Bias in *de novo* germline mutation rates

Context

Many diseases, like schizophrenia or autism, are caused by autosomal disorders. Therefore, understanding the origin of these mutations may help in a medical approach to prevent these diseases.

Another important aspect of this project is a better understanding of natural selection processes. Indeed, a crucial aspect of evolution lies in these *de novo* or spontaneous mutations. Since these mutations are random and usually appear in the germlines spontaneously among a population, it will spread or not within this population, depending on whether this mutation confers an evolutionary advantage or disadvantage. In the latter case, this can cause diseases. Therefore, biases in *de novo* mutation rates may have important implications for dynamics of the evolutionary process and the health of a population.

Goal

The goal of this project was to identify the presence of biases affecting the number of *de novo* germline mutations in the offspring of humans. In other words, we tried to identify what are the factors influencing the probability of spontaneous mutations in the next generation. Furthermore, we focused on single nucleotide mutations taking place in autosomes.

Data

3 different studies have been used for this project :

- *Whole-genome sequencing in autism identifies hot spots for* de novo *germline mutation* (Michaelson *et al*., 2012)
- *Timing, rates and spectra of human germline mutation* (Rahbari *et al*., 2015)
- *Rate of* de novo *mutations, father's age and disease risk* (Kong *et al*., 2012)

Conclusion

Main points revealed during this project :

- Father's age is an important factor for *de novo* mutations
- Between 1.5 and 2.0 mutations in the offspring for each additional year of the father
- The sex in the offspring doesn't seem to play a role in the number of mutations
- Mutations are relatively well distributed between and within the autosomes

Annex - Results

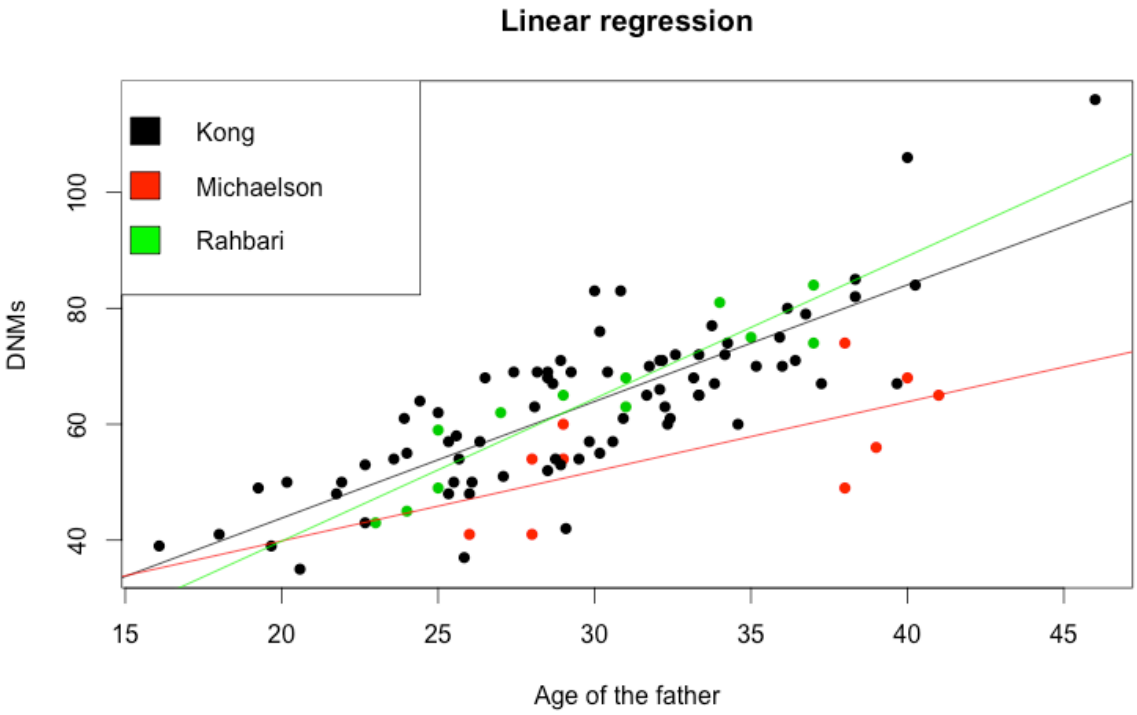

Figure 1 : Linear regression between the age of the father and the number of DNMs mutations. The results strongly suggest that father's age is an important factor for *de novo* autosomal mutations.

