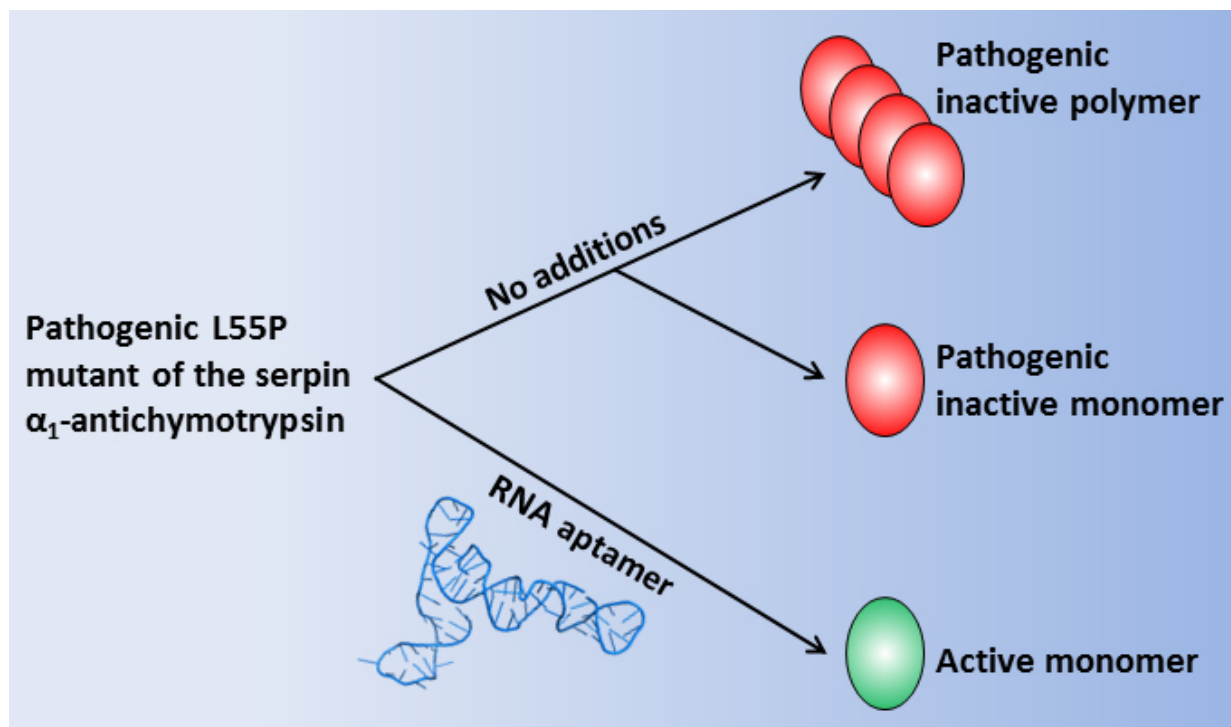


A new way for prevention of pathogenic protein misfolding

June 9 2016, by Lisbeth Heilesen



Incorrectly folded proteins can cause a variety of diseases. Danish researchers have found a solution for preventing this misfolding. Credit: Jan K. Jensen, Aarhus University

Incorrectly folded proteins can cause a variety of diseases. Danish researchers have found a solution for preventing this misfolding.

Several diseases occur when mutations cause misfolding of proteins. These include "serpinopathies" which is a group of rare heritable diseases. They are caused by mutations of so-called "serpin" inhibitors of proteolytic enzymes involved in [blood coagulation](#), tissue remodeling, and other important physiological functions. The [mutations](#) cause misfolding, which results in an inactive serpin and hence overactivity of the corresponding proteolytic enzyme.

The exact symptoms depend on which serpin is misfolded. The best known serpinopathy is α 1-antitrypsin deficiency, which causes liver cirrhosis and lung emphysema. But also other serpins may misfold, for instance anti-thrombin and C1 inhibitor, leading to thrombosis and hereditary angioedema, respectively.

A long standing problem has been that agents preventing misfolding also inhibit the anti-proteolytic functions of the serpins. Working with a mutant of the serpin α 1-antichymotrypsin, a group of Danish researchers has now designed a way of preventing misfolding while leaving the anti-proteolytic effect unabated. The α 1-antichymotrypsin mutation is associated with chronic [obstructive pulmonary disease](#) (COPD).

The [researchers](#) have developed an RNA aptamer, which prevents misfolding and polymerisation of the α 1-antichymotrypsin mutant and does not interfere with its ability to inhibit the target proteases, i.e., cathepsin G and chymotrypsin. One perspective is that similar strategies may be employed by other proteins prone to misfolding.

More information: Jeppe B. Madsen et al. An RNA Aptamer Inhibits a Mutation-Induced Inactivating Misfolding of a Serpin, *Cell Chemical Biology* (2016). [DOI: 10.1016/j.chembiol.2016.04.013](https://doi.org/10.1016/j.chembiol.2016.04.013)

Provided by Aarhus University

Citation: A new way for prevention of pathogenic protein misfolding (2016, June 9) retrieved 11 May 2024 from <https://phys.org/news/2016-06-pathogenic-protein-misfolding.html>

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