Genetic tests for rare anaemias in the area of internet and of NGS (next generation sequencing)

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This talk will address four main questions about the current use and usefulness of genetic tests in rare diseases and rare anaemias (RA). It will focus on new available technical tools for the molecular analysis and on the possibility to order genetic tests online.

Why do we perform genetic tests in rare anaemias? Genetic tests are usually offered to patients with a known or supposed diagnosis of RA, because many such conditions are hereditary. First, they can be mandatory to firmly ascertain (or exclude) the diagnosis of some rare conditions that are difficult to confirm using only clinical or biological tools. In that case, the finding of a molecular anomaly in one (or several) gene(s) implicated in the disease is a powerful diagnostic test. Second, even when the diagnosis has been made, genetic tests may be useful to predict the outcome of the disease (severe or mild) or to prevent complications. Genetic tests are also used to screen for healthy carriers of a given disorder, in order to propose genetic counselling and, if needed, to offer prenatal or pre-implantation diagnosis.

What is new in 2015? Molecular diagnosis has benefited from several important developments during the past decades. One of the main technical revolutions concerns gene sequencing. The original method, called Sanger sequencing, has been (and is still) a very useful technique, but it is time-consuming and expensive. Next Generation Sequencing (NGS) is a new way of sequencing DNA. NGS allows sequencing large panels of genes or performing "exome sequencing", a method permitting the study of all the known coding regions (genes) of the genome.

In addition, genetic diagnosis is now easily performed on different tissues, including blood samples, saliva, hair and even on a single cell. This has made possible the development of various medical and non-medical applications, such as preimplantation diagnosis, forensic genetic tests, but also paternity tests or the search for one's ancestral origins. A number of so-called **direct to consumer tests** (DCT) are now **available online**. The **reliability** of these genetic tests and the problems they pose in terms of security and privacy are questioned.

A second burning subject concerns the new medical and ethical issues raised by the use of a potent method such as NGS, capable of analysing the whole genome of a person. One issue is the inadvertent discovery of other disorders made while looking for something else... this is called **"incidental findings" in gene screens**. In the future, screening for all the pathological or predisposing genetic markers of an individual would possibly become a standard. However today, it looks like if technical progress has gone too fast and human knowledge has to make up the delay. An optimized (new) use of genetic tests has to be set-up, including diagnostic and prognostic purposes, prevention of diseases comprising pre-symptomatic testing. From the patient point of view the main expected advantages are a better diagnosis allowing an optimised care. Other problems, such as privacy (insurances), the use of personal data for research or for commercial purposes are still debated and the legal frame requires several adaptations. Protection by law, (national health authorities, legal entities) and best practice guidelines (scientific societies, rare disease networks) are key modulators but should not be a brake on research and progress.