P-5

Assessment of autoimmunogenic potential of autoimmune disease inducing chmecals using the popliteal lymph node assay

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The popliteal lymph node assay (PLNA) was proposed to predict autoimmunogenic potential of xenobiotics. This study was conducted to establish the popliteal lymph node assay(PLNA) and to investigate the measurement of lymphocyte subsets can be utilized as an additional parameter in PLNA. Chlorpromazine, hydrazine, and streptozotocin, have already been reported to respond positive in the PLNA using mice, and these chemicals also caused autoimmune disorders in humans as autoimmunogens. Wistar rats were injected subcutaneously with 50㎕ of each test substance solution (10, 30 and 100㎎/saline 1㎖) into one foot pad and vehicle(saline) only into the contralateral foot pad of the rats on day 1. PLN weight and cellularity, and lymphocyte subsets were measured on day 7 after treatment of chemicals. Comparison of the control PLN was used to calculate weight and cellularity indices and in absolute weight and cell number compared with PLNs injected with saline in both hind foot pads of rats. The changes in lymphocyte subsets were monitored by flow cytometry and immunophenotyping of lymphocyte subsets stained with a panel of monoclonal antibodies. Not only the weight and cell numbers but also PLN cellularity and weight indices in PLNs treated with these compounds dose-dependently increased at 1.5㎎/rat, 5㎎/rat groups. Treatment with chlorpromazine, hydrazine result in decrease in the percentages of CD8b+ and CD5+ cells, however the proportions of CD45RA+ subset in PLNs was increased. Treatment with streptozotocin result in the most decrease in the percentage of $CD8b^+$ cells at the lowest dose(0.5mg/rat) of the three doses, however this percentage recovered at 5mg/rat from decrease. Proportions of NK cells were increased in every positive groups. These results suggest that the PLNA may be an appropriate screening system for prediction of the autoimmunity-inducing potentials of xenobiotics, and the measurement of lymphocyte subsets could be utilized as an additional parameter in PLNA for evaluation chemicals inducing the potential autoimmune disease.