

## Alpha-1-Antitrypsin mutants as highly effective anti-inflammatory agents

**Prof. Eli Lewis**, the Department of Clinical biochemistry and pharmacology, Faculty of Health Sciences,  
Ben-Gurion University of the Negev, Beer-Sheva, Israel

### Technology

Human Alpha1-antitrypsin (hAAT) is a serum glycoprotein presently prescribed for patients with genetic AAT deficiency. It is administered in the form of a plasma-derived affinity-purified protein. hAAT is also a potent modulator that diverts injurious inflammatory responses towards resolution and healing. Wounds heal faster with topically administered AAT; blood vessels irrigate tissues better and skin regeneration is improved. Prof. Lewis lab has generated number of hAAT derivatives using site-directed mutagenesis or directed evolution approaches to generate hAAT with improved biological activity in cell line. One was mutant named, CPAT. CPAT is 500-fold more anti-inflammatory compared to native hAAT, i.e., the required dose of CPAT should be lower than that of commercially available hAAT and still reaches a blunting of inflammatory signals. In-addition, CPAT demonstrated superiority over serum-purified hAAT in expedition of tissue repair *in vitro* and *in vivo* in several tested models. Last, CPAT has a larger distribution volume and extended half-life *in vivo*. Efficient production of CPAT was demonstrated in HEK293 and CHO cells. In a study held in BGU CPAT was integrated into an emulsive topical aerosol and was shown to expediate tissue repair and recovery *in vivo* in cases of full-thickness skin wounds in an early surgical suture removal model. CPAT treatment is currently tested as potential treatment for corneal injuries and dermal burns as a result from heat or radiation exposure. CPAT production and topical formulations was also recently development.

### Application

Anti-inflammatory agent for various indication. Preclinical and clinical studies already demonstrated the great potential of WT hAAT, also know as alpha-1 proteinase inhibitor, as a therapeutic agent in various indications (Alpha-1 antitrypsin deficiency, Emphysema, Type I Diabetes, Graft versus Host Disease, Lung transplant rejection, Cystic Fibrosis and more). Since the hAAT mutants have superior activity, it can be used in location where small volume are required.

### Advantages

- High anti-inflammatory activity
- Easier and cheaper manufacturing procedure that will reduce the cost of treatment (compare to blood product of WT hAAT)
- The superior anti-inflammatory activity of the rhAAT variants may be used to reduce drug quantities, change drug administration regime or even for additional indications.
- Can be relevant for various indication
- Based on WT hAAT (FDA-approved), may reduce safety profile
- Topical formulation was achieved
- Recombinant-based technology enables low cost compared to plasma-extracted products; this format also reduce the safety concerns and costs associated with blood-borne diseases

### Patent

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