14th Euro-Global Gastroenterology Conference

July 08-09, 2019 | Zurich, Switzerland

Toward understanding the molecular basis of esophageal squamous cell carcinoma

Ming Rong Wang
Cancer Institute and Hospital-CAMS & PUMC, China

Esophageal squamous cell carcinoma (ESCC) is among the most common human cancers, with an overall five-year survival rate of around 20%. To improve the diagnosis and prognosis of ESCC, we performed systematic studies on the molecular alterations in the disease. Frequent gains of chromosomal bands 3q26, 8q24, 11q13, losses of 3p14 and 9p21, amplifications of genes CCND1, EMS1 (CTTN), EGFR, PLK1, SKP2, PRKCI (PKCiota), deletions of CDKN2A/B, FHIT and rearrangements of NTRK3, DTL and PTPRD were found. The mutation profiling was characterized and potential therapeutic targets were identified. We further investigated intratumor heterogeneity (ITH) of the molecular alterations and constructed phylogenetic trees for genomic evolution, in which the mutations of ERBB4, FGFR2, BRCA2, ATM, TP53 and copy number changes of 11q13 and 9p21 were early events and those of PI3K/MTOR pathway, KIT, AURKA, CCND2 and 3q26 were late. By proteomic techniques and immunohistochemistry, multiple proteins were observed with high expression in tumor tissues but negative/low expression in morphologically normal operative margins. Especially, copy number alterations of ANO1, CDKN2A, and high expression of p63 and ANO1 were also present in precancerous lesions (dysplasia). We further explored the mechanisms underlying the development and progression of ESCC and revealed that CRT, CTTN, PKCiota, SKP2 and PLK1 enhanced cell motility and resistance to apoptosis and promoted tumor growth and metastasis via activating the PI3K-AKT pathway, inhibiting beta-catenin degradation and up-regulating the apoptosis suppressor Survivin. These findings extend our understanding of ESCC, providing theoretical foundation for elucidating the mechanisms underlying the tumorigenesis of the esophagus and progression of ESCC and for developing classification biomarkers and therapy targets for ESCC treatment.

wangmr2015@126.com