

In the PROTEAN study we aimed to characterise the expression of proteins on the surface of oesophageal cancer cells that could be recognised by the immune system and hence be targets for cancer vaccines – a new treatment approach that aims to harness patients own immune system to control or eliminate their cancers and which has shown promising results but is dependent upon identifying the best possible targets, known as tumour specific antigens or neoantigens for the vaccines on the tumour cell surface. Current approaches identify these targets indirectly by inferring what they might be from gene mutations or the over expression of genes in cancers- this technique is known to be inefficient with o less than 1 in 10 neoantigens identified actually ending up being useful targets for cancer vaccines. We aimed to evaluate a new technique-mass spectrometry based immunopeptidomics that directly profiles the neoantigens themselves at the tumour cell surface- we hypothesised it would be more efficient than current approaches but it was uncertain if mass spectrometry base immunopeptidomics would be possible on small biopsies of tumours that available from routine diagnostic biopsies of Oesophageal cancer and hence whether it could be used in practice. In PROTEAN we obtained tumour biopsies from 86 patients with oesophageal adenocarcinoma and demonstrated that immunopeptidomics was successful in all cases 100%, thereby demonstrating that it is possible to perform this technique on routinely available diagnostic small tumour biopsies. The results also demonstrated that while there is some overlap the majority (>90%) of neoantigens on each patients are unique to that patients tumour- this suggests that in order to be the most effective they can be cancer vaccines may need to be personalised to the neoantigen targets present in each patients tumour. Interestingly we found that 19/20 neoantigens identified by immunopeptidomics would not have been identified by current approaches based on analysing gene mutations or gene expression (RNAS Seq) thereby demonstrating that immunopeptidomics appears to be a much more efficient way of detecting neoantigens . In summary this study has demonstrated the feasibility and usefulness of a new technique to identify targets for cancer immunotherapies including cancer vaccines, that is much more efficient at identifying the needed targets and we have described for the first time the neoantigen profiles of oesophageal adenocarcinomas, and how they vary from one patient to another. This will enable immunopeptidomics to be investigated further to accelerate the development of new more effective cancer immunotherapy treatments especially cancer vaccines including those personalised precisely against each patient tumour.