Correlation of primary tumor engraftment in immune deficient mice and relapse rate in patients with early-stage non-small cell lung carcinoma (NSCLC).

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Background

Compared to cell lines, primary tumor xenografts potentially are more clinically relevant cancer models as they more closely reflect the phenotype and genotype of the original cancer. However, only a minority of tumors engraft successfully in severe combined immune deficient (scid) mice and can be passaged serially. Although xenograft models are used extensively, few studies have investigated whether tumors that engraft represent a distinct clinical subset. We hypothesized that NSCLC tumors with more aggressive clinical and histological features have greater engraftment capacity than those with a less aggressive phenotype.

Methods

Fresh primary tumors were harvested from NSCLC patients who underwent curative resection. Tumor fragments were implanted into the subcutaneous tissue of non-obese diabetic-scid mice within 24 hrs of excision. Patient characteristics for tumors that engrafted (XG) and did not engraft (No-XG) were compared. Only tumors from patients with >1-yr follow-up were evaluated for time to progression (TTP) and to correlate clinicopathological features with engraftment.

Results

Between March 2005 and October 2008, 110 tumors were implanted. Of these, 45 (41%) engrafted and were passaged serially *in vivo*. Squamous cell carcinomas engrafted significantly more than adenocarcinomas (57% *versus* 26%, p=0.03). There were no significant differences in differentiation grade or clinical stage between the XG and No-XG groups. XG patients had significantly shorter TTP than the No-XG group (10.19 *versus* 18.64 months, p=0.003). In multivariate analysis the ability to form a xenograft was an independent predictor of relapse (HR 4.15 95% CI 1.152-14.94, p=0.03).

Conclusion

Xenograft models can be established from the histological spectra of NSCLC encountered in the clinical setting. The capacity of these tumors to engraft may be predictive of a more aggressive phenotype and poorer clinical outcome.