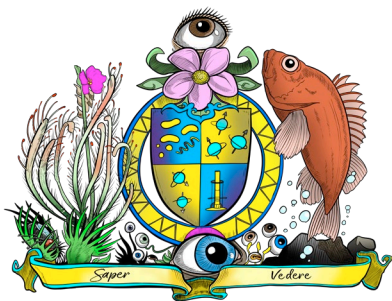


Probing oxidation-induced structural changes in human γ S-crystallin using NMR spectroscopy

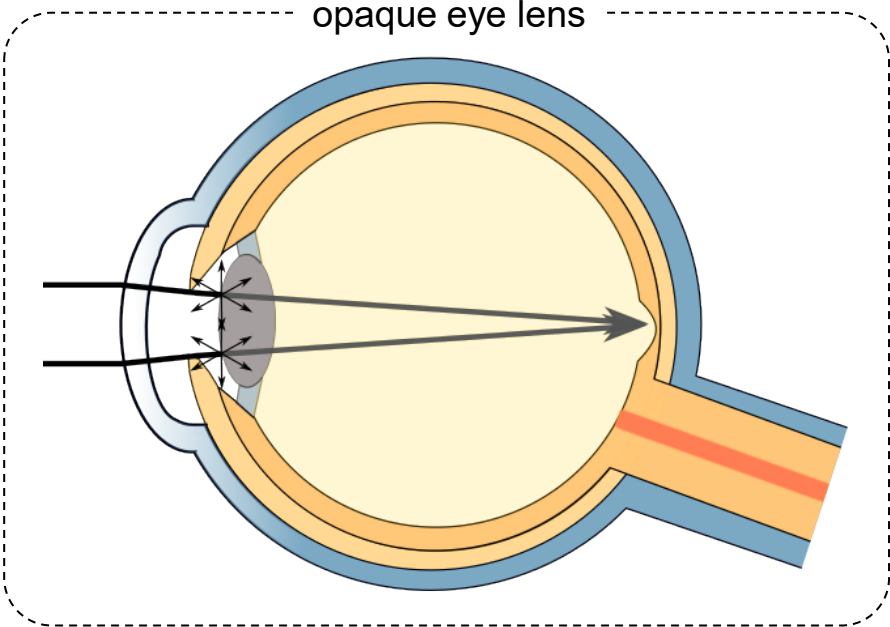
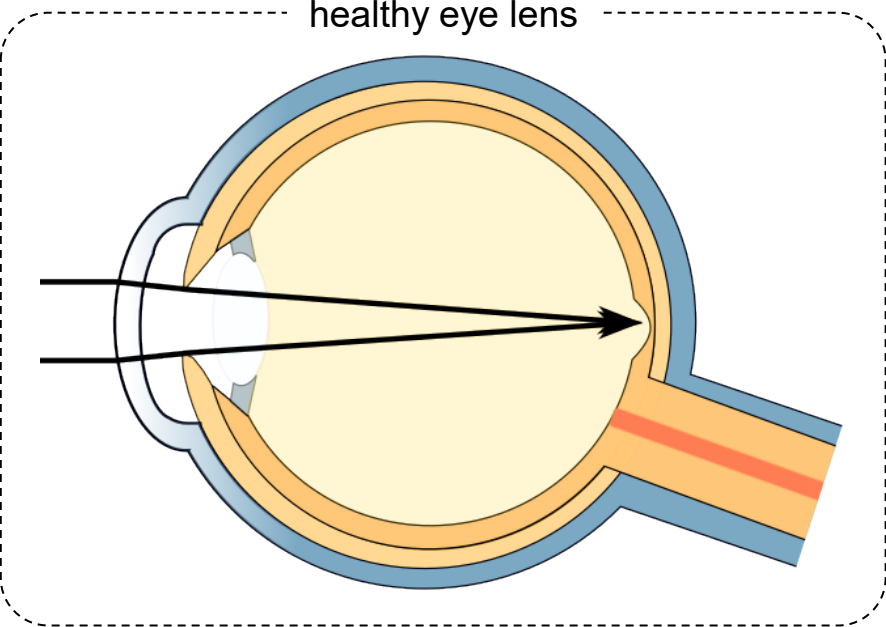


