Potentiated Interferons

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Interferons are complex sets of proteins which have gained recognition due to their ability to inhibit virus replication by cell mediated processes. They also possess anti-cellular and immuno-regulatory properties which in animal systems cause potent anti-tumour effect. Some of the interferons which are involved in this process are : Leukocyte Interferon (IFN- α). Fibroblast Interferon (IFN- β) and Immune Interferon (IFN- γ)[1]. Of these IFN- α and IFN-β have similar physicochemical and biological properties and are also termed as Type I Interferons[2]. IFN-γ does not however share the same molecular homology and is hence termed as Type II Interferon[3]. In addition IFN- γ also activates cell more slowly as compared to IFN- α and IFN- β [4,5] and has more potent anti-cellular [6,7] and immuno-regulatory activities[8] than IFN-α and IFN-β. Studies on the biological differences between Type I and Type II interferons have led to treating the cells with combined preparations of the Type I and II interferons which was observed to cause a potentiation of the anti-umour action.

Effects of Potentiation of Interferon Activity

Potentiation as observed originally in the mouse system showed greater than additive enhancement of the anti-viral action of the interferons[9]. It was observed that the combination of three units of IFN-γ plus twenty six units of IFN- α , which occurs in nature[10], gave a level of protection which was found to be equivalent to 320 units of either IFN alone. As only 29 units of activity was expected on the basis of pure addition a 11 fold potentiation was unexpected. This result however was confirmed be Zerial and Brennan independently[11,12]. Further studies have shown that Type II interferon interacts synergistically with either of the interferons to potentiate anti-viral activity[13].

Role of Receptor Interaction in Potentiation

Interferons do not inactivate the viruses directly. They induce the cell to active the establishment of an anti-viral state. This activation should require binding of the interferon molecules to the receptors on the cell surface. This interferon receptor interaction is expected to trigger production of a second messenger which in turn caused a depression of the host cell genome, causing transcription ad translation of the antiviral proteins. The anti- cellular action of the interferons is also speculated to start in a similar way.

The second messenger substances however to date have not been identified on a firm basis. A transient increase in the c-GMP levels has been observed in interferon sensitive cells[14] but not in the interferon resistant cells[15], which suggest that c- GMP could be the second messenger substance.

The future role for potentiated interferons is uncertain due to main reasons viz.,

1. The most pure IFN-γ preparations appear to contain a protein fragment which inhibits interferon action[16] and so needs removal in order to obtain maximum potency.

2. There are reports about bone marrow suppression which could be a major side-effect in interferon therapy[17].

Certainly a deeper understanding of the complex biochemical processes is required since the combination interferon therapy is indeed promising for anti-viral use.

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