TRANSGENIC APPROACHES IN THE INVESTIGATION OF INNATE IMMUNE CELL SIGNAL TRANSDUCTION

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Recognition is a fundamental characteristic of the immune system, which regulates the immune response through a multi-step mechanism that often leads to the elimination of the triggering agent. Recognition or function defects of the innate immune cells can lead to severe infections or can participate in the escalation of autoimmune disorders. For the proper control of these latter diseases, it is crucial to have a better understanding of the signaling cascades linking immune recognition to immune response.

Experimental genetic modifications (transgenic techniques) have unique roles in the identification of the signaling cascades of several innate immune cells such as monocytes/macrophages, neutrophils or mast cells. The modifications are made in the genome of an experimental animal resulting in a total block of gene transcription, the inactivation of a specific protein segment with enzyme activity or the addition of a new gene. The effects of these transgenic changes can easily be tested in *in vitro* or *in vivo* experimental setups. (Several inflammatory disorders have experimental mouse models, for example the TNF trangenic or the K/BxN (serum transfer) models serve as useful platforms for a better understanding of the pathomechanisms of human autoimmune arthritides.) The identified signaling participants can be potential targets of pharmacological inhibitors. Beyond clarifying the role of a gene/protein in an animal model, it can be an interesting question to identify the function of the molecule in separate cell-lineages, for which the Cre-lox cell-specific knockout technology is a useful method.

The ligand binding of several cell surface receptors (like Fc receptors, integrins or cytokine receptors) can lead to the activation of innate immune cells. During the signal transduction of these receptors (besides several other molecules that are going to be discussed during the presentation) tyrosine kinases often get activated and serve as potential targets of pharmacological intervention in immune-mediated disorders.

We can conclude that transgenic approaches are important in the investigation of signal transduction pathways of innate immune cells that can participate in several systemic autoimmune diseases. A better understanding of the signaling routes of these cells can reveal underlying disease mechanisms and can have beneficial therapeutical effects.