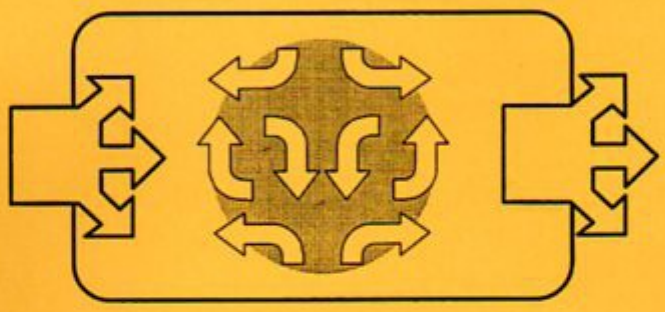
2nd Joint Meeting

Study Groups 'Signal Transduction'
of the German Societies for Immunology and Cell Biology (DGfI and DGZ)
Study Group 'Gene Technology/Biotechnology'
of the Society for Biochemistry and Molecular Biology (GBM)

Signal Transduction: Receptors, Mediators and Genes



Paul-Ehrlich-Institute

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Program and Abstracts

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ACTIVATION OF MITOGEN- AND STRESS-ACTIVATED SIGNAL TRANSDUCTION PATHWAYS IN STELLATE CELLS FROM NORMAL AND FIBROTIC LIVER

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Stellate cells are the main source of hepatic collagen during the development of liver fibrosis. Proliferation as well as differentiation and collagen synthesis of stellate cells are regulated by transforming growth factor-β (TGF-β). It induces in stellate cells isolated from healthy rat liver fast activation of MAPK [1] and SAPK within 10 min. In stellate cells isolated from fibrotic liver no activity of MAPK could be detected after treatment of cells with growth factors. SEK1 and SAPK, however, was found to be activated even in the absence of TGF-β, bFGF or PDGF. Low MEK activity and high levels of MAPK phosphatases MKP-1 and MKP-2 may explain the lack of MAPK activity in the stellate cells of the fibrotic liver.

[1] Reimann, T. Hempel, U., Krautwald, S., Axmann, A., Scheibe, R., Seidel, D. and Wenzel, K.-W. (1997) FEBS Lett. 403, 57-60

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THE REDOX POTENTIAL/ELECTRON TRANSFER IS RESPONSIBLE FOR STRESS PROTEIN OR O_2^--SYNTHESIS AND PROLIFERATION

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The adaption of cells to oxidative stress, to heat shock, to environmental stress etc. is nothing other than their natural defense mechanism for protection against injury. The general scheme of activation of this defense mechanism seems to be the use of stimulatory or inhibitory cytokines/hormones including. For instance, tumor necrosis factor (TNF) and Il-1 control NADPH oxidase (non phagocytes), TNF and Il-1 control collagenase, and gIFN and Il-4 control IgE. In most (or all?) cases, the activation/deactivation of NADPH oxidase (O_2^--production/IgE-synthesis) occurs simultaneously to the expression of former enzymes. The plasma membrane NADPH oxidase is a rather complicated electron transfer system, which resembles probably the most important crossover-, end-/starting point of various signal transduction pathways: Ca^{2+}/Mg^{2+}-sensitive phosphorylation/dephosphorylation (incl. JAK-STAT-g-protein-pathway) of the complex regulates the electron transfer (incl. thiol/disulfid-interchange-FeS-protein) between mitochondria/plasma and nucleus (NADH/ATP-NADPH/K^+-O_2/O_2^---DNA/IgE). Another control is played for instance by arachidonic acid (delivered by PLA_2): The NADPH oxidase belongs then to enzyme systems like insulinR, nAcChR, adenylate cyclase, mit K^+ATPase/ATPsynthase presenting a universal principle of nature.

Kiehl R. (1994) Int. Alk-Ciba Corning Joint Symp., Benzheim; (1995/96) Habilthesis, LMU Munich, Med. Fakultät; (1997) BIOforum 12, GIT Verlag, p. 686-690; (1998) Proc. of the 17th Int. Symp. of the Electrolyte/Blood Gas Intercontinental Working Group on the Confluence of Crit. Care Analysis and Near Patient Testing, Nice; (1998) Biotechnology Int., Universal Medical Press Inc., in press.