Use of Optical Imaging to Predict Tumor Response to anti-EGFR Therapy

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Objective: Current treatment with anti-epidermal growth factor receptor (anti-EGFR) antibody is costly and there are few predictors to determine which patients will respond to therapy. The purpose of this study is to assess whether optical fluorescent imaging can be used to predict tumor response to anti-EGFR treatment.

Study Design: Murine model using head and neck squamous cell carcinoma (HNSCC) xenografts and in vitro imaging of those cell lines.

Methods: SCID mice were xenografted with SCC-1, FaDu, and CAL27 tumor cells and treated with anti-EGFR antibody, cetuximab, to evaluate tumor response. Imaging was performed after systemically injecting the fluorescently labeled bioconjugate cetuximab:Cy5.5 prior to treatment and at four weeks after initial treatment. Fluorescence intensity was determined for each image. To evaluate in vitro fluorescent internalization pattern, the same cell lines were labeled with cetuximab:Cy5.5 and imaged.

Results: In vivo, SCC-1 tumor response was greatest, followed by FaDu and CAL27, with SCC-1 tumors being significantly smaller than control (P=0.0001). In addition, SCC-1 fluorescence was significantly greater than both FaDu and CAL27 (P<0.001). Tumor response corresponded with optical fluorescent intensity. In vitro, cells were evaluated for fluorescence internalization pattern. CAL27, which responded poorly in vivo, demonstrated the greatest internalization followed by FaDu (P<0.05) and SCC-1 cell lines (P<0.0005). Response to treatment appears to be inversely related to fluorescence internalization pattern.

Conclusion: Optical imaging of EGFR-expressing tumor tissue labeled with cetuximab:Cy5.5 may aid in determining which patients are most likely to benefit from cetuximab therapy.

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Summary

Summary of Results. CAL27, which responded poorly to cetuximab therapy had the highest level of internalization (P=0.014). Failure to completely internalize the fluorescently labeled antibody resulted in a favorable response to anti-EGFR therapy.

Response to Cetuximab in vivo

In vivo
Fluorescent Intensity

In vitro
Fluorescent Internalization

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