Scientists take step forward in understanding of oesophageal cancer

September 1 2017

Credit: University of Manchester

Scientists at The University of Manchester have identified some key factors that establish oesophageal cancer cells.

Professor Andy Sharrocks and his clinical collaborator Dr Yeng Ang led a team which used a new approach, looking for molecular signatures within the human genome which act as markers for cancer cells.

The signatures are able to define how the genes in oesophagus cancer are controlled and how this differs from normal oesophageal cells.

By using the information they identified which proteins are activated to drive oesophageal cancer.

The study is published in *PLOS Genetics* and was funded through a Manchester Cancer Research Centre (MCRC) clinical training fellowship to the lead author, Ed Britton, from Cancer Research UK.

And thanks to the work, the scene is set for a new branch of research which may be able to develop leads for generating targeted drug therapies.

Professor Sharrocks said: "Oesophageal adenocarcinoma, a type of oesophageal cancer, has an abysmal survival rate, partly because it is poorly understood at the molecular level. Few, if any, targeted therapies exist.

"It presents late and patients have to endure a brutal chemotherapy treatment regime.

"There has been little progress in understanding this cancer over many years, so we believe this approach might represent a major step forward."

Professor Sharrocks used a revolutionary technique called ATAC-seq which has the potential to reveal molecular changes in individual cancer cells. Previously, scientists were only able to analysis millions of cells at

a time.

Current approaches focus on identifying changes to the DNA code in oesophageal cancer cells. However, the DNA is tightly packed into the nucleus meaning that it is "insulated" from being activated.

The new technique looks at a novel aspect of changes that occur in cancer cells and interrogates the packaging itself. That allows identification of regions where DNA is exposed and hence potentially in an "active" form.

Professor Sharrocks added: "We have validated these results among other data sets by cross checking them and they confirm our findings.

"But most importantly, our research has been driven by data and not by inclination. Before the advent of approaches like ATAC-seq, scientists were forced to be selective in what they analysed. Now it is wholly more scientific."

Dr Catherine Pickworth, science information officer at Cancer Research UK, said: "By identifying two important molecules involved in the development of oesophageal cancer, this study uncovers potential new drug targets for one of the hardest cancers to treat. The next steps will be to find out if drugs can be developed to target these molecules, and if they can be used to treat people with the disease. Survival for oesophageal cancer remains stubbornly low and research like this that tells us more about how it develops is vital to building a full picture of the disease."

More information: Edward Britton et al. Open chromatin profiling identifies AP1 as a transcriptional regulator in oesophageal adenocarcinoma, *PLOS Genetics* (2017). DOI: 10.1371/journal.pgen.1006879