Title: Functional characterization of a SNP (F51S) found in human alpha 1-antitrypsin

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Mutations cause deficiency of antitrypsin proteins, resulting in lung and liver diseases

Many lung and liver diseases are linked to low levels of an enzyme called alpha 1-antitrypsin in the blood. Genetic mutations cause deficiencies to this enzyme, but it is not known exactly how. Researchers focused on one rare mutation called F51S to figure out how it alters the structure of alpha 1-antitrypsin.

To do this, they compared the structure and properties of alpha 1-antitrypsin with an F51S mutation, with those of wild-type, or normal alpha 1-antitrypsin. They specifically observed the expression, trypsin inhibitory activity, polymerization, and thermal stability of these proteins. They found that while the mutation did not affect alpha 1-antitrypsin's trypsin-inhibiting properties, it did cause the protein structure to become more flexible and more sensitive to heat. These changes prevented the enzyme from being released into the bloodstream, explaining why the mutation causes alpha 1-antitrypsin deficiency.

Because there are so many mutations linked to this deficiency with unknown effects (do they make the enzyme nonfunctional or just stop it from being released?), creating therapies that address the different underlying causes can be tricky. That is why our study is important for clarifying the effects of a specific mutation. We also developed a way to study rare mutations associated with disease, which was not frequently done before because the original methods were expensive and effort-intensive. Our study can help doctors identify whether patients are at risk for certain diseases based on the presence of a specific rare mutation.

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