MASSIVE SEQUENCING AND ITS APPLICATION IN HUMAN REPRODUCTION

D. Ramón, F. Codoñer, J. Martínez, L. Pedrola
Lifesequencing SL, Parc Cientific Universitat de València, C/ Catedrático Agustín Escardino 9, edificio B, 46980-Paterna, Valencia, Spain

The current strategy for determining the genetic basis of diseases is to carry out a genome-wide association study with more than one million of single nucleotide polymorphisms that capture much of the common variation in the human genome. This approach is based on the hypothesis that allelic genetic variations that are common in the population will explain much of the heritability of common diseases. The milestones in these studies were the sequencing of the human genome by the International Human Genome Sequencing Consortium and the development of the Human Haplotype Mapping Project by The International HapMap Consortium. In this sense, second-generation massive sequencing technologies (SGMS) have led the way in revolutionizing the field of human genomics. These technologies achieve much higher throughput by sequencing a large number of DNA molecules in parallel, leading to extremely high overall throughput and a resultant low cost per identified base. Actually there are four SGMS technologies in the market: Roche 454 GSFLX Titanium, Illumina Genome Analyzer, Applied Biosystems SOLiD and Helicos HeliScope. The selection of an appropriate sequencing platform is an important consideration and requires a detailed understanding of their characteristics and applications (sources of error, error rate, and speed and cost of sequencing).

In utero disease screening using non-invasive techniques is a key target in reproductive medicine. The use of non-invasive fetal genotyping was suggested several years ago when several groups reported the existence of fetal cells and cell-free fetal nucleic acids in maternal blood. However, the small amount of fetal DNA relative to maternal counterpart was a technical barrier limiting the systematic genotyping to only a few loci. Very recently, the groups of Dr. Lo at the Chinese University of Hong Kong and Dr. Quake at Stanford University reported the use of SGMS technologies to screen for fetal aneuoplidy and fetal trisomy 21. These reports demonstrated the possibility of using maternal blood to test for all genetic traits. In other words, by using SGMS technologies there seems to be no technical barriers to be able to test one maternal blood sample simultaneously for several genetic traits (chromosomal abnormalities, single-gene diseases and/or non-disease genetic traits). Moreover, several commercial firms such as Artemis Health or Sequenom are exploring these new approaches. The future of this kind of testing is a matter of discussion. In this presentation we will discuss the scope and consequences of its use. Also the public controversy about its uses will be presented. Finally, we will present some preliminary results in the field of human exome sequencing that our company have developed in collaboration with IVI.