De novo STRUCTURAL MUTATIONS

Next generation sequencing (NGS) technologies have made it possible to define the rate and patterns of point mutations in the human germline. Defining the rate of structural mutations is more challenging. This is because they are relatively rare and therefore much larger samples would be required. The other reason is that NGS technologies based on short reads (150-300 bp) are not suitable for structural variations. On the other hand, ultra long sequencing technologies (reads >100kb) are prohibitively expensive for large samples. With this limitation in mind, Belyeu et al. (Am J Hum Genet-2021 in press) have used NGS for a family-based study of germline mutations among 9,599 human genomes from 33 families and 2,384 families from an autism dataset. They found a rate of 0.160 events per genome in unaffected individuals. The rate in autism families was significantly higher (0.206 per genome). In both groups 73% of *de novo* structural mutations arose in paternal gametes. At variance with point mutations, they did not find an increase of structural mutations with parental age; this suggests that different mechanisms are involved in point mutations and structural changes.