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A liver-derived immunosuppressive factor is an arginase: identification and mechanism of immunosuppression

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ABSTRACT

We found a substance in culture medium of neonatal pig liver fragments, which suppresses an immune response monitored by ^{3}H-thymidine incorporation using phytohemagglutinin (PHA)-stimulated lymphocytes. We named it as an immunosuppressive factor (ISF). To purify ISF, ammonium sulfate fractionation, DE52, SP-Sephadex, hydroxyapatite, blue Sepharose, heparin Sepharose and Superdex gel filtration columns were used. Using these purification procedures, ISF was purified 1,254-fold, with 9.2% recovery, from the culture medium of neonatal pig liver fragments, and was identified as arginase by its biochemical characteristics including molecular size, amino acid sequences of digested peptides and expression of arginase activity. The addition of ISF caused to decrease in arginine concentration in culture medium and at the same time DNA synthesis was suppressed dose-

dependently, both of which were recovered by the addition of NOHA (N^G-hydroxy-L-arginine), an arginase inhibitor. In addition, the depletion of arginine in culture medium also led to the inhibition of DNA synthesis. These results led us to the conclusion that immunosuppressive effect of ISF was due to arginase activity that decreased arginine concentration in culture medium, not to another function of ISF.

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