

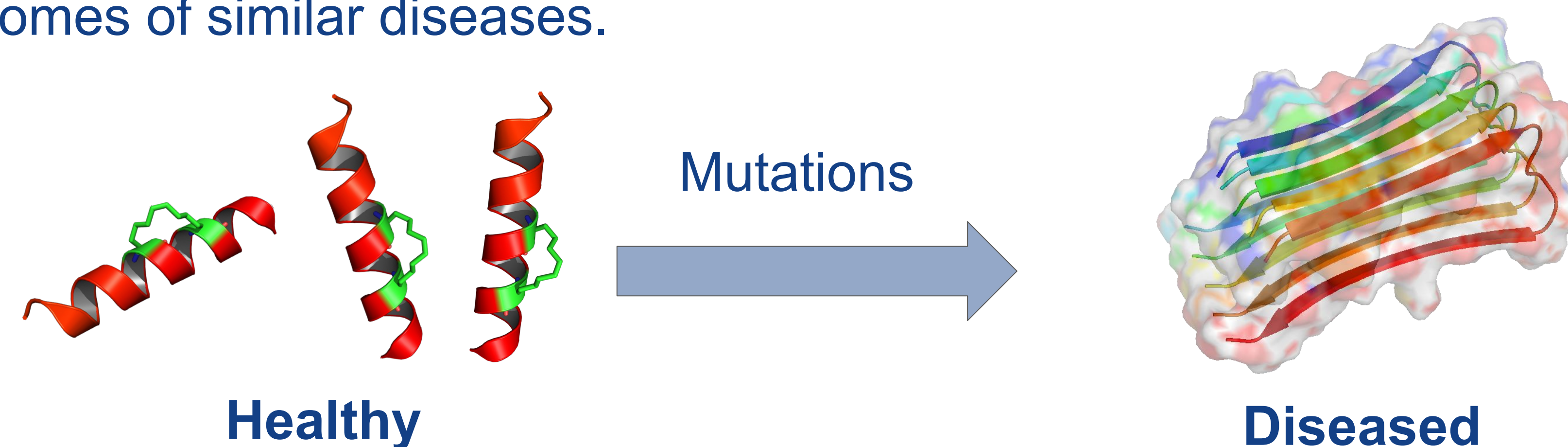
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Introduction & Objectives

Gelsolin protein is known to mutate and form toxic aggregates that deposit throughout organs and cause cell death.

Here, we investigated the extent of and prevention of aggregation in various disease relevant peptides by various biophysical characteristics.

Treating toxic Gelsolin aggregates may be a foundation for improving outcomes of similar diseases.



Key Findings

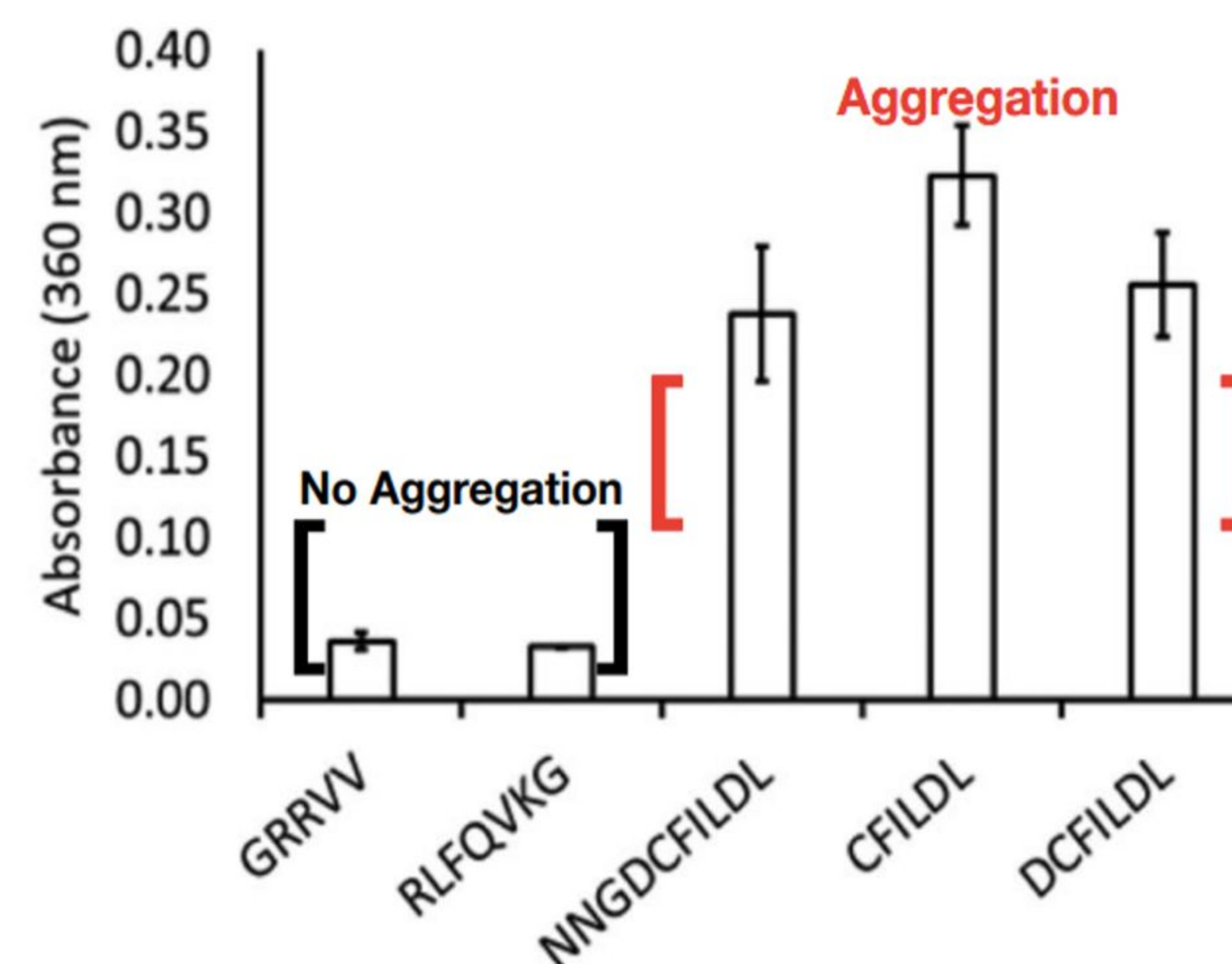
CFILDL-containing protein formed toxic aggregates

