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QUANTITATIVE PROFILING OF HISTONE MODIFICATIONS REVEALS A TUMOR MIGRATION-BIOMARKER IN ESOPHAGEAL SQUAMOUS CELL CARCINOMA

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Esophageal squamous cell carcinoma (ESCC) is one of the most aggressive cancers worldwide (five-year survival rate of only 10%). Unfortunately, such low outcome has only been slightly improved over the last decades. Unlike other tumor types, the molecular mechanisms of ESCC migration remain mostly unexplored. Histones post-translational modifications (PTMs) have been thought to be a group of epigenetic code and abnormal histone PTMs would contribute to cancer propagation. Here, we developed an integrated analysis method and performed a comprehensive profiling of histone PTMs in a paired cell lines, namely nonmalignant human esophageal epithelial cell line SHEE and its malignantly transformed counterpart SHEEC, to investigate potential histone marks related with tumor migration. In total, 11 histone modification types were mapped to 138 amino acid sites on histones, including low abundance of lysine butyrylation, 2-hydroxyisobutuylation, crotonylation, malonylation, and succinylation. 253 different modified histone peptides were further quantified, 17 of which were significantly distinguished between two cell lines. Moreover, we analyzed the relationship between histone PTMs and their regulatory enzymes by combining transcriptome and PTM analysis. Importantly, we found and confirmed that histone H4K20me2 is a unique mark that may be associated with cell migration of ESCC. Finally, this histone mark is confirmed in primary ESCC specimens, implying a possible histone PTM as a biomarker for ESCC diagnosis and treatment.

Biography

Kai Zhang has completed his PhD in 2003 from Nankai University and Postdoctoral studies from ENSCP (Paris), Washington State University, University of Texas Southwestern Medical Centre at Dallas and The University of Chicago. Now he is a Full professor in Tianjin Medical University. He has published more than 60 papers in professional journals such as Angewandte Chemie International Edition, Analytical Chemistry and Molecular and Cellular Proteomics. His current research interest mainly focuses on developing novel mass spectrometry-based proteomics technologies for reliable, sensitive, and comprehensive analysis of proteins and post-translational modifications (PTMs) to decode protein PTM networks and pathways for human health and for biomarker discovery.

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