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Marker found in one in six people could give higher risk of lung and other cancers

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Cancer Research UK scientists have discovered why a gene fault found in around one in six people gives a higher risk of 26 cancer types, according to research published today in *Nature Cell Biology*.

The team, from the Cancer Research UK and Medical Research Council Oxford Institute for Radiation Oncology at the University of Oxford, believe the error involving a gene called RASSF1A could trigger a wide range of cancers and cause resistance to radiotherapy and chemotherapy

treatments, making the cancer harder to treat.

They previously revealed that the gene may be 'switched off' in 17 per cent of people, putting them at a higher risk of cancer.

The researchers have now found that the gene fault works in a similar way to the well-known BRCA gene fault, which increases the risk of breast and some other cancers. They studied the gene fault in mouse cells and cancer cell lines. They found that when the gene, which manages the repair of DNA, is 'switched off', broken DNA cannot be fixed and cancer develops.

Like the BRCA gene, the fault in RASSF1A could help to identify those who will not benefit from chemotherapy or radiotherapy, ensuring they are provided with more appropriate targeted treatments.

Lead author, Professor Eric O'Neill, Cancer Research UK scientist at the Cancer Research UK and MRC Oxford Institute for Radiation Oncology, said: "This important discovery reveals how a single gene fault could trigger the development of a wide range of cancers, especially lung cancer. And crucially it behaves in a similar way to the breast cancer risk gene BRCA which we already know a lot about. This may mean that our progress in understanding how to target genetic faults in breast cancer may also have wider relevance for lung and other cancers.

"The next stage of our work will focus on unravelling if this new gene fault works alone or if it is triggered by environmental factors, like smoking."

Nell Barrie, Cancer Research UK's senior science information manager, said: "Finding the fundamental triggers behind the development of cancer can help us to understand its genetic bedrock, so we can target the

foundations of the disease.

"This important marker could be used to identify patients who will not respond to chemotherapy and radiotherapy, meaning we could divert them to tailored treatments much sooner and boost their chances of survival.

"Personalised approaches will one day enable doctors to treat people based on the genetic fingerprint of their tumour. And we're continuing to invest heavily into research in this area to boost every person's chance of surviving cancer."

More information: O'Neill et al. "RASSF1A–LATS1 signalling stabilizes replication forks by restricting CDK2-mediated phosphorylation of BRCA2." *Nature Cell Biology*. DOI: 10.1038/ncb3035

Provided by Cancer Research UK