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### Genomic biomarkers as predictors of response to immunotherapy

Beer, P A

Wellcome Trust Sanger Institute, UK

**N**ovel immune-oncology therapies have produced dramatic results for some cancer patients. Overall, however, only a small minority of patients derive benefit from these drugs, in the order of 10-15% of those treated. In addition, these agents are associated with significant toxicity due to unrestrained activity of the immune system. There is, therefore, a pressing clinical need to identify biomarkers to identify patients who are most likely to respond to these drugs. Several years' experience with molecularly-targeted anti-cancer therapies has taught us that the biological mechanisms of treatment response and resistance are usually genomically mediated and biologically constrained. Coupled with an understanding

of cancer as a Darwinian process, it is possible to leverage cancer genomic profiling to guide therapy. The same principles are also applicable to immunotherapy, with the cancer genome encoding diverse predictors of response and resistance, including mutational burden & profile, activity of the antigen presentation machinery and function of the intracellular interferon signaling pathway. This talk will examine the current state-of-the-art in genomic biomarkers for immunotherapy response in the light of lessons learned from both molecularly-targeted therapy and from a Darwinian understanding of cancer evolution.

[pbeer@doctors.org.uk](mailto:pbeer@doctors.org.uk)