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Interferon A Natural Key Against To Viral Infections

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ABSTRACT:
Interferons (IFNs) are proteins produced by a variety of cells in the inflammatory response to infections. Their production is triggered by the immune system in response to pathogens or cytokines. Interferon was discovered by Alick Isaacs and Jean Lindenmann in 1957. It was originally thought that interferon could be used as a general anti-viral agent and in anti-cancer therapy. There are many different types of interferons, now known as interferons "alpha," "beta," "gamma" and "lambda," with different cellular receptors and modes of action, and there are possibly 24 different types of alpha interferon. Independently and simultaneously, a group of Japanese scientists found an "interfering factor," which upon subsequent analysis turned out to be interferon, probably of the alpha type.

Key words: Alpha interferon, Beta interferon, Gamma interferon, Applications.

I. INTRODUCTION:

Discovery of Interferon:

No history of virology would be complete without a discussion of interferons and how they led to the discovery and identification of cytokines (small proteins that influence the activity of the immune system and nearby cells), their function in innate immunity, and their pharmaceutical properties as anti-viral and anti-cancer agents. The cloning of the interferon gene and its production in E. coli initiated the biotechnology revolution. As was the case of many other major discoveries in science, interferon was a fortuitous discovery.

In 1957, Alick Isaacs (1921–1965) and a post-doctoral Swiss student, Jean Lindenmann, were studying the phenomenon of "viral interference"—the ability of one virus to inhibit the replication of another virus. When 10-day-old chick chorioallontoic membranes from chick embryos were infected with heat or UV inactivated influenza virus, a material was produced that interfered with subsequent viral replication. The experimental procedure is illustrated in Fig. 7.1. Influenza virus production (or inhibition) was measured by hemagglutination, the ability of the virus to interact and agglutinate red blood cells. They termed the interfering substance "interferon".The end point of the titration was the identification of that well (on a plate of small wells) with partial agglutination; the reciprocal of the influenza dilution thus observed was taken as the interferon titer (concentration).

TYPES OF INTERFERONS AND ITS APPLICATIONS

Interferons:

- Interferons are the set of proteins which are released by virus infected cells in vivo and which reacts with uninfected cells so as to render them resistant to infection to virus.
- It belongs to the class of glycoproteins and cytokines. Interferons are named for their ability to interfere with viral replication.
- However virus-encoded genetic elements has the ability to antagonize the interferon response contributing to viral pathogenesis and viraldiseases
- Interferons have various functions they activate immune cells such as natural killer cells and macrophages they increase host defenses by regulating antigen presentation by virtue of increasing the expression of major histocompatibility complexantigens.
- Immune cells communicate with one another in many different ways, including through the production of cytokines.
- Cytokines are proteins that cells expel, or

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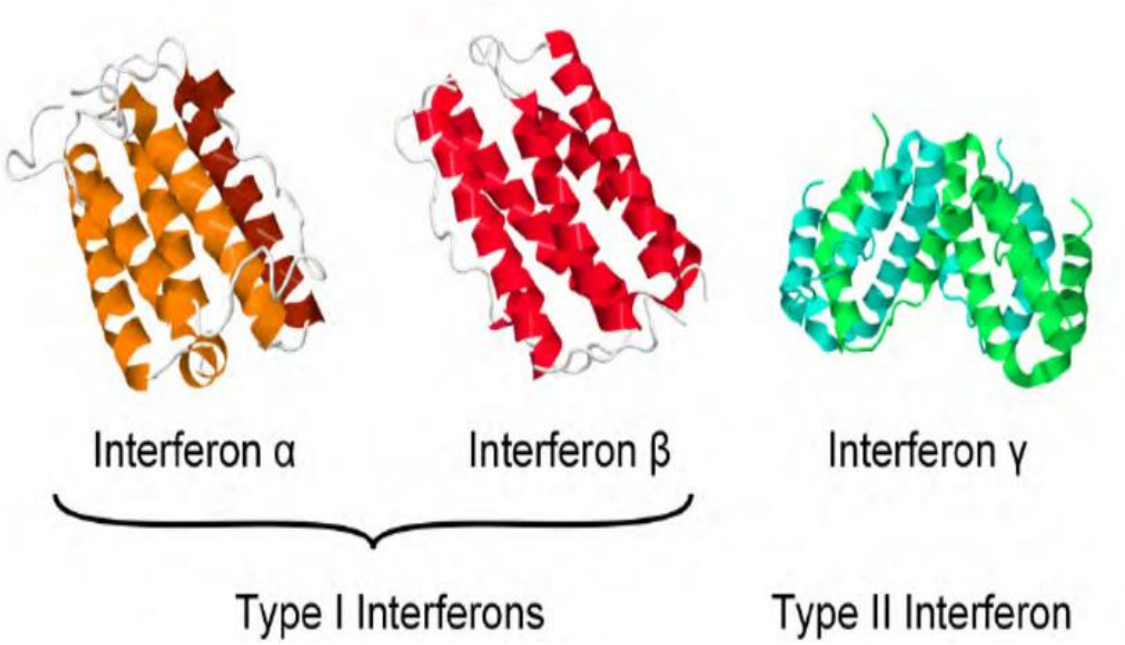
secrete, that can travel to other cells in the body, bind to receptor proteins on the cell surface, and relay a message.

