C-079

CLINICAL RELEVANCE OF A TUMOR-ASSOCIATED ANTIGEN IN MALIGNANT MELANOMA.

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Because of the antigen non-specific nature of immune complex (IC) detection assays, assessment of IC in the circulation of melanoma patients has resulted in inconsistent correlations with their disease course. This investigation was designed to (a) determine the presence of melanoma-TAA in IC of pathological stages I and II melanoma patients and (b) correlate the results with their clinical course. IC were isolated from sera of patients at the time when they had no clinically detectable disease by polyethylene glycol and subjected to the antigenic competition method using radioiodinated melanoma-TAA. Seventy-five percent (15/20) of pathological stage I patients were persistently positive for melanoma-TAA specific IC and developed recurrent disease. The lead time ranged from 4 months to 5 years. Conversely, 76% (13/17) of patients in this group who were negative for melanoma-TAA specific IC remained disease free for up to 8 years. Similar analysis of sequential serum samples from 35 pathologic stage II melanoma patients revealed that (a) patients who had the continuous presence of melanoma-TAA specific IC recurred within 5 years, and (b) patients who were melanoma-TAA specific IC positive at 3-4 weeks post lymphadenectomy, but became negative, remained disease free for 5 years. These results suggest that the persistent presence of tumor-antigen specific IC in stage I and II melanoma patients indicates the presence of subclinical disease. This is in agreement with the natural history of melanoma where delayed relapses have often been reported. Thus monitoring melanoma-TAA specific IC in circulation of patients with melanoma appears to be useful in predicting recurrence of the disease.

C-080

IMMUNOHISTOCHEMICAL RENIN STUDY OF DES-INDUCED SYRIAN HAMSTER RENAL TUMOR.

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The following study was undertaken to determine if diethylstilbestrol (DES) induces renin secreting renal tumors.DES-treatment of a ♂ Syrian hamster resulted in the development of a renal tumor and its serosal metastases, both containing cells with many secretory granules. The tumor was passed serially in DES and non DES-supported ♂ hosts until the tumor became autonomous. All tumor samples were studied immunohistochemically using antiserum to mouse salivary renin (MSR) and three antisera to rat renal renin (RRR). The PAP and VECTOR-ABC-AP procedures were used to stain all tumor sections, mouse kidney sections, rat kidney sections and hamster kisney sections; normal rabbit serum and non-substrate AP controls were used to ascertain non-specific staining. The antiserum to MSR stained 10x more JGAs in the mouse kidney sections than in the hamster kidney sections, and the antisera to RRR stained 7x more JGAs in rat kideny sections than in hamster kidney sections. Even though there were fewer JGAs stained in the hamster kidney sections, all antisera stained the JGAs in the hamster kidney sections and therefore, were used to stain the tumor sections of the DES-induced renal tumor line. Renin positively stained cells were observed in the tumor sections of both DES-supported tumors and autonomous tumors (non-DES-supported). Plasma renin activity (PRA) was determined for tumor bearing host hamsters and compared with the PRA determined for normal adult hamsters; it was higher than normal PRA levels. Therefore, the DES-induced renal tumor line contained cells secreting sufficient renin to raise the PRA above normal.

C-081

GROWTH FACTORS IN THE PATHOGENESIS OF CHRONIC MYELOGENOUS LEUKEMIA (CML)

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The aim of this paper is to study the role of diffusible serum growth factors in the pathogenesis of CML. The detection, quantitation and kinetic studies of these factors were done by standard semi-solid agar colony assay for haemopoietic committed stem cells (CFU-GM) spleen colony forming assay for haemopoietic pluripotent stem cell (CFUs), ^{3}H-thymidine suicide assay to determine the number of CFUs in 'S' phase of the cell cycle and anchorage independent growth of NRK-49F and Balb/c 3T3 fibroblasts by agar colony assay for TGFβ type activity. The results show that at 10% V/V 7 CML sera in chronic phase enhanced human placental conditioned medium (supramaximal) induced CFU-GM colonies by 196.64 ± 41.87% over controls. Similarly 4 CML sera at remission enhanced CFU-GM by 173.4 ± 58.93% and 3 CML sera at blast crisis enhanced by 178.12 ± 72.92% over controls. Whereas, 3 normal sera showed little or no enhancement over controls (121.67 ± 5.77%). This activity is synergistic to supramaximal level of colony stimulating activity. ^{3}H-thymidine suicide assay showed that at 10% V/V 7 CML sera at diagnosis showed a $\bar{x}$ % CFUs kill of 42.53 ± 11.26 as against 1.88 ± 4.2 obtained with 5 sera from normal volunteers. In addition CML sera at all stages of the disease showed enhanced levels of TGF-β type activity as compared to normal sera. These results indicate that CML sera may contain enhanced levels of early growth factors which stimulate proliferation of CFUs resulting in increased CFU-GM pool as seen in CML. The enhanced TGF-β type activity could disrupt bone marrow stromal fibroblast architecture and may have a role in the pathogenesis of this disease.