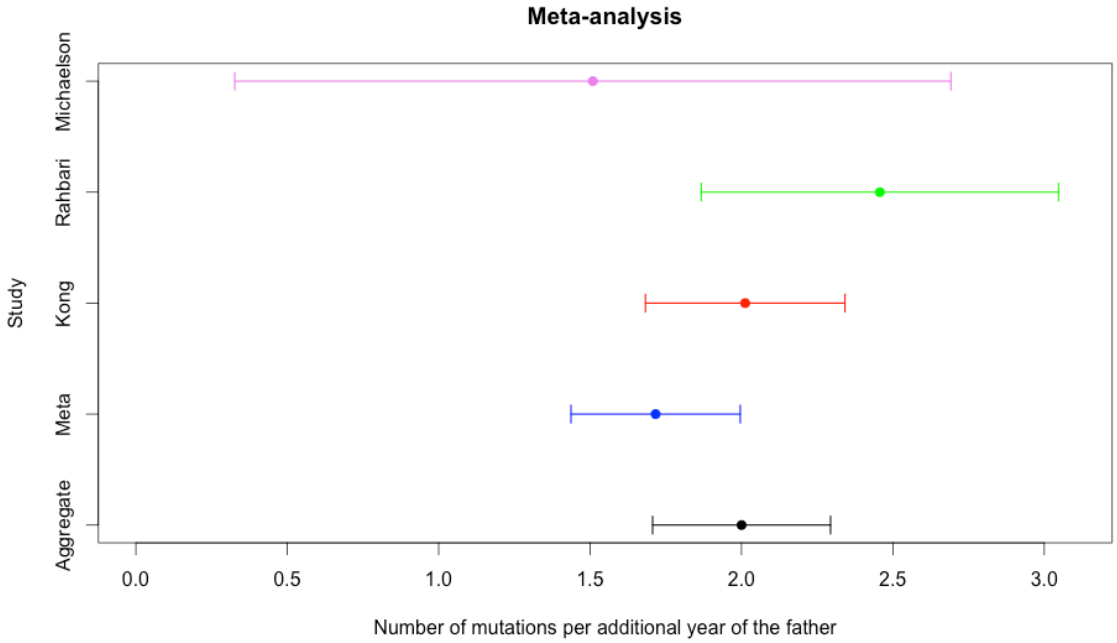

Figure 2 : Meta-analysis performed using a fixed effect model. The segments represent a 95% confidence interval. "Meta" represents a ponderation through the variance of the 3 studies. "Aggregate" represents a combination of the 3 studies, without any ponderation. The results show that there are between 1.5 and 2.0 mutations in the offspring for each additional year of the father. A difference between the studies can also be noticed.

