

WHAT ARE INTERFERONS?

- ◉ Naturally occurring proteins and glycoproteins
- ◉ Secreted by eukaryotic cells in response to viral infections, tumors and other biological inducers
- ◉ Structurally, they are part of the helical cytokine family which are characterized by an amino acid chain that is 145-166 amino acids long

DISCOVERY OF INTERFERONS

- ⊙ 1957
- ⊙ Isaacs and Lindenmann
- ⊙ Did an experiment using chicken cell cultures
- ⊙ Found a substance that interfered with viral replication and was therefore named interferon (**“Interference factors”**)
- ⊙ Nagano and Kojima also independently discovered this soluble antiviral protein

INTERFERON BASICS

- ◉ Interferons play an important role in the first line of defense against viral infections
- ◉ Interferons are part of the non-specific immune system

IMPORTANT FEATURES

- ◉ First recognized by their ability to interfere with viral infections in cultured cells.
- ◉ Does not protect the virus infected cell that produces it.
- ◉ Itself is not the antiviral agent.

It moves to other cells where it induces an antiviral state. (By inhibiting viral replication)

TYPES OF INTERFERON

TYPE I:

Interferon-alpha (leukocyte interferon, about 20 related proteins)
leukocytes, etc

Interferon-beta (fibroblast interferon)
fibroblasts, epithelial cells, etc

TYPE II:

Interferon-gamma (immune interferon)
certain activated T-cells, NK cells

INDUCTION OF INTERFERON

- | | |
|--|---|
| A. IFN-α & β
(Type-I- IFNs) | When prototypic cell of origin is exposed to

-Viruses

-Double stranded RNA

- Cytokines |
| B. IFN-γ
(Type-II- IFNs) | Following a number of immunological stimuli including :-

-T-cell specific antigen
-Staphylococcal enterotoxin -A And
-Mitogens (Phyto haemagglutinin ,Phorbol Ester etc) |

Morley,Michael. The pharmacology of lymphocytes. Barlin Heidelberg. Springer. 1988. print

Properties	Alpha	Beta	Gamma
Current Nomenclature	IFN- α	IFN- β	IFN- γ
Former Designation	Leukocyte	Fibroblast	Immune Interferon
Type Designation	Type I	Type I	Type II
No. Of Genes that code for Family	≥ 20	1	1
Principal Cell Source	Most Cell Types	Most cell Types	Lymphocytes
Inducing Agent	Viruses; dsRNA	Viruses; dsRNA	Mitogens
Stability at pH 2.0	Stable	Stable	Labile
Chromosomal location of genes	9	9	12
Size of secreted protein (Number of amino acids)	165	166	143
IFN receptors	IFNAR	IFNAR	IFNGR