Yeonseong (Catherine) Seo
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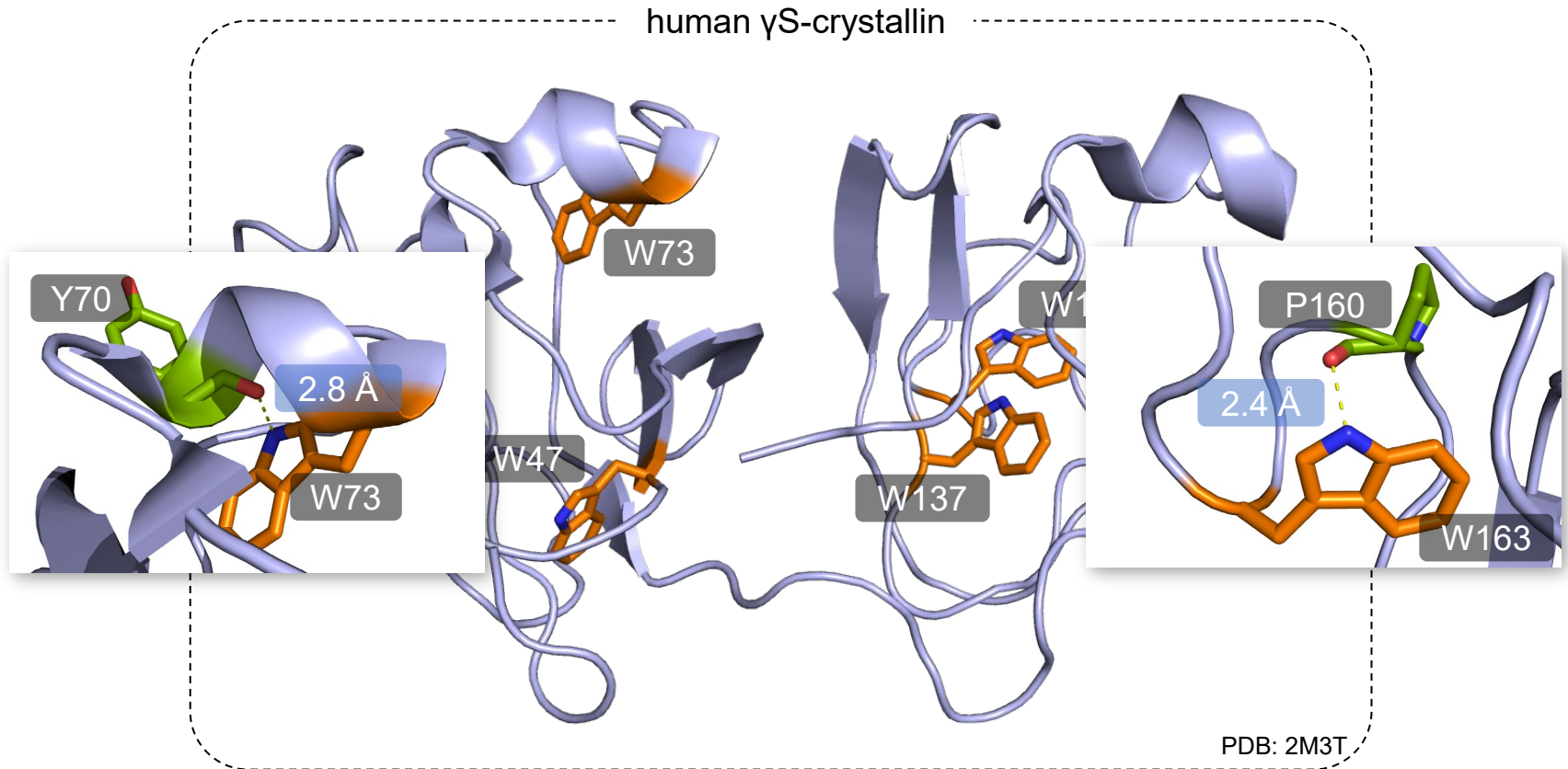
Southern California Pharmaceutical Discussion Group (SCPDG) Meeting
January 29th, 2026

Protein aggregation in the eye lens leads to cataracts



elucidate the molecular mechanisms of crystallin aggregation
for alternative intervention strategies

Tryptophan pairs are at the core of human γ S-crystallin

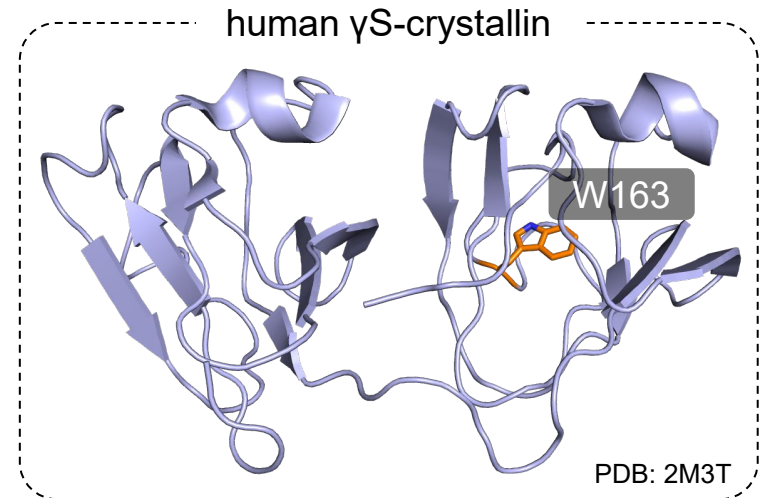


rapid fluorescence quenching via FRET and CT suggests tryptophan residues protect γ S-crystallin from UV damage

