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Thrombin selectively induces transcription of genes in human monocytes involved in inflammation and wound healing

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Abstract

© Schattauer 2014. Thrombin is essential for blood coagulation but functions also as a mediator of cellular signalling. Gene expression microarray experiments in human monocytes revealed thrombin-induced upregulation of a limited subset of genes, which are almost exclusively involved in inflammation and wound healing. Among these, the expression of F3 gene encoding for tissue factor (TF) was enhanced indicating that this physiological initiator of coagulation cascade may create a feed-forward loop to enhance blood coagulation. Activation of protease-activated receptor type 1 (PAR1) was shown to play a main role in promoting TF expression. Moreover, thrombin induced phosphorylation of ERK1/2, an event that is required for expression of thrombin-regulated genes. Thrombin also increased the expression of TF at the protein level in monocytes as evidenced by Western blot and immunostaining. Furthermore, FXa generation induced by thrombin-stimulated monocytes was abolished by a TF blocking antibody and therefore it is entirely attributable to the expression of tissue factor. This cellular activity of thrombin provides a new molecular link between coagulation, inflammation and wound healing.

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Keywords

Gene expression, Inflammation, Microarray technology, Mitogen-activated protein kinases, Protease-activated receptor, Thrombin, Tissue factor