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NEW SEARCH

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Expertise and Research Interests

Our long-term research goal is to better understand the molecular mechanisms, which effect the thyroid-host interactions during the progression of thyroid malignancy and to design methods for changing the extent and type of leukocyte infiltration into diseased thyroids to improve cancer and autoimmune therapies. Papillary thyroid carcinoma (PTC) is the leading endocrine malignancy in the US and accounts for 80% of all thyroid cancers. Furthermore between 5-10% of thyroid cancers present as poorly differentiated carcinomas with high patient mortality. Recent studies have shown the presence of specific rearrangements involving the c-RET tyrosine kinase gene in differentiated thyroid cancers. However, immune recognition of tumor antigens can greatly influence the outcome and extent of disease progression. In patients with autoimmune thyroiditis the high incidence of concurrent cancer is offset by a good prognosis suggesting that a potential tumor specific antigen can evoke effective immune responses preventing tumor spread. One candidate tumor antigen in these malignancies is the RET/PTC oncogenic fusion protein responsible for thyroid cell transformation. Using transgenic mice we have shown that RET/PTC plays a causative role in thyroid neoplasia. Furthermore, some patients analyzed for thyroid disease develop an antibody response to RET/PTC3 protein and 95% of the patients with autoimmune thyroiditis express RET/PTC1 or 3. From these data we hypothesize that RET/PTC or RET/PTC-induced tumor-specific antigen(s) are targets of an immune response leading to lymphocytic thyroiditis and, in predisposed individuals, autoimmune disease. To address this hypothesis we have been using RET/PTC3p53-/- mutant mice, which develop advanced thyroid cancers, to study the tumor specific response against RET/PTC fusion proteins. We plan to decipher the mechanism of RET/PTC induced inflammation and activation in vivo and to target expression of these and newly isolated immunogenic proteins to thyroid tissue in vivo using modified avian retroviruses. These studies will provide a better understanding of human thyroid disease and delineate tissue specific therapies to limit disease progression.

Keywords

Antisense Nucleic Acid; Cancer; Cancer Biology; Cancer Prevention; Carcinogenesis; Carcinogenesis; Developmental Genetics; Embryonic Stem Cell; Genetic Promoter Element; Hematopoiesis; In Situ Hybridization; Laboratory Mouse; Leukemia; Mammalian Embryology; Neoplasm Cancer Genetics; Nucleic Acid Sequence; Oligonucleotide; Retroviridae; Southern Blotting; Transcription Factor; Transfection; Transgenic Animal

Publications

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