

Bertrand Jordan, CoReBio PACA, Marseille: “Genes and Non-Mendelian Diseases: Dealing with Complexity”

ABSTRACT: The first two decades of the new medical genetics (post-recombinant DNA) were marked by resounding successes, such as the isolation of the genes responsible (when defective) for muscular dystrophy, cystic fibrosis, Huntington’s chorea, to name just a few of the more than 1,000 Mendelian genetic conditions whose cause is now known - even though therapy has not progressed very significantly. In contrast, the search for genes involved in common diseases such as diabetes, hypertension, schizophrenia or autism failed miserably in the 1990s, with inconsistent and conflicting results – nevertheless the strong genetic component of these disorders (that also involve environmental factors) has been proved beyond doubt.

In the last 5 or 6 years, thanks to huge progress in technology and analytical methods, it has become possible to identify genes influencing the risk of complex diseases reliably, using the so-called GWAS (Genome-Wide Association Study) approach. The recent development of new generation sequencing promises to accelerate this progress. Yet many problems remain, such as the vexing question of the “missing heritability”, or the difficulty of translating these (now reliable) scientific results into genetic tests with real clinical validity and utility.

I will present these issues using the case of autism (1), one of the disorders for which a strong genetic component has been demonstrated but where the search for causative genes remains difficult and where attempts at developing valid genetic tests have largely failed.

1 Bertrand Jordan. «Autisme, le gène introuvable» (Autism, the elusive gene), Ed du Seuil, Paris 2012.