

EFFECT OF CISPLATIN ON HUMAN BLOOD MONOCYTE FUNCTION IN VITRO.

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Patients treated with cytotoxic drugs have an increased incidence of infections with low-pathogenic microorganisms, including fungi. Since cells of the mononuclear phagocytic system are crucially involved in the resistance against such infections, the in vitro influence of cisplatin on isolated human blood monocytes was evaluated with regard to chemotaxis, chemokinesis, phagocytosis and killing of Candida albicans. Without preincubation cisplatin in concentrations between 100 and 0,000001  $\mu\text{M}$  did not influence their function. With preincubation for 30-120 minutes an inhibition was observed. At 120 minutes the value was 30% of normal ( $P < 0.001$ ). The inhibitory effect was dependent on temperature indicating that cisplatin interfered with function not only at the cell membrane level. These results show that not only is the leukocyte count depressed during chemotherapy, but the involvement of crucial functions is impaired as well. This may predispose the patient to clinical infection.

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## INACTIVE ZYMOGEN FORMS OF PLASMINOGEN ACTIVATORS FROM HUMAN NEOPLASTIC CELLS.

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Inactive zymogen forms of human plasminogen activators with  $M_r$  52.000 (HPA52, the urokinase type) and  $M_r$  66.000 (HPA66, the tissue type) were purified from conditioned culture fluid of glioblastoma cells and melanoma cells, respectively, by affinity chromatography with monoclonal antibodies against each of the enzymes. Both zymogen forms migrate as one band in SDS-polyacrylamide gel electrophoresis under reducing as well as non-reducing conditions, indicating that both consist of one polypeptide chain. Catalytic amounts of plasmin converted both zymogens to active enzymes, which were shown by SDS-polyacrylamide gel electrophoresis under reducing and non-reducing conditions to consist of two polypeptide chains, held together by one or more disulphide bridges. The zymogen forms of the two enzymes differed in their reactivity towards the active site titrant diisopropylfluorophosphate (DFP): in analogy with the active forms pro-HPA66 incorporates DFP, while pro-HPA52 does not at any measurable rate. These findings demonstrate the existence of an additional step in each of the two pathways leading to extracellular proteolysis by plasminogen activation.

## DERIVATION OF MONOCLONAL ANTIBODIES TO TWO TYPES OF HUMAN PLASMINOGEN ACTIVATORS.

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We have derived monoclonal antibodies against a human 52,000- $M_r$  plasminogen activator (HPA52; the urokinase type activator) and a human 66,000- $M_r$  plasminogen activator (HPA66; the tissue type activator). Mice were immunized with impure preparations of the respective enzymes. Screening of hybridomas was based on inhibition of an enzyme assay of the two activators using the impure preparations, supplemented with enzyme-linked immunosorbent assay and SDS-polyacrylamide gel electrophoresis followed by immunoblotting. Five clones of hybridomas producing antibodies to HPA52 and three clones of hybridomas producing antibodies to HPA66 have been isolated. We have characterized the purified antibodies with respect to their strength and specificity in enzyme inhibition. There was no cross-reactivity of monoclonal antibodies raised against one type of plasminogen activator towards the other type. Using affinity chromatography with columns of antibody immobilized on Sepharose, each of the two types of plasminogen activators was purified from conditioned culture medium of human neoplastic cells to homogeneity as evaluated by SDS-polyacrylamide gel electrophoresis.