Accelerated Therapeutics

Targeted Transient Ribosomal Inhibition (TTRI)
and
The Viral Pulmonary Pandemic Stopper (VPPS) Opportunity

The VPPS Opportunity: Inhalable TTRI would serve as a "Viral Pulmonary Pandemic Stopper." By inhalation, the TTRI compound localizes in the respiratory tract, providing full spectrum antiviral activity and anti-inflammatory activity. The full spectrum antiviral activity is because TTRI does not target the virus, but targets the host ribosomes in the respiratory tract that the virus requires for its replication and spread. With this therapeutic option, viral pandemics and viral biological warfare threats would be a thing of the past. And that is just one use of the platform technology.

Relevant Background of TTRI

TTRI: Targeted Transient Ribosomal Inhibition (TTRI) is a platform technology that would provide therapeutic benefit in pulmonary and dermal indications where Antiviral, Anti-inflammatory, or Antiproliferative activity is desired. TTRI is a repurposing as well as a change in route of administration.

The compound is only suited for administration by inhalation for pulmonary indications and topical administration for dermal indications. The compound is NOT suited for systemic injection.

Mechanism of Action: The compound readily crosses cell membranes and binds with high affinity to the peptidyl transferase site on ribosomes, preventing de novo synthesis of proteins for ~ 12 hours per administration, before being intracellularly inactivated by acid catalysis. See Reference Slide 1 for details.

Pharmacokinetics (PK): The compound stays where it is applied and does not go system because of its blood insolubility. Topical application results in 97% retention in the skin. Similarly, inhalation results in its retention in the respiratory tract. Any compound entering systemic circulation is readily metabolized by the liver.

Toxicity: In TTRI, toxicity is defined by duration of inhibition of ribosomal function, or inhibition of de novo synthesis of proteins. Cells can sustain up to 3 days of inhibition without reduction in cell viability. After that, progressive, duration dependent cell death is observed. Accordingly, " 2 days on ,1 day off " regimens are used, unless ablative affect is desired.

Physiological Activity: When inhaled, or topically applied, TTRI provides localized (i.e. "Targeted") Antiviral, Anti-inflammatory, and Antiproliferative (cytostatic) activity in the respiratory tract , or patch of skin to which it is applied, respectively.

TTRI and the Viral Pulmonary Pandemic Stopper Opportunity

Overview : Localizing the compound in the respiratory tract by inhalation, combined with its Antiviral and Anti-Inflammatory activity, makes TTRI an ideal solution for new or unknown pulmonary viruses.

Antiviral Activity: Viruses require use of host ribosomes to synthesize the proteins required for their replication and spread (because viruses lack the genome to synthesize ribosomes). Preventing ribosomes from functioning, prevents viral replication and spread. It is not necessary to know what strain of virus has infected the target area as TTRI shuts down ANY virus that requires use of host ribosomes (i.e. all known viruses). Furthermore, TTRI shuts down every single protein that needs to be synthesized by the virus. As an example, the influenza genome codes for 10 proteins. Current drugs like Tamiflu inhibit one of those 10. TTRI inhibits all 10.

Anti-Inflammatory Activity: The anti-inflammatory activity stems from ribosomal inhibition in tissue resident mast cells in the respiratory tract, and hence inhibition of de novo synthesis of protein mediators of inflammation such as cytokines and leukotrienes. See Reference Slide 2 for details.

Intellectual Property: The use of TTRI as an inhalable pulmonary Anti-inflammatory was covered under our US pat. 7,012,091 until May of 2024, however the patent maintenance fees were not paid in 2018 because of lack of investor interest.

A patent application was filed in 2009 for the use of TTRI as a Dual Action Pulmonary Antiviral and Anti-inflammatory. While several other TTRI patents had been granted, the assigned examiner rejected the application in 2015 under the obviousness objection (i.e. “it should have been obvious to one skilled in the art”.) Because of the circumstances surrounding the application, the inventor suspects the data made its way to China, and the absence of a patent precluded its development in the US.

Value Proposition: New viruses arise from genetic reassortment in co-infected cells, as well as random mutations. New biological warfare viruses can be engineered or simply raised by co-infecting birds and passing the genetic reassortment product by air stream across to primates to isolate and harvest new viruses that are suitable for bio warfare purposes.

The value proposition against a new virus is that a country would not undergo the mortality and financial devastation, such as the US did with COVID-19. Having the Viral Pulmonary Pandemic Stopper would yield mortality numbers similar to those that China and Iran are reporting.

The value proposition against a bio warfare virus is without measure. It is estimated that more soldiers died in WW1 of Spanish Flu than of all ordinance combined. If a highly contagious bio warfare variant of H5N1 is unleashed by an attacker, killing 80% of a population, military included, any war would over before it even started. It would be the end of the US as we know it.

