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CPE-deltaN : a powerful diagnostic and predictive biomarker for metastasis in different types of human cancers

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Abstract

Metastasis is a major cause of mortality in cancer patients. Currently, few accurate biomarkers exist for predicting future metastasis to guide therapy. Here we report that CPE-deltaN, a splice isoform of the carboxypeptidase E gene is a prognostic biomarker. CPE-deltaN drives metastasis by interacting with histone deacetylase 1/2 to up-regulate expression of metastatic gene Nedd9. CPE-deltaN mRNA is elevated in human metastatic colon, breast, prostate, head and neck, glioblastoma and HCC cell lines. In clinical studies on 99 patients with hepatocellular carcinoma (HCC), a common cancer worldwide, CPE-deltaN mRNA quantification in the resected primary tumor (T) and normal surrounding tissue (N) established a T/N cut off value which predicted future intra-hepatic metastasis at 2 years with high sensitivity (92%) and specificity (76%), independent of cancer stage (J. Clin. Invest. 121:880-892, 2011). Additionally, a study on 68 patients with colorectal cancer showed that T/N of CPE-□N mRNA above the cutoff accurately diagnosed metastatic tumors. In another study, resected PHEO/PGLs having very high CPE-deltaN mRNA copy numbers accurately predicted future metastasis or recurrence in patients diagnosed with benign tumors at time of surgery, versus low copy numbers in post surgery, disease-free patients, with sensitivity and specificity values of 100%. Thus CPE-deltaN is a powerful biomarker for diagnosing and predicting future metastasis and recurrence in HCC, PHEO/PGL and colorectal carcinoma patients, superior to the histopathological diagnosis currently available. On-going clinical studies suggest that CPE-deltaN is a prognostic biomarker for other types of cancers as well which will be discussed.

Biography

Dr. Y. Peng Loh completed her PhD from the University of Pennsylvania, PA., in Molecular Biology and did postdoctoral studies at the National Institutes of Health and the Max Planck Institute in Germany. She is the Head of the Section on Cellular Neurobiology, NICHD, National Institutes of Health, USA. She has published more than 200 papers in reputable journals and book chapters and serves on the editorial board of several journals. She has also won prestigious awards including the FASEB Excellence in Science Award and NIH Director's awards for her Science and Mentoring.