Next Generation Sequencing: A Change of Paradigm in Molecular Diagnostic Validation

Abstract

Next Generation Sequencing (NGS) is beginning to show its full potential for diagnostic and therapeutic applications. In particular, it is enunciating its capacity to contribute to a molecular taxonomy of cancer, to be used as a standard approach for diagnostic mutation detection, and to open new treatment options that are not exclusively organ-specific. If this is the case, how much validation is necessary and what should be the validation strategy, when bringing NGS into the diagnostic/clinical practice? This validation strategy should address key issues such as: what is the overall extent of the validation?; should essential indicators of test performance such as sensitivity of specificity be calculated for every target or sample type?; should bioinformatic interpretation approaches be validated with the same rigour?; what is a competitive clinical turnaround time for an NGS-based test and when does it become a cost-effective testing proposition? While we address these and other related topics in this commentary, we also suggest that a single set of international guidelines for the validation and use of NGS technology in routine diagnostics may allow us all to make a much more effective use of resources.

Key words: NGS, validation, technology

The recent paper by Tothill et al. in one of the recent issues of *Journal of Pathology* [1] illustrates an intelligent application of complex genomic information in a very specific clinical problem. Both fresh-frozen and formalin-fixed paraffin embedded samples of patients with cancers of unknown primary (CUP) were analysed with next generation sequencing (NGS) technology. In 75% of the patients tested, the results revealed new therapeutic options, as well as certain signatures that are “etiological” in nature and, as such, are indicative of a