Author's response to reviews

Title: IGF-I induced genes in stromal fibroblasts predict the clinical outcome of breast and lung cancer patients

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Dear Editor

Please find attached our manuscript “IGF induced genes in stroma fibroblasts predict the clinical outcome of breast and lung cancer patients” which we would like to submit for publication in “BMC Medicine” as a research article.

IGF-I has multiple effects on tumor initiation, development and progression and its effects on the cancer cells have been well described. However solid tumors consist not only of malignant epithelial cells but rather form organ like structures with a stroma consisting of fibroblasts, inflammatory cells and endothelial cells. An endocrine or paracrine stimulus like IGF-I therefore might influence both: the tumor cells and the stromal cells. The goal of this study was to characterize the effects of IGF-I on the cancer cells and the stromal fibroblasts in parallel. To this aim, we used an ex vivo culture model to simulate the effects of IGF-I on tumor cells and primary stromal fibroblasts and determined associated gene expression changes with cDNA microarrays. On the molecular level, cancer cells and fibroblasts showed common and distinct response patterns to stimulation with IGF-I. Interestingly a set of genes induced by IGF-I in the stromal cells proofed to have a high prognostic power in early stage and metastatic breast cancer and also in adenocarcinomas of the lung, indicating that it plays an important role in some but not all of the tumors of different tumor entities.

We think these results might be of interest to the readers of BMC Medicine because for the first time we systematically characterize the effects of IGF-I stimulation on global gene expression in primary fibroblasts from the human breast and from breast cancer. Considering the emergence of anti-IGF targeted therapies we think that an in vitro model linked to a prognostic gene expression signature might be of interest not only for modeling the effects of IGF blockers on the tumor stroma, but also as a baseline to test it as predictive marker to select patients deriving a benefit form these therapies, since it might represent the effect of an activated IGF-I signaling axis.

Thus, our manuscript should be of equal interest to researchers studying cancer genomics, specifically the genomics of the tumor stroma or global gene expression profiling in breast cancer and lung cancer and researchers interested in cancer cell biology.

With the hope that our manuscript is of interest to BMC Medicine, I remain