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Influence of a Bovine Spleen Extract on Immunological Responses in Mice

L. Millerioux, M. Lenfant, D. Oleson and E. Mayadoux

Centre de Recherches sur les Maladies du Sang (Prof. *J. Tanzer*), CHU La Milètrie, Poitiers, et Institut de Cancérologie et d'Immunogénétique, Hôpital Paul-Brousse, Villejuif, France

Abstract. The presence of immunological stimulatory and inhibitory activities has been detected in a bovine spleen extract F prepared by acetic extraction of an acetonic powder. F was fractionated after water dilution, by ultrafiltration on an Amicon PM-10 membrane. Two successive ultrafiltrates (mol. wt. $< 10{,}000$) are obtained: U_1 which contained the largest pool of the low molecular weight substances, and U_2 which was shown previously to be enriched in an immunosuppressive peptide.

The biological activities of U_1 have been studied compared to those of U_2: 1. Added to mouse spleen cells culture, U_1, at low dose, stimulated ^{3}H-thymidine incorporation into the DNA of the cells, but inhibited it when large dose was added. In this test, U_2 was devoid of stimulatory action. 2. When injected into mice sensitized with sheep red blood cells, three distinct activities were detected: U_1 was inhibitory at the sensitization period; at the last step of differentiation of the lymphocyte, U_1 was stimulatory at low dose and inhibitory at large dose. As assessed by Biogel P-2 chromatography, this last activity was attributed to the presence in fraction U_1 of the immunosuppressive peptide previously characterized in U_2.

The immune response is a complex biological process which is controlled by a series of negative and positive regulatory factors which can be antigen-dependant or not.

Some natural non-antigen-specific immunoregulatory factors have been described in serum fractions and in various lymphoid tissue extracts. They are characterized by their non-species specificity and bring to mind the properties of 'chalone' as described by *Bullough and Laurence* [1969].

In a recent review, *Miller and Habicht* [1977a] have compared various procedures to extract from lymphoid tissues endogenous regulators of the lymphocytic immune system. These authors have emphasized the difficulties in reproducing and evaluating the published results because the extraction and purification procedures described in the literature are, at least, as numerous as the starting materials (fifteen different sources were cited).

Furthermore, in a complementary study measuring serum fraction activities on im-