LOSS OF THE KERATIN CYTOSKELETON IS NOT SUFFICIENT TO INDUCE EPITHELIAL MESENCHYMAL TRANSITION IN A NOVEL KRAS DRIVEN SPORADIC LUNG CANCER MOUSE MODEL

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Epithelial-to-mesenchymal transition (EMT), the phenotypical change of cells from an epithelial to a mesenchymal type, is thought to be a key event in invasion and metastasis of adenocarcinomas. These changes involve loss of keratin expression as well as loss of cell polarity and adhesion. We here aimed to determine whether the loss of keratin expression itself drives increased invasion and metastasis in adenocarcinomas and whether keratin loss leads to the phenotypic changes associated with EMT. Therefore, we employed a recently described murine model in which conditional deletion by Cre-recombinase leads to loss of the entire keratin multiprotein family. These mice were crossed into a newly generated Cre-recombinase inducible KRAS-driven murine lung cancer model to examine the effect of keratin loss on morphology, invasion and metastasis as well as expression of EMT related genes in the resulting tumors.

We here clearly show that loss of a functional keratin cytoskeleton did not significantly alter tumor morphology or biology in terms of invasion, metastasis, proliferation or tumor burden and did not lead to induction of EMT. Further, tumor cells did not induce synchronously expression of vimentin, which is often seen in EMT, to compensate for keratin loss. In summary, our data suggest that changes in cell shape and migration that underlie EMT are dependent on changes in signaling pathways that cause secondary changes in keratin expression and organization. Thus, we conclude that that loss of the keratin cytoskeleton per se is not sufficient to causally drive EMT in this tumor model.