Toxic aggregate formation was prevented by small molecules

Protein mutations caused unique behaviour based on mutation location

Existing toxic aggregates could convert healthy protein to a toxic aggregate

Results



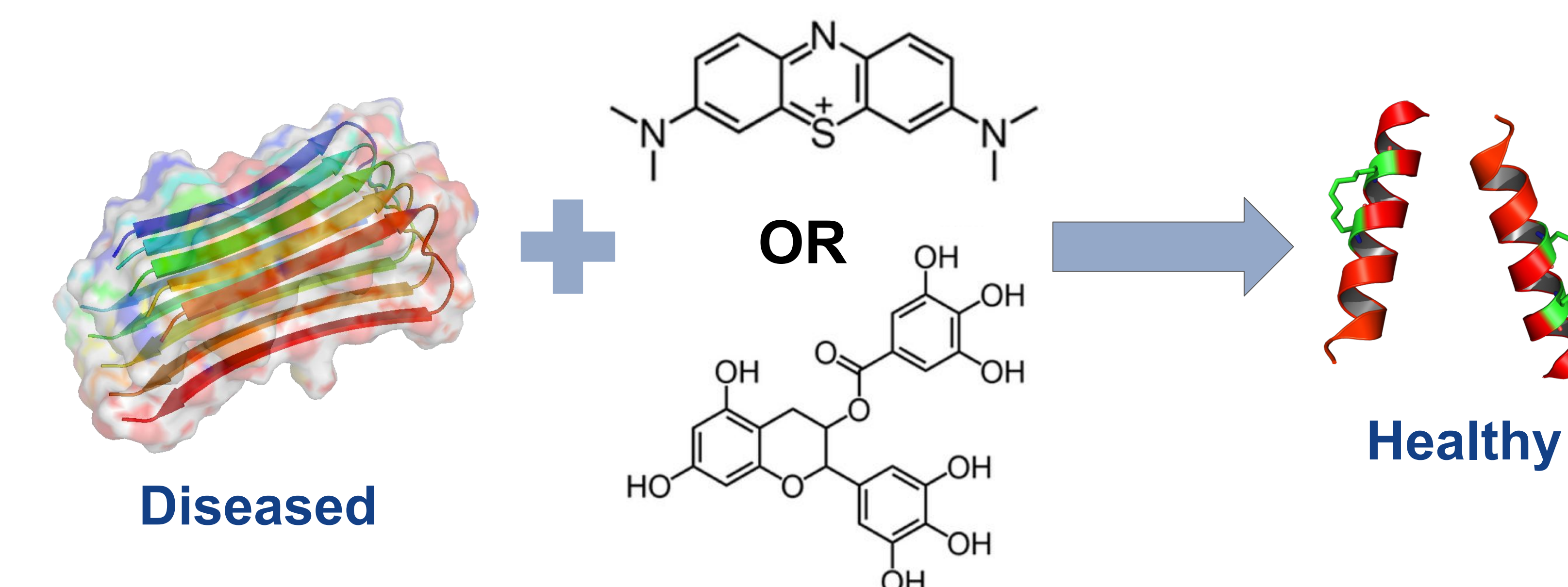
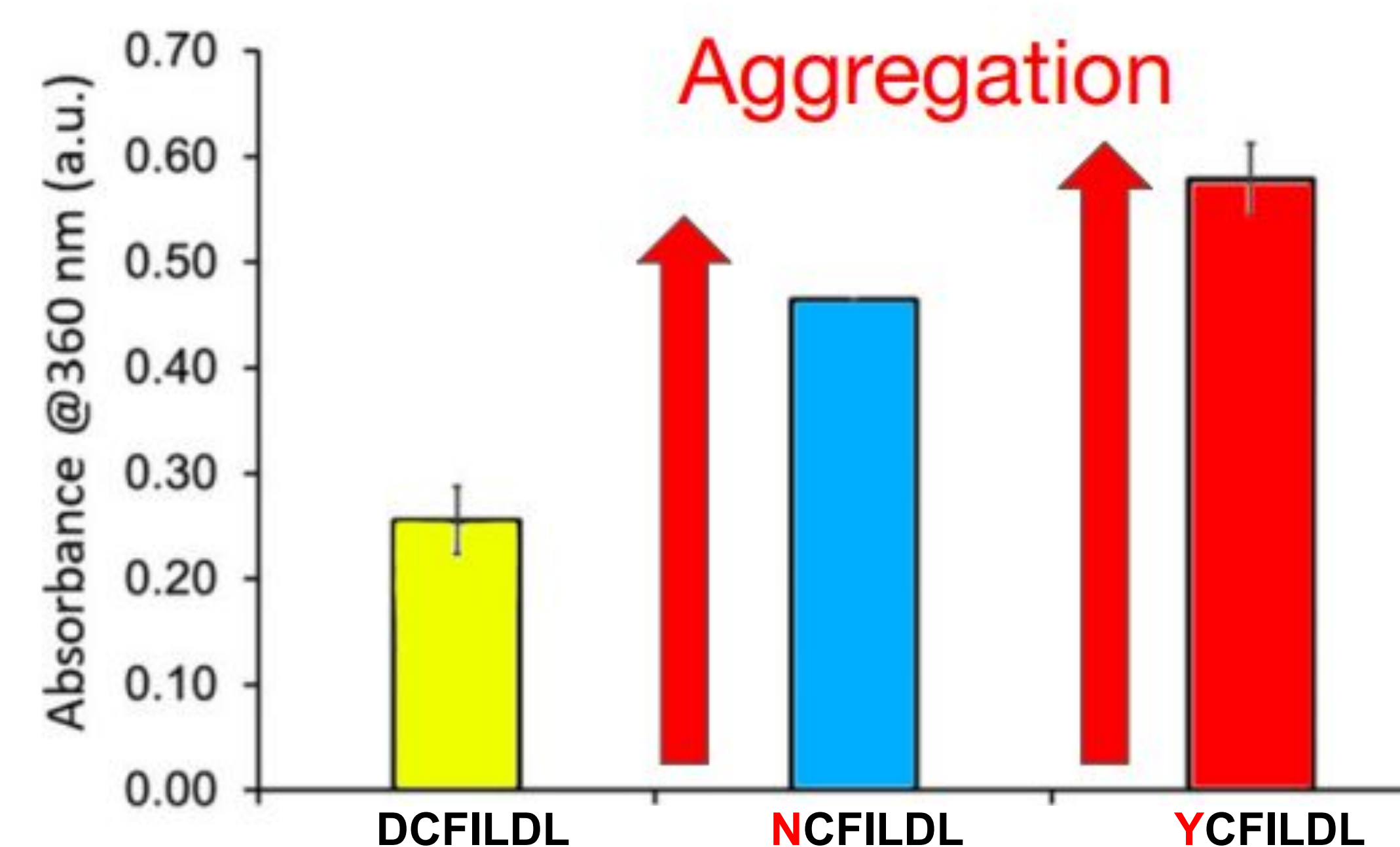
Specific peptides were more susceptible to toxic aggregate formation.

Toxic aggregating peptides met specific criteria:

1. Hydrophobic
2. CFILDL sequence
3. Acidic
4. Low isoelectric point

Mutations proximal to the CFILDL sequence impacted the aggregation and their toxicity.

The use of small molecules inhibited toxic aggregates.



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Solomon, J. P., Page, L. J., Balch, W. E., & Kelly, J. W. (2012). Gelsolin amyloidosis: genetics, biochemistry, pathology and possible strategies for therapeutic intervention. *Critical Reviews in Biochemistry and Molecular Biology*, 47, 282–296.
<https://doi.org/10.1007/s11010-021-04085-6>