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WHAT'S INSIDE

epithelial cells and their associated stroma. During breast carcinogenesis, these stromal-epithelial interactions are increasingly deregulated. Stromal fibroblasts in invasive breast carcinomas (i. e., carcinomas associated fibroblasts, CAF) differ from fibroblasts associated with normal breast. These differences include the production of increased amounts of type-specific collagens, the over expression of various growth factors, proteases and protease inhibitors, and acouisition of the myofibroblast phenotype, characterized by alpha-smooth muscle actin (SMA) expression. SMA functions to stop the migraton of breast fibroblasts and contributes to the contraction of myofibroblasts. These activities involve alterations in adhesion moleculares and cytoskeletal organization, which also affect expression of other molecules, such as extracellular matrix (ECM) proteins and proteases, by fibroblasts. In this project we test the hypothesis that expression of SMA is responsible for much of the CAF phenotype. RNA interference was utilized to inhibit expression of SMA in CAF. SMA-inhibited and SMA-expressing CAF were compared for the expression of a variety of cell adhesion mole%ules, ECM proteins, and ECM modulating proteases. We demonstrate that SMA in CAF affects the expression of several cell adhesion molecules, ECM proteins and ECM.
DTIC
Cancer; Epithelium; Mammary Glands; Muscles

20040059125 Loyola Univ. Chicago, Maywood, IL
Effects of Androgen Ablation on Anti-Tumor Immunity
Kast, W. M.; Sep. 2003; 61 pp.; In English
Contract(s)/Grant(s): DAMD17-02-1-0244
Report No.(s): AD-A421972; No Copyright; Avail: CASI; A04, Hardcopy

Androgen ablation (AA) constitutes the most common therapy for the treatment of advanced prostate cancer. While initially effective at reducing tumor burden, most patients recur with androgen insensitive disease. There exists a clear need to augment the clinical efficacy of hormone-based therapies, and immunotherapy of prostate cancer represents a promising approach for achieving such augmentation. Moreover, our data indicate that AA affects the immune system both systemically as well as at the prostate. Castration of mice stimulates B and T lymphopoiesis, thymic and bone marrow hyperplasia. The induction of apoptotic cell death following androgen ablation is accompanied by an inflammatory infiltrate comprised predominantly of activated T cells. This AA induced autoimmune-like response exerts limited anti-tumor activity in a mouse prostate cancel model, but the anti-tumor effect is potentially synergistic with CTLA-4 blockade, which promotes the development of autoreactive T cells. We have used the first year of this proposal to obtain and produce all necessary reagents (genes, tumor cell lines, hybridomas, purified antibodies) to position ourselves for studying the effects of AA on prostate cancer immunity as these effects might significantly influence the ability of a tumor-bearing host to mount an effective immune response.
DTIC
Ablation; Cancer; Hormones; Males; Prostate Gland; Tumors

20040059128 Columbia Univ., New York, NY
Dynamic Functional Mammoscopy: A Non-Ionizing Imaging Technique Enhancing Early Detection of Breast Cancer
Smith, Suzanne J.; Apr. 2003; 22 pp.; In English; Original contains color illustrations
Contract(s)/Grant(s): DAMD17-98-1-8054
Report No.(s): AD-A421983; No Copyright; Avail: CASI; A03, Hardcopy

During the third and final year of this study, we focused on improving the imaging technology of Dynamic Functional Optical Mammoscopy (DFOM) and focused on technique on refining existing weaknesses in specificy identified during the second year of study. In addition, we summarize the case studies and analysis of data obtained during the first two years. This data included optical imaging of patients scheduled for biopsy of breast lesions. These patients were recommended for core or excisional breast biopsy on the basis of equivocal mammographic and ancillary clinical findings within ACR BI-RADS(TM) categories 3 or 4. Analysis of test results of 117 patients showed that DFOM modality detected cancer in 13 of the 15 patients in whom biopsies confirmed malignant lesions, giving a sensitivity of 87%. DFOM also correctly identified 79 of 102 benign lesions giving a specificity of 77%. In clinical practice, the adjunctive use of DFOM would have decreased the percentage of biopsies that turn out to be benign from 102/117 (87%) to 23/117 (20%). The negative predictive value, the chance that a negative DFOM result truly indicates a benign lesion, was 79/81(98%) for the cases included thus far. While encouraging, these results suggest the need for further patient studies on_specificity.
DTIC
Cancer; Clinical Medicine; Detection; Images; Imaging Techniques; Mammary Glands