

CELLULAR RESPONSE TO THROMBIN ACTION

Summary

Thrombin is plasma serine protease generated in the blood coagulation cascade. Active form of human thrombin: α -thrombin is a 36 kDa molecule consisting of 2 polypeptide chains (A and B) covalently linked by a single disulfide bond. Thrombin is mostly associated with blood coagulation and fibrinolysis. However, thrombin is also able to induce biological responses of different cells presented in the vicinity of enzyme generation. These responses are mediated by protease activated receptors (PAR), which are members of the 7-transmembrane G protein coupled receptors family. PARs are abundantly presented on blood platelets, endothelial cells, monocytes, T-lymphocytes, fibroblast, smooth muscle cells, neurons and tumor cells. Thrombin stimulates platelets activation leading to their aggre-

gation, shape change and secretion of the contents of platelet granules. PAR activation on endothelial cells and blood vessels smooth muscle cells causes vasodilation. Endothelial cells activated by thrombin also exhibit on their surface expression of P-selectin, E-selectin and adhesion molecules (ICAM-1 and VCAM-1). Activation of PAR-1 receptor in monocytes results in increased secretion of proinflammatory cytokines. PAR signaling stimulates cell growth, differentiation and proliferation. These effects are important in healing of injured tissues. Thrombin promotes angiogenesis in developing tumors and facilitates their metastasis. The different effects of thrombin action indicate that this enzyme is one of the most multifunctional serine protease.