- One important class of cytokines is interferons (IFNs), which play a vital role in protecting cells against viral infections.
- In fact, theName "interferon" reflects the fact that these cytokines were discovered based upon their ability to interfere with the production of viral particles.

TYPES OF INTERFERONS:

- Based on the type of receptor through which they signal, human interferons have been classified into three major types :

S.no	TYPES	SOURCE
1.	Alpha-interferon	Monocytes and B-Lymphocytes
2.	Beta-interferon	Fibroblasts and epithelial cells
3.	Gama-interferon	T-cells



Interferon type 1/ Alpha interferon:

- All type 1 interferons bind to specific cell surface receptor complex known as the Alpha interferon receptor that consists of IFNAR1 and IFNAR2chains.
- In general, type 1 interferons are produced

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when body recognizes a virus that has invaded it. They are produced by fibroblasts andmonocytes.

- However the production of type 1 IFN-a is inhibited by another cytokine known asinterleukin-10.
- Once released type 1 interferons binds to specific receptors on target cells, which leads to expression of protiens that will prevent the virus from producing and replicating its RNA andDNA.
- Alpha interferon can be used to treat hepatitis B and Cinfections.

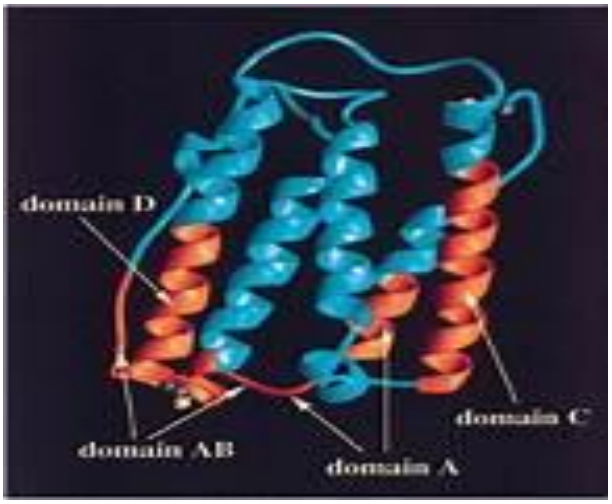
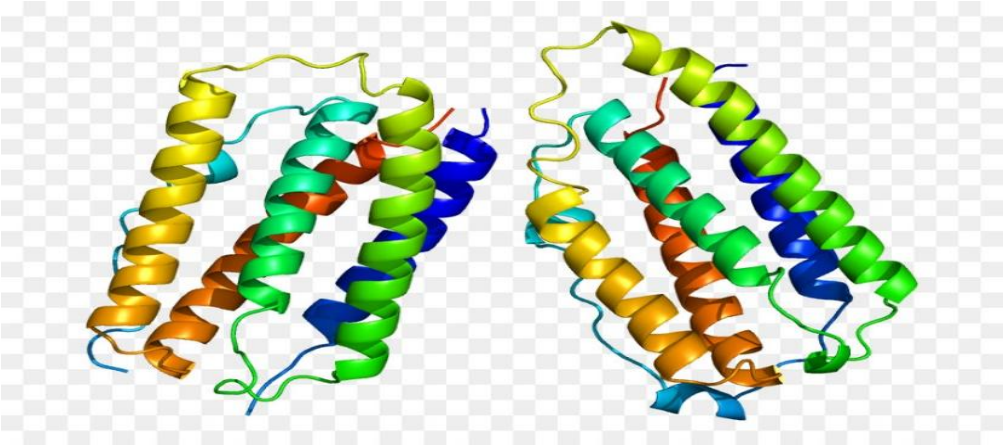