W163 is surface-exposed and thus oxidation-prone

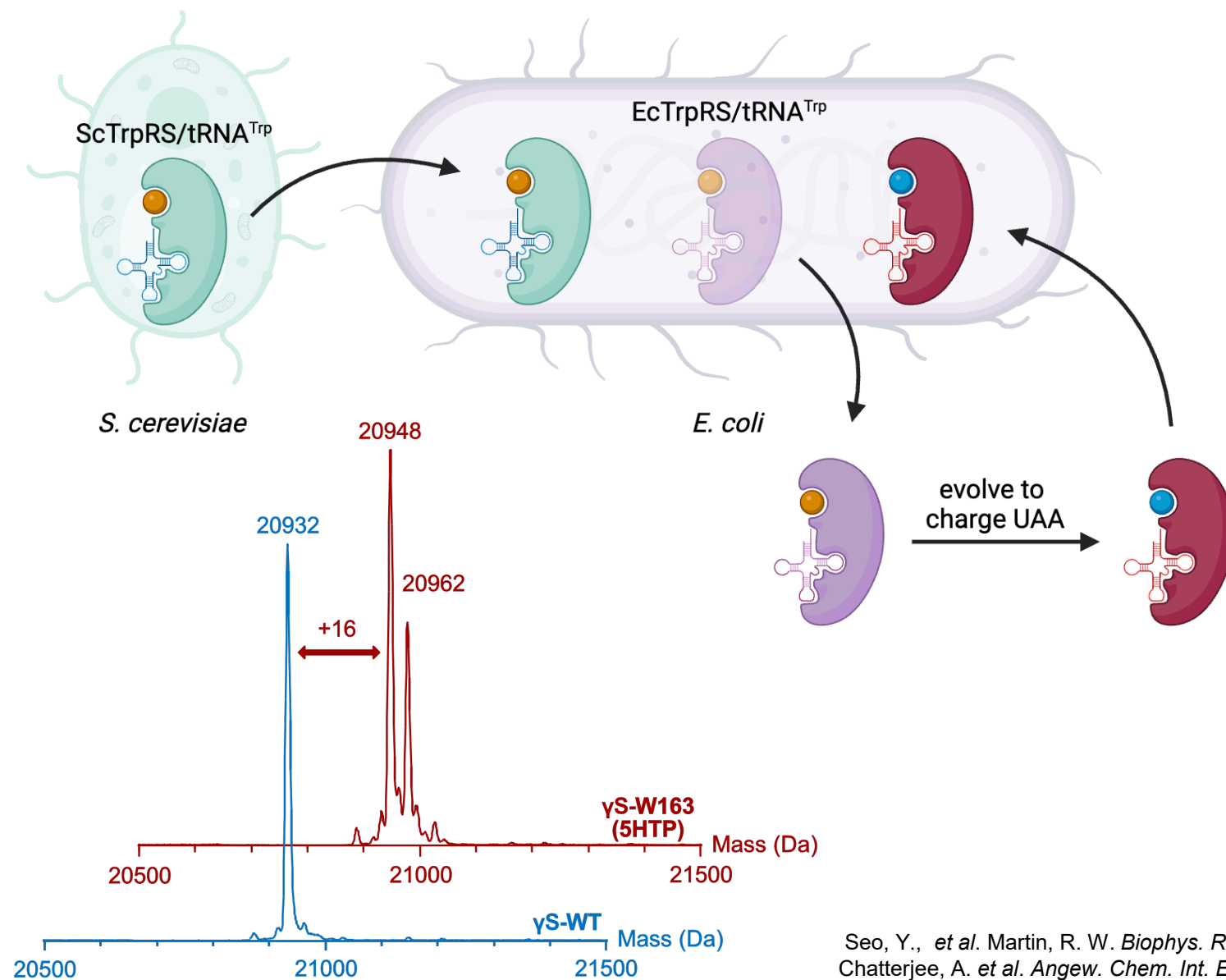
Table 1. Oxidation Sites Identified in γ and UV Irradiated H γ S^a

