THE IMMUNOSUPPRESSIVE ACTIVITY OF PLASMIC DEGRADATION PRODUCTS OF HUMAN FIBRINOGEN.

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Plasmic cleavage of human fibrinogen leads to generation of immunosuppressive activity not expressed by the intact molecule, and which is demonstrable in vitro and in vivo. This activity is not associated with the high molecular weight derivatives X, Y, D and E, but is present in the small dialyzable peptide fraction obtained from plasmic digestion. The peptides inhibit in a non-toxic fashion, the stimulation of "H-thymidine uptake and blastogenesis of lymphocyte by phytohemagglutinin (PHA) and alloimmune cells (MLC) under conditions of both macrophage dependence and macrophage independence. The peptides also suppress the plaque-forming cell response of mice to sheep red blood cells in vivo. Approximately 30 μg peptides/culture leads to a 50% inhibition of the PHA and MLC systems, and approximately 400 μg/mouse produces a 50% suppression of the plaque-forming cell response. Intact fibrinogen chains exhibit negligible activity, but plasmic digests of Aα chain are suppressive. Consistent with derivation from the Aα chain was the demonstration that the activity was generated from limited plasmic digest of fibrinogen which produced fragment X, and this activity was soluble at 80°C for 10 minutes. The release of the active peptide by limited plasmic degradation, and the activity of these peptides at physiologic concentrations suggests that this system may be of importance in vivo in association with local fibrinogenolysis or fibrinolysis at sites of thrombus. This has been in part substantiated by the experimental initiation of fibrinogenolysis in vivo with streptokinase.