Medical Xpress

Study opens door to targeted treatments for esophageal cancer

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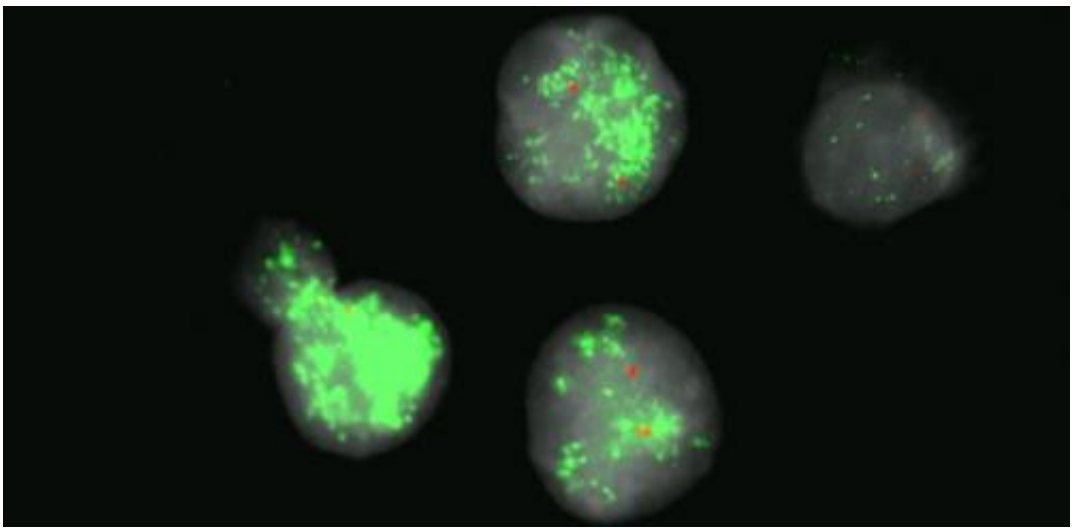

Multiple copies of the TRIM44 gene in an oesophageal cancer cell line. Credit: Professor Rebecca Fitzgerald and Dr Johnny Ong

Scientists have discovered that oesophageal cancer can be classified into three different subtypes, paving the way for testing targeted treatments tailored to patients' disease for the first time.

This discovery, published in *Nature Genetics* today, could help find drugs that target specific weaknesses in each subtype of the disease, which could make treatment more effective and boost survival.

The scientists, funded by Cancer Research UK and the Medical

Research Council, looked at the complete genetic make-up of 129 oesophageal cancers and were able to subdivide the disease into three distinct types based on patterns detected in the DNA of the cancer cells called signatures.

The first subtype they found had faults in their DNA repair pathways. Damage to this pathway is known to increase the risk of breast, ovarian and prostate cancers. Patients with this subtype may benefit from a new family of drugs called PARP inhibitors that kill cancer cells by exploiting this weakness in their ability to repair DNA.

The second subtype had a higher number of DNA mistakes and more immune cells in the tumours, which suggests these patients could benefit from immunotherapy drugs already showing great promise in a number of cancer types such as skin cancer.

The final subtype had a DNA signature that is mainly associated with the cell ageing process and means this group might benefit from drugs targeting proteins on the surface of the cancer cells which make cells divide.

Professor Rebecca Fitzgerald, lead researcher based at the MRC Cancer Unit at the University of Cambridge, said: "Our study suggests we could make changes to the way we treat oesophageal cancer. Targeted treatments for the disease have so far not been successful, and this is mostly down to the lack of ways to determine which patients might benefit from different treatments. These new findings give us a greater understanding of the DNA signatures that underpin different subtypes of the disease and means we could better tailor treatment.

"The next step is to test this approach in a clinical trial. The trial would use a DNA test to categorise patients into one of the three groups to determine the best treatments for each group and move away from a one-

size-fits-all approach."

Each year around 8,800 people are diagnosed with oesophageal cancer in the UK and just 12 per cent survive their disease for at least 10 years. Cancer Research UK has prioritised research into oesophageal cancer to help more people survive the disease by bringing people together, building infrastructure and developing the next generation of research leaders.

Professor Peter Johnson, Cancer Research UK's chief clinician, said: "Being able to distinguish distinct types of oesophageal cancer is a genuinely new discovery from this work. For the first time we may be able to identify and test targeted treatments designed to exploit the cancer's specific weaknesses. Although survival rates from oesophageal cancer have been slowly rising in the last few years they are still far too low, and this research points the way to a completely new way of understanding and tackling the disease."

More information: Secrier, M. et al. Mutational signatures in esophageal adenocarcinoma reveal etiologically distinct subgroups with therapeutic relevance *Nature Genetics*, 2016. nature.com/articles/doi:10.1038/ng.3659

Provided by Cancer Research UK