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SPP1 overexpression is associated with poor outcomes in ALK fusion lung cancer patients without receiving targeted therapy

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The screening of non-small cell lung cancer (NSCLC) tumors for anaplastic lymphoma receptor tyrosine kinase (ALK) gene rearrangements is important because of the dramatically favorable therapy response to ALK inhibitor. However, the exact mechanism of poor survival in ALK fusion lung cancer patients without receiving targeted therapy is unclear. In this study, total of 521 tumor specimens from Chinese patients with lung cancer were screened for ALK fusion by immunohistochemistry (IHC) and confirmed by fluorescence in situ hybridization (FISH). As results, there were no cases of coexisting EGFR and ALK mutations identified. Fourteen cases (2.7%) harbored ALK fusion, including eight solid adenocarcinomas with signet ring cell features, four acinar adenocarcinomas with cribriform pattern containing mucin, one adenosquamous carcinoma and one micropapillary adenocarcinoma with mucin. Six (42.9%) of fourteen patients with ALK-positive lung cancer had stage disease, and five ALK-positive patients treated with platinum-based chemotherapy had poor outcome (all patients were dead and the mean survival time was 12 months), compared to 72 months for patients with ALK inhibitor therapy. Furthermore, Five ALK-positive cases were analyzed by whole exome sequencing (WES) and via direct transcript counting using a digital probe-base (NanoString) to explore the driver genes. Deregulation of PI3K/AKT signaling pathway in ALK-positive lung cancer was demonstrated by WES analysis, and significantly increased mRNA of ALK, ROS1, MET, SPP1 and PI3K signaling pathway was identified by NanoString assay. The concordance between NanoString, IHC and FISH methodologies for detecting ALK fusion was 100%. Significant overexpression of SPP1 protein in ALK-positive lung cancer was confirmed by IHC compared to paired adjacent normal tissues and ALK-negative cancers. Thus we concluded that SPP1 overexpression is associated with poor outcomes for patients with ALK fusion lung cancer without receiving targeted therapy and PI3K/AKT/SPP1 pathway may become the promising targets in patients with aggressive lung cancer.

Biography

Dr. Fei Pei obtained her ph.D degree in medicine from department of Pathology, School of Basic Medical Sciences, Third Hospital, Peking University Health Science Center, Beijing, China in 2004. Currently Dr. Pei is a research and clinical associate professor and Co-PI of Peking University Health Science Center. Her research interests mainly lie in the fields of cancer biology. She has published more than 20 scientific publications since 2011.