LETTER to the EDITOR

Stathmin 1, a Therapeutic Target in Esophageal Carcinoma?

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Dear Editor

I read with great interest the article by Wang and colleagues (Wang et al., 2014), which investigated the impact of Stathmin 1 expression in outcome of a cohort with 100 esophageal carcinoma patients and found that high levels of Stathmin 1 was associated with low differentiated tumors, invasion, metastasis, higher tumor grade and negatively impacted survival. Several studies converge with the findings reported by Wang and colleagues and provide important evidences of the participation of Stathmin 1 in malignant phenotype of esophageal carcinoma.

Stathmin 1 (also known as Oncopotein 18, OP18) is a polypeptide with 18 kDa, which acts as a microtubule-destabilizing protein, integrates multiple signaling pathways, and providing cell cycle progression, survival and migration (Belletti and Baldassarre, 2011). The first evidence that Stathmin 1 has a role esophageal carcinoma was the identification of a gain-of-function mutation in STMN1 gene (Q18E) in esophageal carcinoma samples, and its mutation presented a potential for *in vitro* and *in vivo* malignant transformation (Misek et al., 2002). Latterly, Holmfeldt and colleagues reported that STMN1 Q18E mutation contributes to chromosomal instability (Holmfeldt et al., 2006).

Using 2-DE and immunohistochemistry analysis, Liu and colleagues (Liu et al., 2013) reported that Stathmin 1 was highly expressed in 101 out of 143 esophageal carcinoma samples and found an association with the tumor grade: high Stathmin 1 expression was found in the highest tumor grade. Interestingly, Stathmin 1 silencing reduced the migration capacity of the esophageal carcinoma cell lines (Liu et al., 2013). Accordingly, studies performed by Wang and colleagues (Wang et al., 2011) and by Akhtar and colleagues (Akhtar et al., 2014b) demonstrated that Stathmin 1 silencing is able to reverse the malignant phenotype of esophageal carcinoma cells, including reduced cell proliferation, cell cycle progression, migration, invasion and tumorigenicity, and increased apoptosis.

Recently, Akhtar and colleagues (Akhtar et al., 2014a; Akhtar et al., 2014b) also provides additional evidences of Stathmin 1 role in the esophageal carcinoma. Stathmin 1 overexpression was found in 100 out of 174 pN0 esophageal carcinoma patients and Stathmin 1 was an independent predictor factor for lymphatic metastasis recurrence (Akhtar et al., 2014a). In addition, Stathmin 1 overexpression was observed 31 out of 63 distal esophageal adenocarcinoma patients and it was associated with lymph node metastasis and high tumor grade (Akhtar et al., 2014b).

In order to verify whether Stathmin 1 could be a target in cancer, several groups have proposed different approaches in attempts to inhibit Stathmin 1 function *in vivo* and the results have been promises. For instance, the GDP366, a dual inhibitor for Stathmin 1 and Survivin, reduced dramatically the malignant phenotype of cancer cells *in vitro* and *in vivo* (Shi et al., 2010). In another study, Phadke and colleagues (Phadke et al., 2011), using small hairpin RNA approach in vivo, showed that inhibition of Stathmin 1 reduced xenograft tumor growth in a mice model. Accordingly, Akhtar and colleagues (Akhtar et al., 2014c) tested the local injection of lentivirus-delivered shRNA targeting Stathmin 1 as approach, and found a significant regression in the cell growth of pre-established xenograft tumors in mice.

Collectively, these studies point out Stathmin 1 as a potential prognosis marker and a promising therapeutic target in esophageal carcinoma. Although novel strategies targeting in Stathmin 1 had been developed and applied to other types of cancer, the application of these strategies in the esophageal carcinoma models are of interest and require future investigation.

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