

DZL News

„BAMBI“– a potential new therapeutic target for non-small-cell lung cancer

Characteristic for non-small-cell lung cancer (NSCLC) is early metastatic disease and high mortality. Researchers at the German Center for Lung Research (DZL), located at the Airway Research Center North (ARCN) and the Translational Lung Research Center Heidelberg (TLRC), have identified a potential new therapeutic target for NSCLC. It is based on the differential regulation of the TGF- β signaling pathway by its pseudo-receptor BAMBI. The study is published today in the online issue of *Cancer Research*.

The endogenous protein TGF- β (Transforming Growth Factor β) exerts a dual role in carcinogenesis. In normal cells and early carcinoma, TGF- β acts as a tumor suppressor by promoting programmed cell death of malignant cells. However, as the tumor progresses TGF- β signaling switches to promote cancer progression, invasion, and tumor metastasis. In this study, the TGF- β signaling pathway was shown to be activated in lung tumor tissue obtained from late stage NSCLC patients and dysregulation of various target genes was observed, which in turn resulted in an increased metastatic potential of cells. It was demonstrated that depending on the expression level of the negative regulator of the TGF- β signaling cascade, the pseudo-receptor BAMBI, the activation of the signaling cascade is reduced. As BAMBI was much less expressed in NSCLC lung tumor tissue, it is proposed that this promotes the activation of the TGF- β signaling cascade and thus tumor progression. Further investigations into the reasons for the reduced expression of BAMBI in lung tumor tissue, suggested that increased DNA-methylation is responsible for the silencing of the gene that expresses BAMBI.

So, what happens if BAMBI is restored in tumor cells? May these tumor cells lose their malignant potential? These questions were addressed in further cancer cell lines and animal model experiments. In cancer cell lines, restoration of BAMBI resulted in a reduced invasiveness of tumor cells. "These results demonstrate the importance of quantitative time-resolved examinations to unravel key mechanisms that contribute to cancer progression" states Ursula Klingmüller (German Cancer Research Center, Heidelberg). In an animal model, injection of cells with restored BAMBI function resulted in fewer and smaller tumors. In summary "our findings suggest that blocking the TGF- β signaling pathway provides a new option for treatment of lung cancer" says Torsten Goldmann (Leibniz Research Center, Borstel), who jointly led this project with Ursula Klingmüller.

The study published in Cancer Research is the result of a successful cooperation along the translational chain between ARCN and TLRC, both members of the German Center for Lung Research (DZL). On the part of ARCN, scientists at the Leibniz Research Center in Borstel, the LungenClinic in Grosshansdorf and the University Hospital Schleswig-Holstein in Kiel contributed to this project. On the part of the TLRC, scientists at the German Cancer Research Center (DKFZ), Heidelberg University and University Hospital Heidelberg contributed to this project.

Further Information: Marwitz S, Depner S, Dvornikov D, Merkle R, Szczygiel M, Müller-Decker K, Lucarelli P, Wäsch M, Mairbäurl H, Rabe KF, Kugler C, Vollmer E, Reck M, Scheufele S, Kröger M, Ammerpohl O, Siebert R, Goldmann T, Klingmüller U (2016) Downregulation of the TGF- β pseudoreceptor BAMBI in non-small cell lung cancer enhances TGF- β signaling and invasion. *Cancer Research* 2016 May 17 [Epub ahead of print]

External link to the article: <http://cancerres.aacrjournals.org/content/early/2016/05/17/0008-5472.CAN-15-1326>