Other Indications: Other pulmonary indications include use of TTRI’s Antiproliferative activity (cytostatic, requiring prolonged administration for cytotoxic affect) for use in Pulmonary Chemosurgery (US 6,559,178), removal of both solid and liquid obstructions in COPD (US 7,015,244), and any other pulmonary indication that would benefit from Antiviral, Anti-Inflammatory, or Antiproliferative Activity. All of the other TTRI patents have not had their maintenance fees paid because of lack of investor interest.

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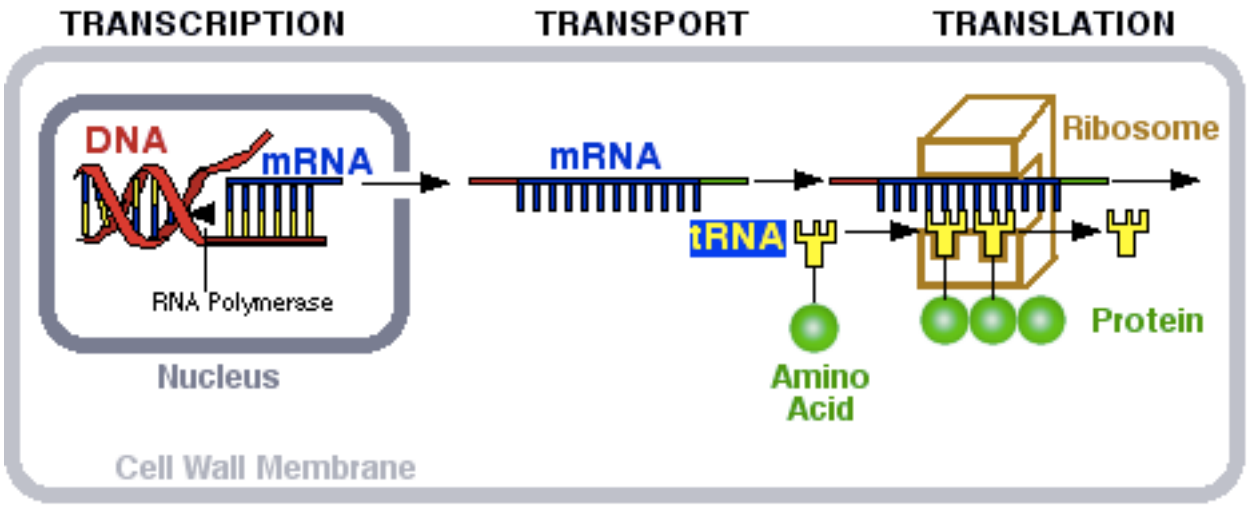
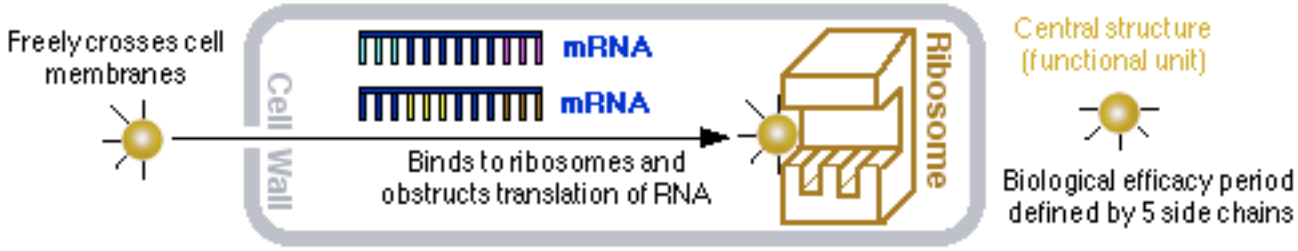
Reference Slide 1 - TTRI MOA

Synthesis of proteins in eukaryotic cells is achieved by a process that involves 1) Transcription of DNA into mRNA in the nucleus, 2) Transport of the mRNA strand to the ribosome (made up mostly of rRNA), and 3) complimentary base pair binding of tRNA with an attached amino acid, whereby the mRNA strand is translated into a protein.



The TTRI compound binds with high affinity to the peptidyl transferase site on ribosomes, preventing translation of RNA into proteins.

