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Comprehensive analysis of the DNA methylation landscape in esophageal adenocarcioma and Barrett's esophagus

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This study describes the esophageal cancer methylation landscape and its impact on gene expression. Genes aberrantly methylated suggest a mechanism that could lead to genomic instability and chromothripsis. A CIMP-like subtype with potentially worse clinical outcome was also identified. The incidence of esophageal adenocarcinoma (EAC) has risen more than 600% in the last 30 years. EAC has a poor outcome with only 13-20% of patients surviving five years. Barrett's esophagus (BE) is a precancerous precursor of EAC. This is the first study to explore methylome, transcriptome and encode data to characterize the role of methylation in EAC. We investigate the genome-wide methylation profile of 125 EAC, 19 Barrett's esophagus (BE), 85 squamous esophagus and 21 normal stomach. Transcriptome data of 70 samples were used to identify changes in methylation associated with gene expression. BE and EAC showed similar methylation profiles, which differed from squamous tissue. Hyper-methylated sites in EAC and BE were mainly located in CpG-rich promoters. Genes aberrantly methylated showed enrichment for pathways involved in tumorigenesis including cell adhesion, TGF and WNT signaling. Also genes involved in chromosomal segregation and spindle formation were aberrantly methylated. The methylation profiles revealed two EAC subtypes, one associated with widespread CpG island hyper-methylation overlapping H3K27me3 marks and binding sites of the Polycomb proteins. These subtypes were supported by an independent set of 89 esophageal cancer samples. The most hyper-methylated tumors showed worse patient survival.

Biography

Lutz Krause undertook his undergraduate studies in Computer Science and completed his PhD in Bioinformatics and Genome Research. In 2008 he has joined the Nestle in Lausanne, Switzerland, where he studied the role of the gut microbiota in health and disease. In 2010 he moved to Australia to the QIMR Berghofer Institute and in 2014 he joined the University of Queensland Diamantina Institute, to pursue his research on biomarker discovery and genetics of complex diseases. In collaboration with the Princess Alexandra Hospital, his research aims at the identification of biomarkers that help clinicians choosing the optimal treatment for individual EAC patients.

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