Hedgehog inhibition results in the upregulation of pro-tumourigenic αvβ6 integrin expression and function in cancer

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OBJECTIVE: Aberrant Hedgehog (Hh) signalling has been reported in a number of cancers, and Hh inhibitors are in clinical trials. We have previously reported αvβ6 integrin upregulation in cancer. The objective of this study was to examine the relationship between Hedgehog signalling and αvβ6 integrin.
STUDY DESIGN:To examine a link between Hh and αvβ6, we overexpressed Gli1 in immortalised keratinocytes. Three-dimensional organotypic assays were used in vitro; and archival human clinical samples were used for in vivo studies.

RESULTS: Suppressing Gli1 significantly increased αvβ6 expression, promoting tumour cell motility and stromal myofibroblast differentiation. In vitro findings were supported using human clinical samples, where αvβ6 and Gli1 were inversely expressed in different cancer types.

CONCLUSIONS: Gli1 and αvβ6 are inversely expressed in tumours, and Hh targeting promotes pro-tumourigenic cell functions in vitro. This may have clinical significance, given the incidence of secondary malignancies (including head and neck cancer) in patients treated by Hh inhibitors.