Structural variation in the genome of Monozygotic Twins

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The cell dedicates a lot of energy for maintaining its genomic integrity, but no system is perfect. For thousands of years the human life expectancy was relatively stagnant. The genetic stability in humans was not tested beyond a certain age limit. But in the past century, the life expectancy has increased by almost 20 years in many developed countries due to the leaps in modern medicine. Such sudden change in the increase in human lifespan has put the cells under considerable strain for maintaining its genetic integrity. The incapacity to deal with these changes is thought to have led to many genetic defects, which were often passed on through generations. These genetic instabilities and variations have led to a growth in various diseases and disorders in humans in recent decades.

Currently "ageing" is one of the least understood biological phenomenons. Many studies are currently underway to explain the genetic and epigenetic mechanisms underlying the ageing process in humans. It is popularly believed that ageing causes an accumulation of rearrangements in the genome, which lead to irreparable damage, diseases or even fatality. It has also been recently found that all the cells in the body arising from a single fertilized event do not have the same genetic composition, as was previously assumed, and is referred as '*somatic mosaicism'*. Due to mosaicism a small percentage of somatic cells in the body have a slightly different genomic content then the rest of the cells.

Monozygotic twin's are an excellent model for studying genetic variations occurring throughout the lifetime of a human being. As we know, the genetic makeup of the twins is theoretically the same, as they arise from the same zygote. We have selected monozygotic twin pairs, which are either discordant in their phenotype (one twin healthy and the other being affected by asthma or other autoimmune disease) and/or at two different ages. Our aim was to try to relate a phenotypic difference among twins to a genotype change. Moreover we investigated the quantity and the localization of genetic changes that occur over time, by comparing two populations of twins differing in their age (namely one "young" and one "old"). We wanted to demonstrate that the human genome accumulates structural rearrangements with age.

Copy Number Variation Analysis (CNVs) using arrays from manufacturers like Illumina BeadChip and Roche NimbleGen were used to compare the genomes of these pairs of MZ twins. The aim was to confirm if the aberrations shown by Illumina would also be reciprocated on Nimblegen arrays, where both these platforms are independent. Initially we worked on 18 SNP probes, which showed point mutation in one of the twin when compared to other. Later we went after larger genetic rearrangements, which were shown by multiple patients at the same loci by Illumina arrays and then confirmed further by Nimblegen. We studied 20 such loci with apparent large aberrations (500bp-8kb) by cloning and sequencing techniques.

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