Great genetic variation in pancreatic cancer, study shows

November 9 2010

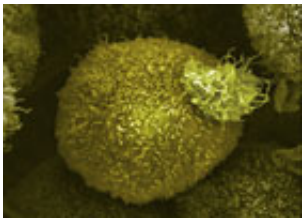

Image: Pancreatic cancer cell. Credit: Anne Weston, LRI, CRUK, Wellcome Images.

A new study published recently in *Nature* details the complexity of genetic variation found in pancreatic cancer cells. The ability to identify and understand the early mutations involved with the disease may lead to the discovery of new drug targets.

Around 97 to 98 per cent of people with pancreatic cancer die within five years of diagnosis. The disease is so deadly because it often exhibits no symptoms, and hence is only diagnosed when at an advanced stage.

The genetic changes behind pancreatic cancer are complex and varied, with tumour cells exhibiting a variety of genetic mutations. New research from scientists, including those from the Wellcome Trust Sanger Institute, sequenced the DNA from the primary and secondary tumours, known as metastases, of 13 patients in order to compare the mutations.

The sequencing revealed that 17 per cent of the genomic mutations were shown to cause a distinctive pattern of DNA rearrangement, which the researchers have termed a 'fold-back inversion'.

"Of all the types of cancer we've studied, this particular DNA rearrangement seems to be distinctive for pancreatic cancer," explains Dr. Peter Campbell, from the Wellcome Trust Sanger Institute, who led the research.

This fold-back inversion is caused when a DNA region is duplicated following a breakage. These breaks can occur repeatedly during cell division, leading to an explosion of genomic instability.

This instability is found early on in the development of pancreatic cancer and can lead to the incorrect expression and deletion of genes. Given the random nature of mutations, there can be huge genetic differences between cells in the same pancreatic tumour.

Once a pancreatic tumour cell has gained the necessary mutations, it is able to move around the body, forming metastases. What this research showed is that the cancer cells continue to mutate even after they have left the pancreas, potentially enabling the tumour cells to survive in other organs, such as the lungs or liver.

"Why would a pancreatic cell be able to survive in the lung? There's no reason for that to happen," asks Dr. Campbell. "Our results suggest the cancer cells do not stop evolving once they start invading tissue - metastases seem to be able to 'fine tune' their genome to be able to survive in different hostile environments," he adds.

More information: Campbell PJ, et al. The patterns and dynamics of genomic instability in metastatic pancreatic cancer. *Nature* 28 October 2010.