) weather may have promoted human migrations in Europe and the Near East. With the intensification of agriculture and domestication, milk and dairy consumption would have provided a good nutritional component to farmers diets. It has also been hypothesised that there is a positive correlation between LP frequency and latitude and it led Flatz and Rotthauwe to say that due to the small amount of Vit D and calcium content in milk, LP could have provided a good supplement of both against the lack of sunlight due to higher altitudes, with the lack of sunlight being the selective pressure advantaging LP in adults altitude adaptations in Tibetans. With the modern human migration out of Africa, humans would have encountered many obstacles such as extreme temperatures, new pathogens and higher altitudes - these new environments would have been responsible for being agents of natural selection, causing natural adaptations. One example of this acquired adaptation is the adaptation of the Tibetans to the hypoxic environment of the high altitude Tibetan plateau.

The positive selection in this example can be seen in the hypoxia pathway gene EPAS1. This gene was found to be associated with differences in haemoglobin concentration at higher altitudes. The selected haplo-type is found only in Denisovans and in Tibetans, also present at a very low frequency in Han Chinese populations. The Tibetan plateau itself is inhospitable to humans, due to a cold climate, low atmospheric oxygen pressure and limited resources. Because of the Tibetans adaptations that confer higher fertility that acclimated women of low-altitude origin and lower infant mortality, the Tibetans successfully settled in the plateau. Women of lower altitude origin tend to have problmes bearing children at higher altitudes with their children having typically low birth weights compared to children of women with high altitude origin. The origin of the Tibetan high - altitude adaptation was discovered using exome and single nucleotide polymorphism (SNP) array data. The results showed, that in most cases, EPAS1 was involved – a transcription factor induced under hypoxic conditions, as the gene with the strongest signal of Tibetan specific selection. SNP variants in EPAS1 showed strong associations with expected levels of haemoglobin in many of the studies. Those subjects carrying the derived allele have lower haemoglobin levels than individuals homozygous for the ancestral allele. Introduction of genetic variants from archaic Denisovan – like individuals into the Tibetan gene pool was likely to be the source of the adaptation.