The emerging role of aquaporin 5 (AQP5) expression in systemic malignancies

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To the editor,

We read with great interest the recent article entitled “AQP5 silencing suppresses p38 MAPK signaling and improves drug resistance in colon cancer cells” published in *Tumor Biology*, identifying that aquaporin 5 (AQP5) can participate in mediating colon cancer pathogenesis and drug resistance as well as recurrence in colon cancer [1]. To date, AQP5, ubiquitously found in mammalian cells such as mammary gland, is a membrane of transmembrane proteins that play significant roles in water and small solute transport across epithelial and endothelial barriers [2]. Interestingly, emerging data suggests that AQP5 expression may participate in the growth and progression of a number of systemic malignancies besides colon cancer [1].

In mammary malignancies, for instance, Lee et al. [3] in a recent study of AQP5 expression in individuals with early breast cancer (EBC) reports that nearly 60 % of the patients were immune-positive for AQP5. Simultaneously, AQP5 overexpression was significantly connected with survival for the patients with estrogen receptor/progesterone receptor-positive and human epidermal growth factor receptor 2-overexpressed EBC. AQP5 may be an independent prognostic marker of survival for the EBC patients after curative surgery. Similarly, another study [4], conducted in Chinese populations to explore the expression profile of AQP0-12 in breast cancer tissues and corresponding normal tissues, concluded that AQP5 was expressed mainly in cell membranes within cancer tissues, but absent in normal breast tissues. In addition, AQP5

expression was associated with cellular differentiation, lymph node invasion, and tumor staging. Similarly, a study by Jung et al. have found that AQP5 expression in breast cancer cells with the loss of polarity of ductal epithelial cells was seen during the progression of breast carcinoma [5]. Moreover, the tumor proliferation and migration were markedly attenuated secondary to shRNA-induced or hyperosmotic stress-induced reduction of AQP5 expression. Ultimately, it comes to a conclusion that AQP5 may exert effects on breast cancer cell growth and metastasis.

In esophageal malignancies, for instance, in esophageal squamous cell carcinoma (ESCC), AQP5 expression is also high. The silence of AQP5 expression can inhibit the tumor proliferation and G1-S phase progression [6]. Induction of apoptosis accompanies the above changes. Furthermore, the AQP5 siRNA-transfected tumor cells show significant increase in p21 and decrease in CCND1 mRNA expression, indicating that AQP5 expression may modulate cell proliferation and survival as well as prognosis of ESCC. Interestingly, a recent study discovers that co-expression of AQP3 and AQP5, not each alone, is correlated with advanced invasion depth, aggressive lymph node status, and positive distant metastasis, together with the poor prognosis in overall and disease-free survival [7], demonstrating for the first time that combined detection of the expression of AQP3 and AQP5 may help to predict the progression and the prognosis of ESCC patients.

A similar expression of AQP5 is seen in lung malignancies. It augments MUC5AC and MUC5B mucin production via mediating the epidermal growth factor receptor (EGFR) signaling pathway, which may play fundamental roles in enhancing metastasis potential in lung adenocarcinoma [8]. Similarly, AQP5 also can increase the potential of tumor proliferation and metastasis in lung malignancies. It mediates these effects by virtue of activation of the EGFR/ERK/p38 MAPK signaling pathway [9]. As a result, the expression of proliferating

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cell nuclear antigen and c-myc, good markers for cell proliferation, are accentuated.

The above examples clearly illustrate the significant role of AQP5 in tumor growth and progression in systemic malignancies. Further studies are needed to identify agents that may mediate AQP5 expression and thereby may be of benefit in mitigating AQP5-induced tumor growth and progression in systemic malignancies.

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Conflicts of interest None

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