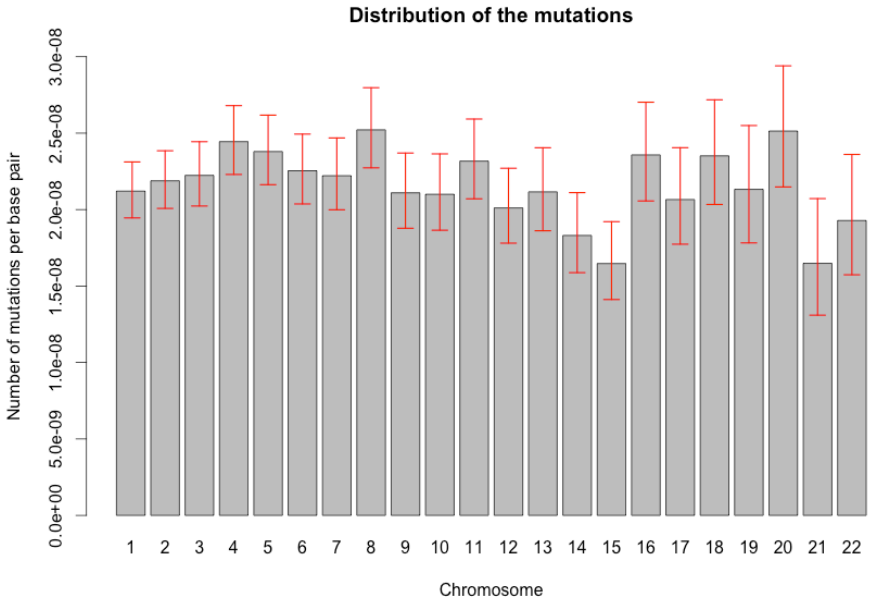

Figure 3 : Number of mutations per base pair between the 22 human autosomes. The results indicate that the mutations are quite well distributed between the 22 autosomes.

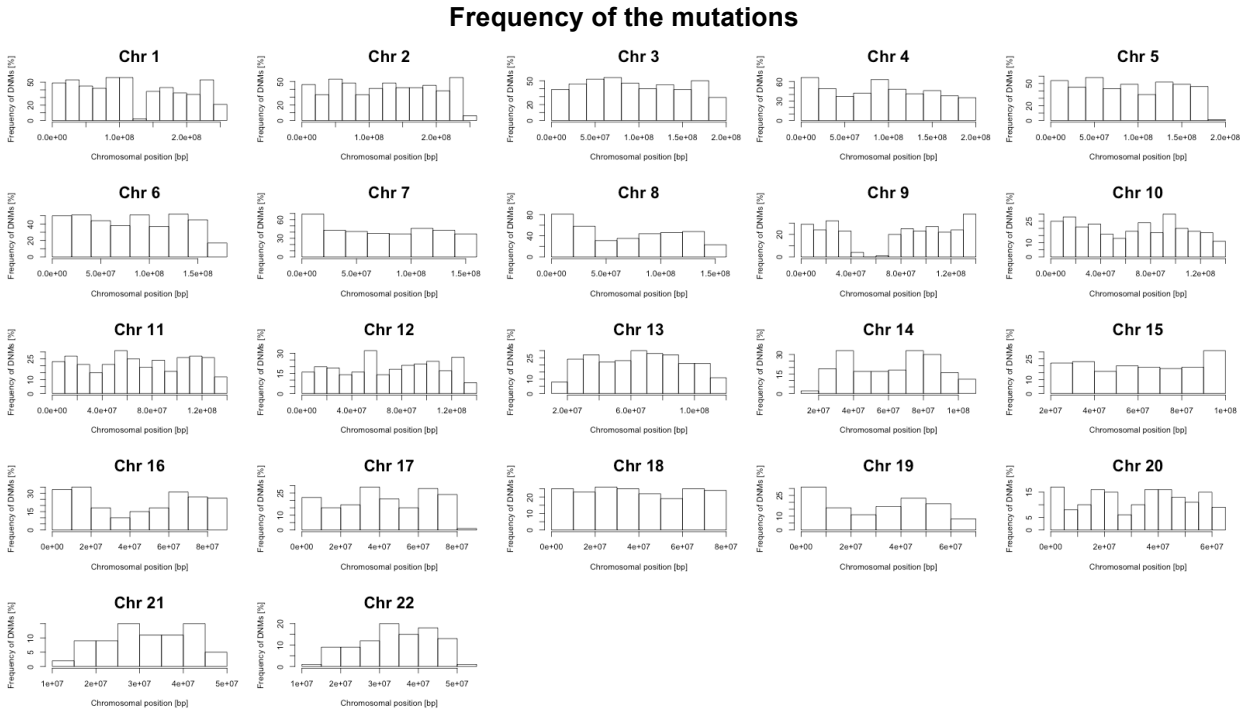

Figure 4 : Frequency of the mutations along the 22 autosomes. The results reveal that the mutations are relatively well distributed along the different autosomes.