The phosphorylation-specific association of STMN1 with GRP78 promotes metastasis in breast cancer

Abstract

Stathmin1 (STMN1), which exhibits a complicated phosphorylation pattern in response to various extracellular signals, is associated with cancer metastasis, but the involved signaling mechanisms are poorly defined. In this context, we found that phosphorylation of STMN1 at Ser25 and Ser38 was specifically required to maintain cellular migration capability and associated with a poorer disease-free survival (DFS) in breast cancer. In addition, glucose-regulated protein of molecular mass 78 (GRP78) was identified as a novel phospho-STMN1 associated protein based on the STMN1 Ser25/Ser38 phosphorylation. This phosphorylation-dependent interaction is regulated by MEK kinase, and required for STMN1-GRP78 complex stability and STMN1-mediated migration. In respect of its clinical signature, a prognostic model based on phospho-STMN1 and GRP78, which was more accurate than the TNM staging system, was established to assess individuals' metastatic risk for patients with breast cancer. Collectively, our findings document roles of phosphorylation states of STMN1 in associating with GRP78 and promoting metastasis in breast cancer, providing the clinical insights of cancer-specific modifications in malignancies.