

Better diagnosis, less cost

Murdoch Mactaggart learns of initiatives bringing reduced costs through earlier and more accurate diagnosis.

Healthcare now relies heavily on technology. Medicine has consequently become extremely complex, with the half-life of specialist knowledge perhaps no more than five years.

However, the potential for saving costs through early and accurate diagnosis is substantial.

Even more exciting are glimpses of the future, developments such as personalised medicine where diagnoses using genetic information or molecular-level analyses will be used to tailor therapies specific to individuals and with high probabilities of success.

Sensitive but not specific

"Precise diagnosis is essential in order to select the right therapy," explains Dr Mike Evans, CEO, Oxford Gene Technology (OGT). "People vary widely and until you understand exactly what's wrong, using more precise molecular diagnostic methods, you can't select the best therapeutic approach."

Biomarkers are biological indicators of a physiological condition, perhaps an infection, chronic disease or trauma. One example is prostate-specific antigen (PSA), a protein found at elevated levels in the serum of men with some prostate disorder. PSA is highly sensitive but is not very specific, good at identifying a prostate-related problem but poor at identifying what the problem actually is.

"With high PSA levels the actual disease could be a clinically benign enlarged prostate, a prostate infection, an indolent form of prostate cancer requiring only monitoring, right through to a potentially fatal cancer requiring urgent treatment," says Dr John Anson, OGT's VP of Biomarker Discovery. "This uncertainty means a large number of men have precautionary procedures such as needle biopsies or even have their prostates removed, which can lead to significant side-effects."

Because of disease complexity and variations between individuals it's almost impossible for a single biomarker to identify disease without giving false positives or failing to distinguish between benign and aggressive conditions, at least in early-stage diagnosis. OGT's research approach is instead to develop biomarker panels which offer excellent sensitivity but which also offer precise indicators to specific conditions.

"We've run a successful pilot study" adds Anson "and we're currently running a validation study of 1,800 different samples including patients with aggressive prostate cancer, with other cancers and with other relevant conditions. The aim is to identify aggressive prostate cancer early and so save more lives, avoid unnecessary procedures and hence also save considerable amounts of money."

"Our biomarker discovery platform currently focuses on prostate cancer" adds Anson "but the technology has broad applicability, not only to other cancers but particularly to autoimmune diseases. We've done some preliminary work on lupus, something notoriously difficult to diagnose. That's the start of a programme to broaden the utility of the technology and show its applicability to other conditions, so facilitating early diagnosis and bringing further cost savings."

Improving chromosome analysis

OGT is also working in the area of cytogenetics, or chromosome analysis, specifically developing micro-array



techniques which give high precision results. This builds on the academic work of OGT's founder and current chairman, Sir Edwin Southern, Emeritus Professor of Biochemistry at Oxford University.

"The current approach, karyotyping, brings positive results in perhaps 5% of cases," says Evans "Our array comparative genomic hybridisation, aCGH, improves that greatly, identifying positively in up to 25% of cases. This not only brings clear healthcare benefits to sufferers and their families but also reduces costs greatly. However, implementing aCGH is not a trivial exercise and so although we supply the product we also work with NHS clinical centres in offering specialist cytogenetics services through our own high throughput array lab in Oxford."

"There are numerous syndromes variously associated with learning difficulties. Down's Syndrome is straightforward to identify but others are not and these new tests will help paediatricians identify such syndromes immediately postnatally. This should allow earlier implementation of appropriate counselling and help to lead parents to specific support groups, as well as reducing costs greatly."

Benefit or costly disaster?

Around 258,000 men die annually worldwide from prostate cancer but because most prostate cancers are relatively benign many elderly men live with the disease for years before dying from something else.

The problem is one of accurate diagnosis. A 1993-2001 study of nearly 77,000 US men, published in the New England Journal of Medicine in 2009, showed that PSA screening and resulting treatment had virtually no effect on mortality in men of 55+. A European study 1990-2006, also published by the NEJM in 2009, suggested some benefit to PSA screening but estimated that 1410 men would need to be screened with 48 being treated to prevent one death.

Professor Richard Ablin, the physician who discovered PSA in 1970, has come out strongly against general PSA screening, describing it as a 'profit-driven public health disaster', 'peddled by drug companies' and wasting some \$3 billion annually in the US. The issue is not just waste but the serious side-effects which the 98% of men being treated unnecessarily risk. Early and accurate diagnosis of aggressive prostate cancer will not only improve survival rates but also reduce greatly these unnecessary side effects and associated human and monetary costs.



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