

Research Projects:

Overview: Our bodies are equipped by defense mechanisms and thereby escape the infection of bacteria and viruses. In the host defense against virus infection, a family of cytokine, which is called interferon (IFN), plays an important role. Although the interferon was discovered as a protein that shows an antiviral activity, it has thereafter been understood that interferon can display a variety of biological activities including suppression of cell proliferation, anti-tumor effect, and modulation of immune responses. Recently it has been suggested that interferon is involved in other biological processes such as ontogeny, cell differentiation, obesity, carcinogenesis and cranial nerve cell function, although the details have not been clarified still enough. On the other hand, application of the pleiotropic activities of interferon in the medical treatment is also advanced: for instance, therapy with interferon is actually authorized in chronic hepatitis C. Further progress of the interferon research will extend the possibility of its use in the treatment. The current research in our laboratory focuses on the study on the physiological roles of interferon in various aspects ranging from basic life-science to clinical applications.

1) Analysis of interferon-induction and -action mechanisms: The host defense mechanism against bacterial or viral infection is initiated by recognition of the body elements of the microorganisms including their nucleic acids, which induces the production of some kinds of cytokines (inflammatory cytokines) including interferon (innate immune responses) and then develops adaptive immune responses. It is suggested that the induction of interferon can be influenced by various endogenous or exogenous stimulations (stress) besides the microorganism infection, and that the interferon system may take part in stress responses as well as maintenance of the homeostasis of the living body. Deciphering molecular and cellular mechanisms of tissue-specific interferon induction and of interferon action is expected to extend our understanding of physiological roles of interferon.

2) Investigation of the relationship between interferon

Recent Publications

- Watanabe, Y. Fifty years of interference. *Nature Immunology* **5**, 1193, 2004.
- Maruyama, M., et al. Subcellular Trafficking of Exogenously Expressed Interferon- β in Madin-Darby Canine Kidney Cells. *J. Cell. Physiol.* **201**, 117, 2004.
- Kawano, H., et al. Improved anti-cancer effect of interferon gene transfer by sustained expression using CpG-reduced plasmid DNA. *Int. J. Cancer*, in press, 2007.

system and diseases: Because of a variety of physiological functions of interferon as above mentioned, elucidation of relations between interferon system and various diseases is thought to be important from the point of view of the disease treatment; it is suggested that tumor formation or cancers, autoimmune diseases, and some hereditary disorders involve with abnormality of the interferon system. However, the research on this issue has been insufficiently pursued, remaining future development.

3) Application of interferon to medical treatment and interferon gene therapy: Based on the multiple activities of interferon, it has already been applied clinically as an anti-cancer drug or an antiviral drug, for all that its precise action mechanisms remain not to be well known. Effects of its use together with other medicines have insufficiently been investigated. Therefore, further progress in basic study on interferon is eagerly desired for improving interferon-mediated therapies. Moreover, gene therapy that uses interferon gene-expression vectors or the interferon gene-transduced cells is a promising technique, basic studies on which are still needed to increase the possibility of its broad clinical application.

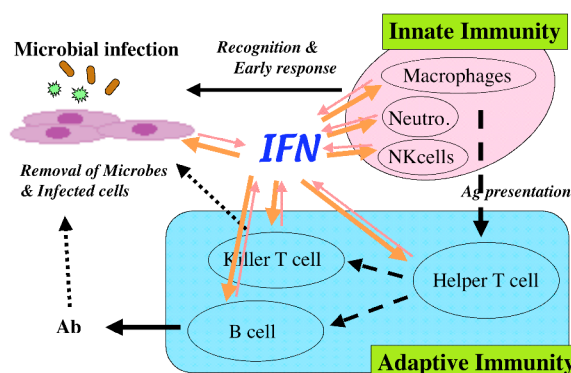


Fig: Interferon (IFN) in the immune system. All cells in the figure are capable of producing interferon and are susceptible to interferon action.