



IL-36 proteolytic processing Inhibitors

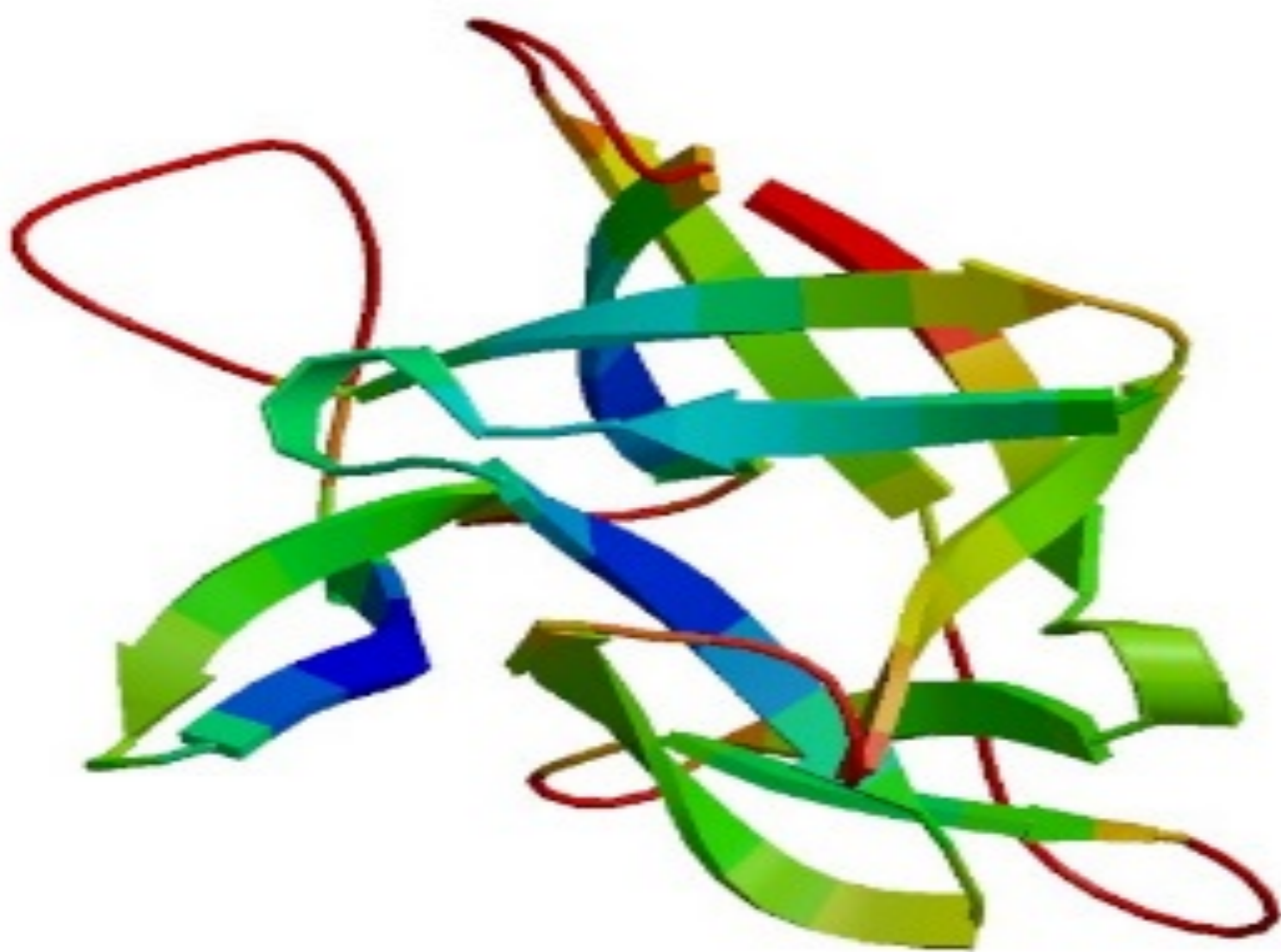
Treatment for Inflammation

Overview

The technology describes strategies, as well as novel chemical entities, for the inhibition of the proteolytic processing and activation of members of the Interleukin-36 (IL-36) family of cytokines- which play a role in promoting inflammation, especially inflammation of the skin as is observed in psoriasis.

Individuals that carry loss-of-function mutations in the IL-36 receptor antagonist (IL-36RA) display a severe and highly debilitating form of psoriasis, called generalized pustular psoriasis.

We have identified the proteases that activate IL-36alpha, IL-36beta and IL-36gamma and demonstrate that inhibition of these proteases (specifically elastase and cathepsin G) greatly attenuates the biology activity of IL-36 family cytokines.



IL-36 gamma

Technology

Following on from this discovery, specific novel polypeptide entities have been developed that are capable of blocking the activation of IL-36 cytokines by cathepsin G and elastase;

Glu-Pro-Phe-CMK; Ala-Phe-Leu-Phe-CMK; Lys-Ala-Leu-CMK, Arg-Ala-Val, Asp-Thr-Glu-Phe, Ala-Pro-Leu, Pro-Gln-Arg, Arg-Pro-Leu and derivatives thereof are capable of inhibiting the processing and activation of IL-36 family cytokines by neutrophil granule proteases

Applications

These novel small (<400daltons) polypeptide inhibitors of proteases have a therapeutic potential for inflammatory conditions where excessive or deregulated IL-36 signalling may have a function in disease pathology, such as psoriasis. Specifically, direct therapeutic utility as inhibitors of neutrophil granule proteases (Cathepsin G, Elastase and proteinase 3) in inflammatory diseases.

The application of small molecule inhibitors directly onto affected areas of skin circumvents a major disadvantage of current therapies for psoriasis and related skin diseases, namely the systemic delivery of potent immunosuppressive drugs or neutralizing antibodies that could make patients vulnerable to sporadic infections.



Psoriasis is a chronic skin disease that affects over 100,000 people in Ireland alone and is estimated to affect 2-4% of the population in western countries. Market reports predict that the world psoriasis drug market will be worth \$8.9bn in 2018. Those products, treating that indication generated £6bn in 2012 according to 'Psoriasis Treatment: World Drug report 2013-2023'

Technology and Patent Status

A priority patent had been filed with the European patent office; EP14185397.8

The opportunity

Trinity College is seeking to collaborate and/or licence the technology to an pharmaceutical company for development and commercialisation.

Market

Therapeutics: Synthesis, Formulation, Processing and Drug Delivery

IP Status

Priority Application filed
EP14185397.8

Opportunity

Research collaboration,
Available to license

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