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Abstract Article

Hylonome

Effect of anti-TGF-β antibodies in syngeneic mouse models of metastasis

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With advances in detection and treatment of primary tumors, secondary tumors (metastases) are largely responsible for cancer patient mortality. While transplants of human tumor cells have been useful for studying factors which inhibit primary tumor growth, newer animal models allow for studies of seeding and growth of secondary tumors in various organs as well as measures of the effects of possible treatments on tumors in multiple sites.

Of the many molecules which have been implicated in metastasis, transforming growth factor beta, TGF-β, is of particular interest in studies of cancer-related bone destruction because of its known involvement in bone development and turnover[1-4] as well as in bone repair[5]. Consistent with its pleiotropic activities, TGF-β can affect tumors in multiple ways[6-12]. Its direct effects include modulation of tumor cell growth, differentiation, and migration, while its indirect activities include regulation of immune function, extracellular matrix production, and angiogenesis[6-12].

In order to better understand the role of TGF-β in cancer, we set up and characterized several animal models and established quantitative endpoints for the analysis of primary and secondary tumors. To this end, anti-TGF-β antibodies were tested in syngeneic, immunocompetent mice using cell lines derived from spontaneous tumors or oncogene-driven tumors. Quantitative endpoints were used to measure tumor number and size as well as destruction of soft and hard tissues. Using these animal models, we found that inhibition of TGF-β has distinct effects on primary tumors and secondary lung and bone tumors in a manner related to the nature of the animal model. Thus, our models have allowed us to distinguish between the various tumor-associated biological activities of TGF-β.

In conclusion, similar to the heterogeneity observed in human tumors, animal models also show varied responses to treatment. Our results have important implications for the use of animal models for testing various possible cancer treatments. Use of different *in vivo* systems may assist in the elucidation of specific pathways for tumor growth and metastasis as well as discovery of methods to stratify patients as part of personalized cancer therapies.

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