The Odds of Survival: Targeting treatment for ovarian cancer

Key facts – Ovarian Cancer

- Ovarian cancer is the fifth most common cancer in UK women
- Every year there are many newly diagnosed cases:
  - 7,000 in the UK
  - 45,000 in the EU27
  - 225,000 worldwide
- Despite some progress, the 5-year survival rate remains low, at around 35%
- Clinicians lack tools for early detection and effective treatment

The Problem

Treatment for ovarian cancer has improved over the past 20 years, mainly as a result of improved surgery and the introduction of new chemotherapy drugs. Still, compared with improvements in survival rates for breast and colon cancer, progress has been modest. Why is this?

The main reason is that early diagnosis of ovarian cancer is difficult. To make matters worse, current chemotherapy has serious side effects and benefits only about 70% of patients. Identifying the patients for whom chemotherapy does not help would spare them unnecessary side effects and can guide them to alternative therapies.

Challenges ahead

A lot of research is required for the development of biomarkers that can indicate response to chemotherapeutic drugs. Although many gene sets have been identified, their ability to predict reaction to therapy is still inadequate for clinical use. Tumour genomes vary greatly and change quickly, and the molecular mechanisms behind drug resistance have not been fully explored. Consequently, the task of predicting likely therapeutic effects is particularly challenging.

Personalising treatment

Before submitting patients to severe therapeutics, it would be better to identify biological traits, or biomarkers, that indicate whether a patient will respond or not. Of particular interest are genes and proteins that have a role in drug resistance. Such genes could be used to test tissue samples in the clinic directly.

Novel technologies such as microarrays and next-generation sequencing make it possible to investigate the activity of the whole genome at one time. For instance, microarrays can inform us if genes are switched on (expressed) or off (idle). Similarly, proteomics methods measure the amount of active (phosphorylated) or inactive (unphosphorylated) protein. These techniques are particularly suitable for identifying biomarkers. They can be used to classify tumours based on which protein pathways are in use and the mutated genes they carry. Using this information, each patient can be guided to a tailored treatment.

Genomics research

Using microarrays, we have found genes that have important roles in drug resistance. Chemotherapy triggers a cascade of gene activity that changes dynamically over time. These genes operate together to modulate important cellular functions such as the cell cycle, DNA repair and apoptosis (cell suicide).

Sets of such critical genes are able to predict survival and drug resistance in patients.

Proteomics research

To gain a more detailed picture, we have also investigated activation of critical proteins. Several cell-signalling pathways, such as PI3K/AKT, Wnt and mTOR were activated at various time points after treatment.

Who are we?

Scientists and medics at the School of Biology at St Andrews, in collaboration with the Breakthrough Cancer Unit (Western General Hospital, Edinburgh), work together to discover biomarkers for chemotherapy resistance in ovarian cancer. Clinical, genomic and proteomic data from cancer samples are analysed using cutting-edge technologies and computational techniques.