Human genetics – mapping the future of medicine

Human genetics and drug discovery are now inextricably linked, with large pharmaceutical companies, small biotech and even academic laboratories turning to sequencing data to identify potential targets for new therapies. But is this information being used to the best effect? And does genetic testing have a role to play in helping today's patients as well as tomorrow's? Dr Pierre-Alain Menoud, Scientific Manager for Molecular Diagnostics at Unilabs in Lausanne, Switzerland, discusses the potential benefits of genetic testing for both the understanding and treatment of disease.

Dr Pierre-Alain Menoud, Scientific Manager for Molecular Diagnostics at Unilabs

When I started in molecular diagnostics in 2002, oncogenetics was still in its early days, with very few tests available. Despite this, there was huge interest in the potential of genetic testing for the diagnosis of various cancers – such as chronic myelogenous leukemia, prostate and lung cancers – and the field quickly evolved in terms of both diagnostic testing and pharmacogenetics. The sequencing of the human genome or genes related to cancers has undoubtedly led to a number of breakthroughs in the understanding and diagnosis of numerous cancers but, more importantly, continues to provide potential therapeutic targets and treatment strategies.

The success of pharmacogenetics approaches in oncology is well documented – the most famous example being the detection of HER2 over-expression for treatment with monoclonal antibody trastuzumab (Herceptin®) – with a huge potential market around the world. The high cost of most cancer therapies, combined with the range of adverse side effects and diversity of disease types, has made this type of genetic susceptibility testing (companion diagnostics) standard practice prior to commencing therapy for many cancers. Unfortunately, the use of pharmacogenetics is still relatively rare outside of oncology, despite the huge potential economic and patient benefits. The reasons for this are complex, but essentially come down to a combination of two factors: the relatively low cost of other therapeutics compared with chemotherapy agents, and a lack of understanding of the potential patient benefits among physicians.

One field which is just beginning to explore pharmacogenetics as a way of improving treatment is psychiatry. Many patients in this field receive long-term treatment in the form of antidepressants or antipsychotics, yet a large proportion respond poorly to treatment, either in terms of low efficacy or adverse side-effects. These issues can significantly impact on the patient's general health – leading to escalation of their condition, metabolic

complications or other, indirectly-related health problems – meaning there are large potential health and economic benefits to improving treatment strategies. As the cost of genetic testing continues to fall, both health insurance companies and healthcare providers are increasingly looking to pharmacogenetics to help individual patients, with many genetics laboratories reporting very high success rates for improving prescribing practices and patient outcomes for psychiatry.

Since the Human Genome Project first reported the complete mapping of the human genome in 2003, the general public has also become far more aware of genetic testing. In addition to the benefits offered by companion diagnostics, many patients are now looking for genetic 'explanations' of congenital disease, even those which do not yet have any known treatment strategies. Similarly, physicians are increasingly finding themselves relying on specialist molecular diagnostics facilities to provide insight into individual cases across a broad range of disciplines, helping to identify relevant genetic tests for everything from coagulation and anesthesia for surgical procedures to prenatal genetics and medically-assisted procreation.

The diverse range of medical specialties now served by genetic testing laboratories means that individual centers can no longer support the required level of expertise across every field. While each laboratory can provide expertise in one or two disease areas – more for large, centralized facilities such as Unilabs – no one center can maintain comprehensive knowledge of every genetic abnormality. Instead, laboratories need easy access to sequencing data, current understanding and prescribing practices from across the globe, to aid physicians and, ultimately, improve patient care. This is where the molecular diagnostics industry has a role to play. To fully benefit from the information that genetic testing – and particularly next generation sequencing – can provide, we need to develop systems that offer full data interpretation; taking the raw data from sequencers, automatically processing and analyzing it, then searching relevant databases to identify specific mutations, related scientific papers and even treatment strategies. This would not only provide physicians with the information required to act on the results they receive, but would also free up resources for more clinical research – further improving patient care in the long term.

At the other end of the spectrum, the ever-increasing demand for testing means that sample numbers will continue to rise steadily for molecular diagnostics laboratories around the globe. This requires high throughput, reliable automation of pre-analytical sample processing and set-up. While the liquid handling technologies required for this already exist, we need complete solutions that are reliable and easy to use, while still providing the flexibility necessary to work with various sequencing chemistries and assay technologies. NGS is just beginning to benefit from this approach, with automated library preparation now available, but even more needs to be done to provide user-oriented solutions that minimize turnaround times for analysis and the risk of human errors.

> "We need complete solutions that are reliable and easy to use."