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Comment on:

Functional MUC4 suppress epithelial-mesenchymal transition in lung adenocarcinoma metastasis. Gao L, Liu J, Zhang B, Zhang H, Wang D, Zhang T, Liu Y, Wang C. Tumour Biol. 2013 in press

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To the editor,

Gao and collaborators have investigated the role of MUC4 in lung cancer and have concluded that loss of MUC4 results in epithelial mesenchymal transition via beta catenin nuclear translocation and that MUC4 expression is correlated with a risk of lymph node metastasis in a 20 lung adenocarcinoma patients cohort [1]. This surprising analysis is contradictory to most of the scientific knowledge and literature regarding MUC4 contribution in epithelial cancers that is very hardly discussed in their manuscript.

MUC4 was originally identified and characterized in our laboratory [2, 3]. Research conducted in mucin laboratories around the world has clearly documented MUC4 roles in

numerous cancers from different organs such as ovary, pancreas, oesophagus or lung. It is now established that MUC4 plays an important role in the behaviour of epithelial tumor cells. Inhibition of MUC4 expression by siRNA or stable ShRNA leads to reduced proliferation, motility, and increased cellular aggregation or chemoresistance [4-9].

Notably, MUC4 was previously suggested as an oncomucin in lung cancer. High MUC4 expression in small-sized lung adenocarcinomas correlates with a poor survival rate in a 185 patients cohort [10]. Analysis of another important cohort of 100 non-small cell lung carcinomas (NSCLCs) showed that MUC4 represses apoptosis [11]. Gao et al do not confront their results to already published literature in that matter.

The relationship between MUC4 and EMT is also conflicting since MUC4 was shown to suppress EMT in lung adenocarcinoma in the present study [1] whereas MUC4 overexpression in ovarian cancer leads to decreased expression of epithelial markers and occurrence of mesenchymal markers *via* upregulation of Twist1, Twist2 and Snail transcription factors and FAK signalling pathway [12]. Collectively, these results mean that MUC4 may regulate EMT in both ways.

Altogether, this clearly illustrates that caution should be kept as to using MUC4 as a marker of favourable prognosis because of the conflicting reports regarding both its involvement in tumor progression in lung cancer and more specifically in EMT and subsequent metastasis.

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