

Dual-specificity phosphatase 6 (DUSP6): a review of its molecular characteristics and clinical relevance in cancer

ABSTRACT

Mitogen-activated protein kinases (MAPKs) are the main regulators of cellular proliferation, growth, and survival in physiological or pathological conditions. Aberrant MAPK signaling plays a pivotal role in carcinogenesis, which leads to development and progression of human cancer. Dual-specificity phosphatase 6 (DUSP6), a member of the MAPK phosphatase family, interacts with specifically targeted extracellular signal-regulated kinase 1/2 via negative feedback regulation in the MAPK pathway of mammalian cells. This phosphatase functions in a dual manner, pro-oncogenic or tumor-suppressive, depending on the type of cancer. To date, the tumor-suppressive role of DUSP6 has been demonstrated in pancreatic cancer, non-small cell lung cancer, esophageal squamous cell and nasopharyngeal carcinoma, and ovarian cancer. Its pro-oncogenic role has been observed in human glioblastoma, thyroid carcinoma, breast cancer, and acute myeloid carcinoma. Both roles of DUSP6 have been documented in malignant melanoma depending on the histological subtype of the cancer. Loss- or gain-of-function effects of DUSP6 in these cancers highlight the significance of this phosphatase in carcinogenesis. Development of methods that use the DUSP6 gene as a therapeutic target for cancer treatment or as a prognostic factor for diagnosis and evaluation of cancer treatment outcome has great potential. This review focuses on molecular characteristics of the DUSP6 gene and its role in cancers in the purview of development, progression, and cancer treatment outcome.

Keyword: Dual-specificity phosphatase 6; MAPK signaling; Cancer; Chemoresponsiveness; Chemoresistance