Molecular Pathology Services Section Front Page

Molecular pathology is a discipline that seeks to describe and understand the origins and mechanisms of disease at the level of macromolecules (for example DNA, RNA and protein) largely using patient samples.

Stratified Medicine

Individual diseases are defined based on a common set of signs and symptoms as well as diagnostic tests. However, these shared signs and symptoms can arise from a variety of disruptions to underlying mechanisms. For example, patients with type I and type II diabetes both present with high blood sugar levels over a prolonged period. However, this common presentation has different causes; Type 1 diabetes results from the body's failure to produce enough insulin and Type 2 diabetes from cells failing to respond properly to insulin. This means that not everyone who is classified with the same disease will necessarily experience the same rate of disease progression or respond equally well to the same drugs. By classifying and understanding the molecular differences between the different groups or strata of people with a shared condition we hope to more accurately diagnose them, better understand how their conditions will progress, and determine which treatments are most likely to be effective. The improved stratification of patients therefore has the potential to deliver significant health and economic benefits.

Diagnostic molecular pathology: the challenge ahead

The scope for both targeted therapeutics and targeted diagnostics is extensive. Even with existing targeted and conventional therapies, the range of candidate predictive and prognostic markers expands on a month-by-month basis. Validation of even a fraction of such markers will require further development of complex molecular diagnostic assays. Given the molecular complexity and heterogeneity of tumors, it is not unrealistic to propose that, within the next 5 to 10 years, diagnostic reporting of 10s to 100s of different molecular variants will be essential to provide relevant information to facilitate appropriate treatment decisions to be made.

Already significant numbers of "molecular diagnostic pathology" assays of varying utility and cost are being offered in different jurisdictions worldwide. These range from in situ based analysis of protein expression, gene copy-number/amplification, to mutational analysis, expression arrays of 10s to 100s of genes.

The clinical challenge addressed ranges from prediction of response to specific therapies (mostly single gene/mutation assays at present), through prediction of residual risk or prognosis following treatment (increasingly multigene assays) to improved molecular classification (diagnosis) of

tumors. As assays increase in complexity, we are experiencing a rapid switch from in situ manually or visually assessed approaches to multiplex analyses of mRNA, CNA and mutations. As the number of targeted therapies increase, so will the complexity and diversity of molecular diagnostic assays required to provide appropriate diagnostic information for personalized or targeted medicine approaches. In many cancers there is already a requirement for anatomical, expression, mutational and CNA data to be reported on the same tumor sample.