Fig:1. **Alpha interferon**

Interferon type 2/ Betainterferon:

- This is also known as immune interferon and is activated by interleukin- 12.
- Beta interferon is also released by cytotoxic T cells and alpha interferon are T helpercells
- They block the proliferation of the type-2 T helpercells
- Beta interferon binds to interferon GR which consists of IFNGR1and IFNGR2chains

Fig: 2.**Beta interferon**



Interferon type 3/ Delta interferon:

- Signal through a receptor complex consisting of ILIOR2 andIFNLR1
- Discovered more recently than type 1 and type 2 interferon recent information demonstrates the importance

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of type 3interferon in some types of virus or fungalinteractions

- In general type 1 and 2 interferon are responsible for regulating and activating the immuneresponse.

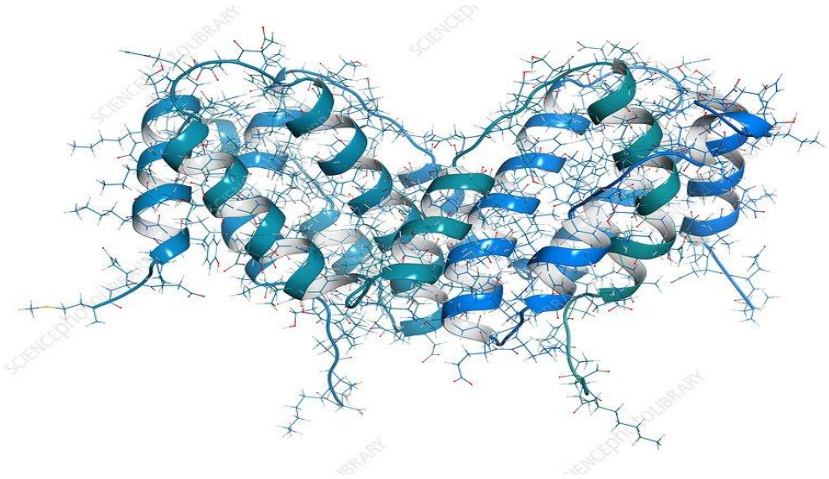

Fig:3 **Gamma Interferon**

Applications of interferon:

- Interferons could be ideal agents for combating viral diseases. They inhibit viral multiplication at such low concentration which is non-toxic to uninfectedcells.
- One interferon can inhibit many viruses. But there are certain draw-backs which stand in their use.
- Firstly, for application in humans, interferon must be of human origin, though interferons produced in monkey kidney cell cultures are also effective inhumans.
- Interferons are produced in very small quantities and it is difficult to get them in sufficient quantity in pure form for clinicalapplication.
- Another factor is that interferons are effective only for short periods and as such can be used against only acute infections, likeinfluenza.
- The difficulty of obtaining sufficient quantity of pure interferon for clinical use has been overcome by cloning the α-IFN and β-IFN human genes in bacteria andyeast.
- By growing these transgenic organisms in mass culture, it has been possible to obtain clinically usable interferons in sufficiently large quantities.
- Alpha-interferon has been marketed in 1984 under the trade name Intron A.
- In the following years, this biotechnologically produced interferon has been approved for clinical use against diseases like genital herpes caused by herpes-virus, hepatitis B andC.
- Beta-interferon has also been biotechnologically produced and marketed under the trade name betaseron. It has been used in a disease called multiplesclerosis.
- A recombinant g-interferon has been found effective against an inherited chronic disease, called granulomatousdisease.

II. CONCLUSION:

It has been replaced in the treatment of viral infections by small molecules that inhibit specifically viral enzymes, and such molecules may have fewer side effects. Interferon is still an important molecule to study since it elucidates the workings of the immune system. It is an important "backup" in the event of a sudden outbreak of an unknown virus epidemic. Interferon later became a standard treatment for a number of types of human cancers, including hairy cell leukemia, Kaposi's sarcoma in AIDS patients, chronic myelogenous leukemia (CML), and papilloma infections.

Interferon has also been used in many clinical trials with inconclusive results. A small group of asymptomatic HIV-infected individuals were treated with IFN-α2b: 41 % had decreased viral titer, and no patients in the IFN-α group developed AIDS-defining opportunistic infection, compared with 5 patients in the placebo group . However, 35 % of the patients in the treatment group withdrew from the study because of the severity of the side effects. Other clinical trials have not been so successful.

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