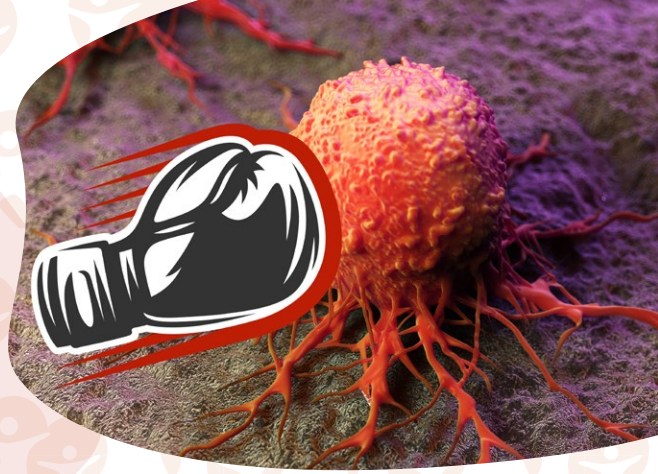


WHAT IF WE COULD FIND NEW TOOLS IN THE FIGHT AGAINST CANCER?



It's possible to speed up progress even more on targeted cancer treatments

Promise: Two teams of scientists led by the Wellcome Trust Sanger Institute and the Broad Institute have, with the help of CRISPR genome editing, built up a database that identified genes that could make for attractive drug targets.

Did you know? More than 1,300,000 people died of cancer in 2013 across all EU countries, making it the second leading cause of mortality. The research detailed here can contribute to the European research and innovation mission on cancer.

The people behind the solution:

"Thanks to CRISPR, we can provide guidance in a data-driven way and at genome-scale on what are the therapeutic targets worthy to be put forward for the development of the next generation of anti-cancer drugs."

Francesco Iorio,
Wellcome Sanger Institute

There are many types of cancer and many causes that lead to cancer, making the science of finding anti-cancer drugs a challenge. Nevertheless, scientists at the Wellcome Trust Sanger Institute and the Broad Institute succeeded in opening the door to treating a range of cancers by mapping dependencies between genes. CRISPR genome editing proved essential in this research by allowing a massive number of targets (genes) to be screened, selectively silencing these targets and recording the effect. Whereas not too long ago it took a whole PhD to silence a single target gene, in the study described here CRISPR took on 18 000 targets. CRISPR is a precision genetic engineering tool which allows scientists to change individual letters of the genetic code with high efficiency and relative ease.

The data gathered led to the discovery of a dependency between so-called MSI-high cancers and the Werner syndrome ATP-dependent helicase or WRN. Cancer arises when oncogenes (which are responsible for tumour formation) arise and tumour suppression genes are disrupted; both occur by way of mutation. Many oncogenes are mutated forms of normal genes involved in cell growth. Tumour suppression genes can be DNA repair genes, which prevent mutations and thereby prevent oncogenes from arising.

MSI-high cancers have a specific malfunctioning tumour suppression gene that causes "microsatellite instability". This form of DNA damage is easily identifiable and occurs in 15% of colon cancers, 22% of gastric tumours, at least 20% of endometrial cancers and 12% ovarian cancers. Now, thanks to the data collected, the researchers found that when the WRN gene was silenced in cell lines of these cancers the cells would die. The likely reason is that WRN was also involved in DNA repair and cells, even cancer cells, cannot survive without any DNA repair at all. In other words, there was a dependency on WRN in MSI-high cancers. What makes WRN an attractive drug target is that this dependency is common to many cancers and that it is synthetically lethal, meaning that cells die only when both the MSI-causing gene and the WRN gene are disrupted. This leaves healthy cells to go on with their normal life unharmed. However, notwithstanding this scientific discovery, still much work lies ahead before any drugs can be made available to patients.

Genome editing is

#InspiredByLife

Credit picture: Wellcome Sanger Institute, Genome Research Limited



REFERENCES:

<https://www.nature.com/articles/s41586-019-1103-9>
<https://www.nature.com/articles/s41586-019-1102-x>
<https://www.fiercebiotech.com/research/using-crispr-to-identify-new-cancer-drug-target>
https://www.eurekalert.org/pub_releases/2019-04/wtsi-ncd040919.php