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Biological Functions of Interferons and Interferon-Induced Genes

Type I IFNs are well established therapeutic agents for the treatment of life-threatening viral infections and also of several forms of cancer. Nevertheless, molecular studies of viral replication have revealed that most viruses have developed escape mechanisms and exert varying degrees of resistance towards the antiviral effects of IFN. Clinical use of IFN in tumour therapy often only results in partial and short-lasting responses. One likely reason is that in many in malignant cell lines IFN signalling pathways are impaired preventing a robust response to IFN treatment.

The pleiotropic biological effects exerted by IFN originate from a still increasing number of >300 individual genes induced by IFN and a substantial number among these genes display as yet unknown functions

Work in our lab is focussing on the identification and characterization of these genes *in vitro* and *in vivo*.

One of them, named *IFRG28*, is permanently expressed in macrophages due to their low constitutive IFN- β synthesis. Analysis of the promoter revealed the presence of three Interferon-Stimulated Response Elements (ISRE) which exclusively responded to IFNs. Inactivation of either two out of three ISRE elements proved that each ISRE is functional although there are individual differences in activity following IFN treatment. Mutation of all three ISRE sites, however, resulted in complete unresponsiveness of the promoter. To study the expressed *IFRG28* gene, monoclonal antibodies were generated

which detected the mouse protein already 2h after IFN treatment. Actinomycine D and Cycloheximide treatment of IFN-stimulated cells revealed an unexpected long biological half life of more than 8h for both mRNA and protein.

Immunofluorescence studies showed an even granular distribution of the protein mainly in the cytoplasm of IFN treated cells.

Selected Publications:

Finke, D. et al.
Elevated levels of endogenous apoptotic DNA and Interferon alpha in complement C4 deficient mice: implications for induction of SLE
Eur.J.Immunol. 37: 1702-1709, 2007

Bachmann A, Zawatzky R, Rosl F.
Genetic redundancy in human cervical carcinoma cells: Identification of cells with "normal" properties.
Int.J.Cancer 120:2119-26, 2007

Samuelsson, C.V.et al.
Transformation of mouse fibroblasts alters the induction pattern of type I IFNs after virus infection.
Biochem. Biophys. Res.Comm. 335: 584-589, 2005