High DDR1 mRNA and protein expression across human tumor types correlate with epithelial composition of the tumor microenvironment

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Background
Discoidin Domain Receptor 1 (DDR1) is a collagen-binding receptor tyrosine kinase expressed by tumor cells which has been implicated in cancer invasion, progression, and immune exclusion. A first-in-human trial of a DDR1-targeted therapy is underway. The relationship between *DDR1* mRNA, DDR1 protein, and the epithelial composition of the tumor microenvironment across tumor types has not been established and has the potential to influence indication and patient selection for DDR1-targeted therapies.

Methods
Human tumor samples (n= 93) from a range of epithelial and non-epithelial tumor types were evaluated by bulk RNA-sequencing and multiplex immunofluorescence (mIF) of DDR1 and pan-cytokeratin (CK). Tumor-stromal segmentation was determined by image analysis for epithelial tumors with epithelium defined by CK positivity in the tumor bed. Correlative analyses were done to relate *DDR1* mRNA expression to DDR1+ cell density, proportion of tumor cells expressing DDR1, and proportion of tumor epithelium.

Results
A high proportion of tumor cells (median of >0.7) expressed DDR1 across all epithelial tumor types. DDR1 expression was uniformly low in non-epithelial tumors evaluated (desmoid tumors, additional indications forthcoming). Moderate correlation was observed between *DDR1* mRNA expression and DDR1+ cell density across tumor types ($R=0.31$, $p<0.01$). In epithelial tumors, both *DDR1* mRNA and protein were correlated with the percentage of epithelium ($R=0.30$ and 0.46, respectively; both $p<0.01$), with significant variance between tumor types.

Conclusion
DDR1 is expressed in a high proportion of tumor cells across a range of epithelial tumor types, suggesting potentially broad application of DDR1-targeted therapies. As expected, since DDR1 is primarily expressed by tumor cells, both mRNA and protein expression levels are correlated with the proportion of tumor epithelium. The degree of correlation between *DDR1* mRNA and protein appears to be tumor type specific, possibly due to differences in DDR1 protein density in DDR1+ cells and/or contamination of bulk RNA with adjacent tissue. Assessment of DDR1+ cell density may be more accurate for patient selection in certain tumor types.