Poster Presentation

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Studies of Human Interleukin 24

J. Lubkowski[1], D. Zhang[1], S. Kotenko[2], A. Wlodawer[1]

[1]National Cancer Institute at Frederick, Macromolecular Crystallography Laboratory, Frederick, Maryland, USA, [2]University Hospital Cancer Center, New Jersey Medical School, Department of Biochemistry and Molecular Biology, USA

In this report we present our progress in the functional and structural studies of human interleukin 24 (hIL-24). Interleukins and interferons (cytokines) together with their cognate receptors form a 'front-end' of convoluted signaling networks, responsible for an immune-response to the presence of various pathogens. Cytokines are subjected to vigorous research related to their role in human physiology and disease and potential therapeutic uses. After many years of intense studies, information on some of cytokines is absent or limited, partly because new members are still being identified as well as due to difficulties of generating significant amounts of active preparations. A sub-family of 'IL-10-related cytokines' also called the cytokine receptor type 2 family (CRF2) comprises nine members. One of CRF2 members is interleukin 24 (IL-24). The most interesting biological feature of human IL-24 (hIL-24) is its tumor inhibitory activity, observed in vitro for several cancer cell lines. IL-24 signals through the receptor complex comprising the high-affinity chain (IL-22R1 or IL-20R1) and the secondary, low-affinity chain (IL-20R2). Structure of IL-24 is currently unknown, although it is expected to be similar to those of other members of the CRF2 family. However, in silica analysis indicates several differences in the molecule of IL-24 when compared to its close homologues. One of more interesting is lack of two canonical disulfide bonds, found in all other interleukins from the CRF2 family, due to missing needed Cys residues. While an alternative, unique disulfide bond in IL-24 is possible, the appropriate experimental evidence is missing. Native IL-24 is N-glycosylated. Although this modification appears dispensable for biological activity of related cytokines, its role in IL-24 is not clear. We have expressed insoluble hIL-24 in bacteria and refolded it subsequently into a soluble, functional form. The mass spectrometry analysis confirmed presence of a single disulfide bond. Our non-glycosylated variant of hIL-24 activates the cognate receptor as efficiently as commercial preparations from eukaryotic sources. We observed, however, that stability of refolded hIL-24 is somewhat compromised. Subsequently, we plan investigating the structural properties of this cytokine.

Keywords: interleukin, IL-10 family, cancer