ANTIVIRAL MECHANISM OF INTERFERON

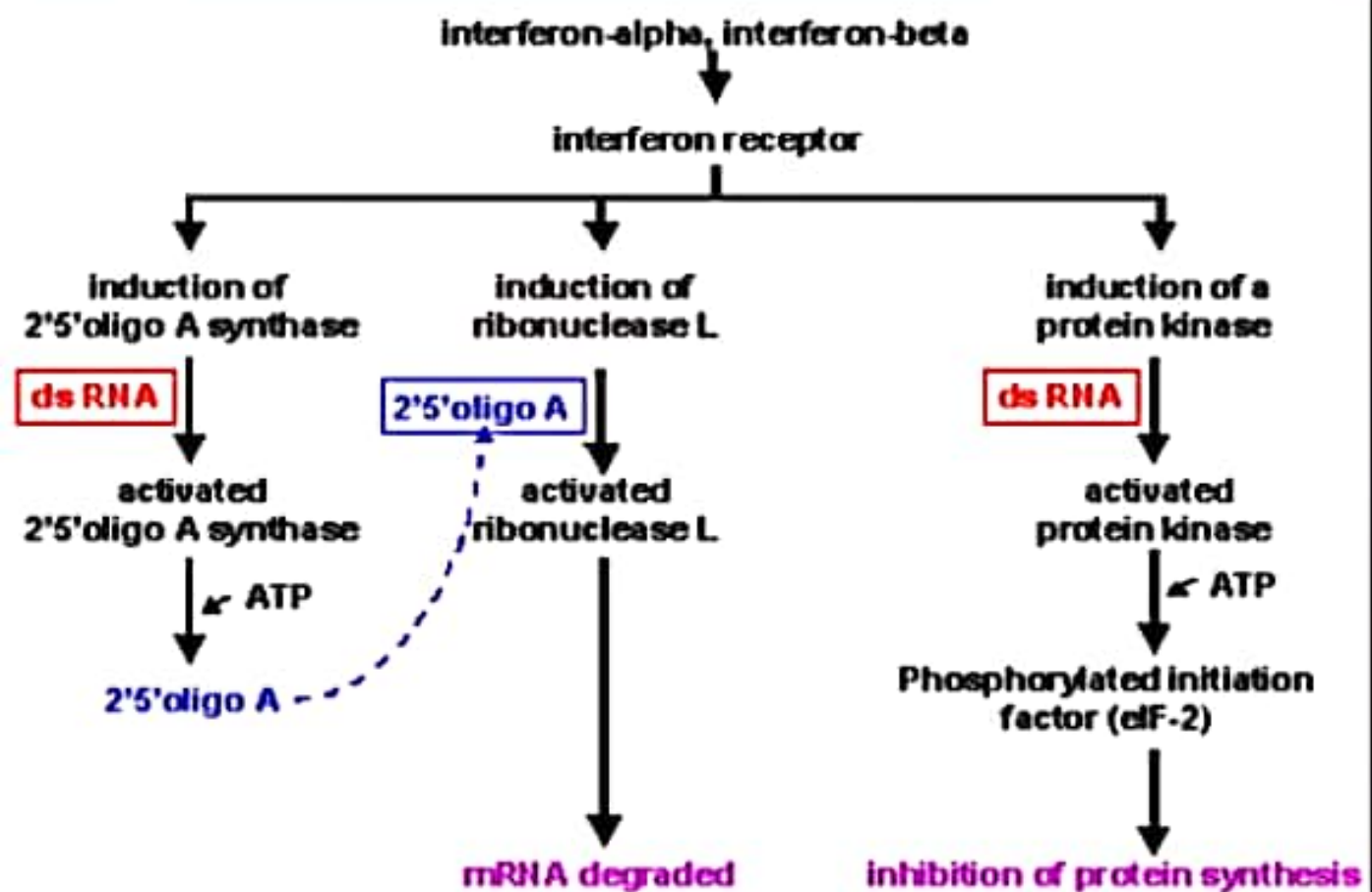
- ⊗ However its best understood anti-viral mechanism is:
 - 1. Block viral mRNA synthesis
 - 2. Block translation of viral mRNA

- Mx proteins
- 2',5' oligo(A) synthetase and ribonuclease L
- PKR, double stranded RNA dependent protein kinase

- ⊗ Mx proteins (myxovirus proteins) are induced by interferon
 - Block viral RNA polymerase
 - Block transport of viral nucleoproteins (influenza virus) into nucleus

- ⊗ 2',5' oligo(A) synthetase and ribonuclease L
 - This enzyme gets activated by dsRNA
 - Unique ability to synthesize oligos of A in the 2'- 5' linkage, norm is 3'-5' linkage
 - Poly(A) oligos bind ribonuclease L and activate it ⇒ mRNA is destroyed
 - Both cellular and viral cells may die

ANTIVIRAL MECHANISM OF INTERFERON



THERAPEUTIC USES OF INTERFERONS

- ⊙ Interferons-alpha and -beta have been used to treat various viral infections.
- ⊙ One currently approved use of interferon- IFN- α is in the treatment of certain cases of acute and chronic hepatitis C and chronic hepatitis B.
- ⊙ Interferon-gamma has been used to treat a variety of disease in which macrophage activation might play an important role in recovery, eg. lepromatous leprosy, .
- ⊙ Since interferons have anti-proliferative effects, they have also been used to treat certain tumors such as melanoma and Kaposi's sarcoma.