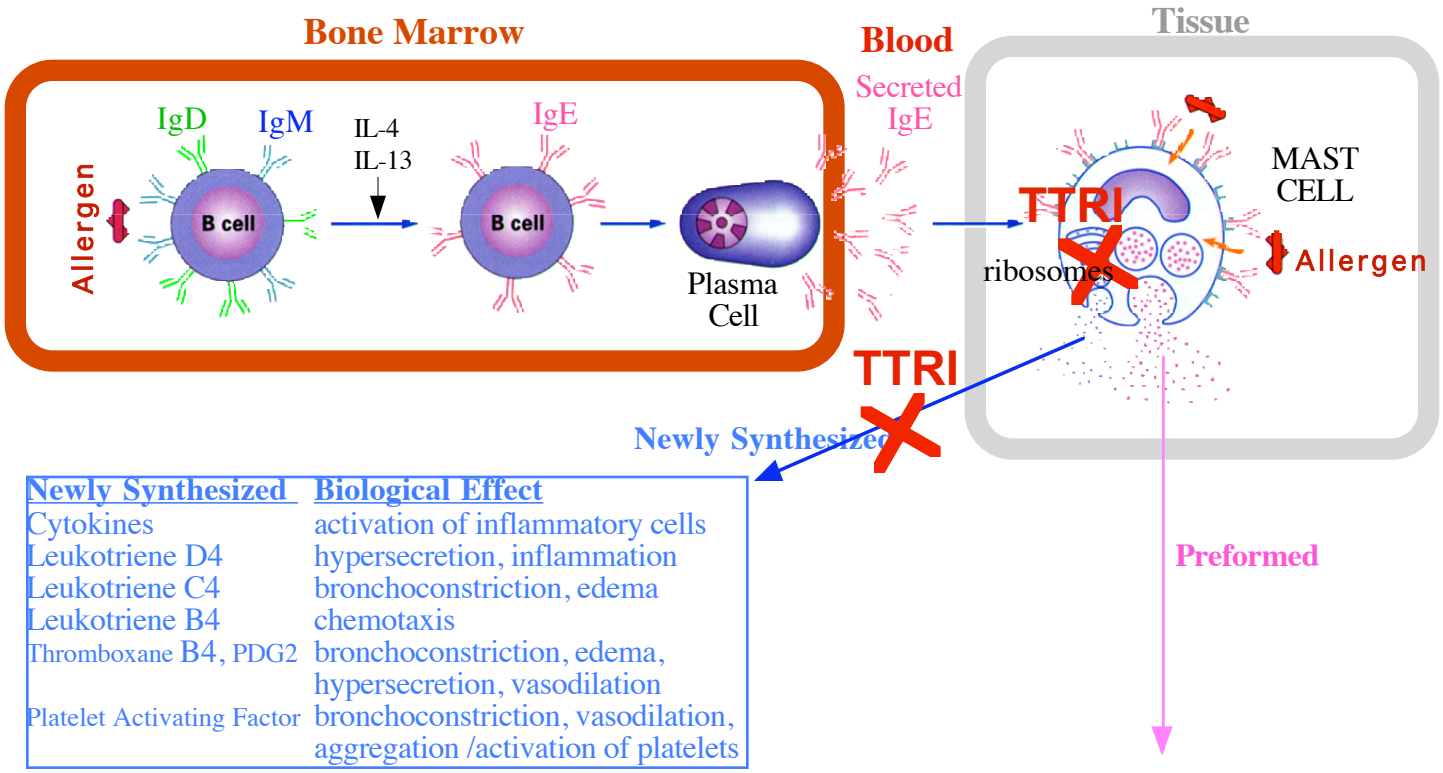


Reference Slide 2 - TTRI Anti-Inflammatory Activity

TTRI blocks ribosomes of tissue resident mast cells, preventing de novo synthesis of Newly Synthesized mediators of inflammation such as Cytokines and Leukotrienes (list shown in the blue box below).

TTRI will not inhibit release of the preformed mediators of inflammation stored in the tissue resident mast cells. However, TTRI will prevent de novo synthesis of these mediators.

Human Inflammatory Response to Allergens



Newly Synthesized	Biological Effect
Cytokines	activation of inflammatory cells
Leukotriene D4	hypersecretion, inflammation
Leukotriene C4	bronchoconstriction, edema
Leukotriene B4	chemotaxis
Thromboxane B4, PDG2	bronchoconstriction, edema, hypersecretion, vasodilation
Platelet Activating Factor	bronchoconstriction, vasodilation, aggregation /activation of platelets

Preformed	Biological Effect
Histamine	bronchoconstriction, vasodilation
Heparin	inhibition of blood coagulation
Tryptase	activation of C3
Kallikrein	generation of kinins, edema,vasodilation
Eosin. Chemotactic Factor A (ECF-A)	chemotaxis of eosinophils
Neutro. Chemotactic Factor (NCF IL-8)	chemotaxis of neutrophils