residue number	peptide	modification
1–10	G <u>S</u> KTGTKITF	K3 ⁻¹
42–72	VEGGT <small>W</small> AVYERP <small>N</small> FAGY <u>M</u> YILPQGEYPEYQR	M59 ⁺¹⁶
73–79	<u>W</u> MGLNDR	M74 ⁺¹⁶
102–125	GDFSGQ <u>M</u> YETTEDCPS <u>I</u> MEQ <u>F</u> HMR	M108 ⁺¹⁶ M119 ⁺¹⁶ M124 ⁺¹⁶
132–146	<u>V</u> LEGVWIFYELPNYR	V132 ⁺¹⁶ or L133 ⁺¹⁶ L142 ⁺¹⁶
159–174	KPID <u>W</u> GAASPAVQ <u>S</u> FR	W163 ⁺¹⁶
20–36	RYDC <u>D</u> CD <u>C</u> AD <u>F</u> HTYLSR	C23 ⁺³² C25 ⁺³² C27 ⁺³²



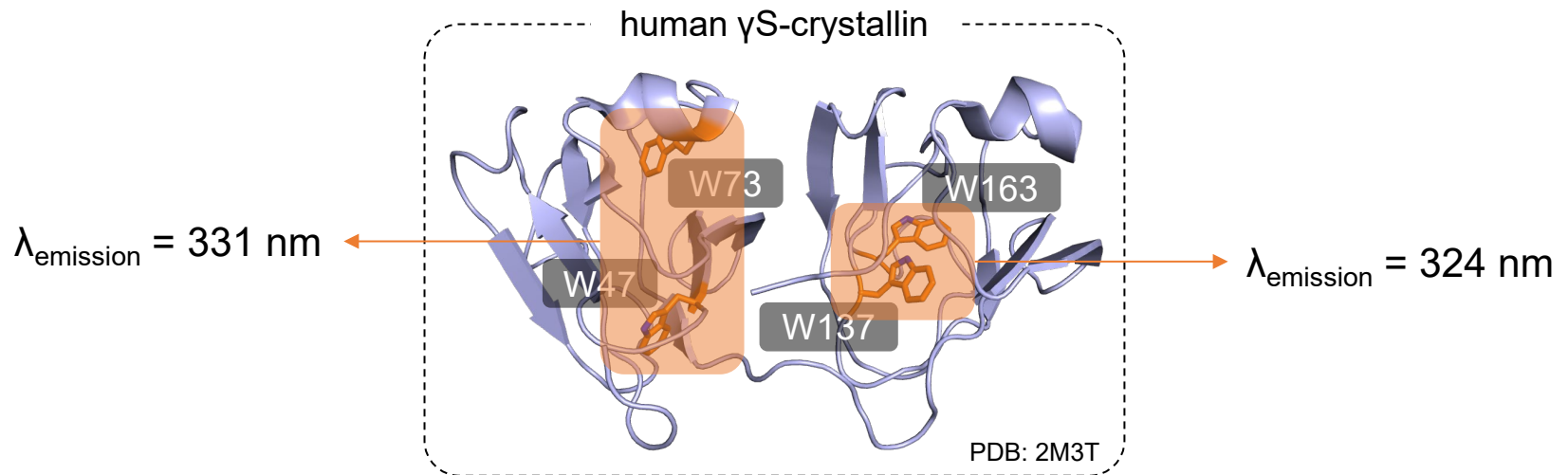
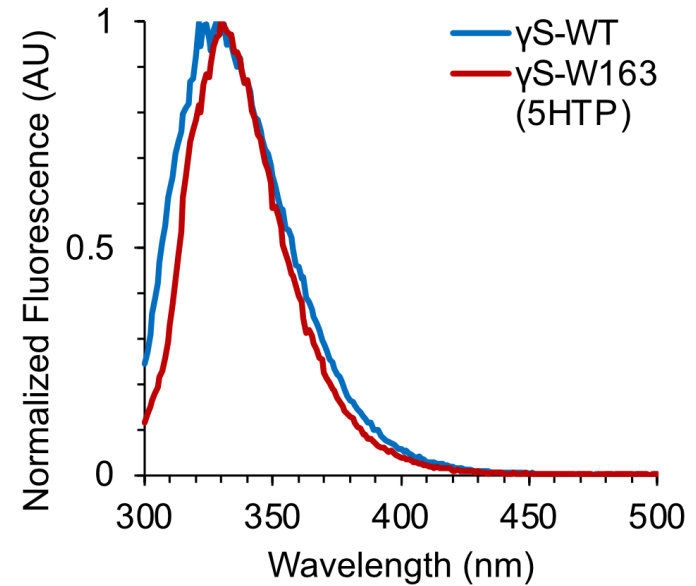
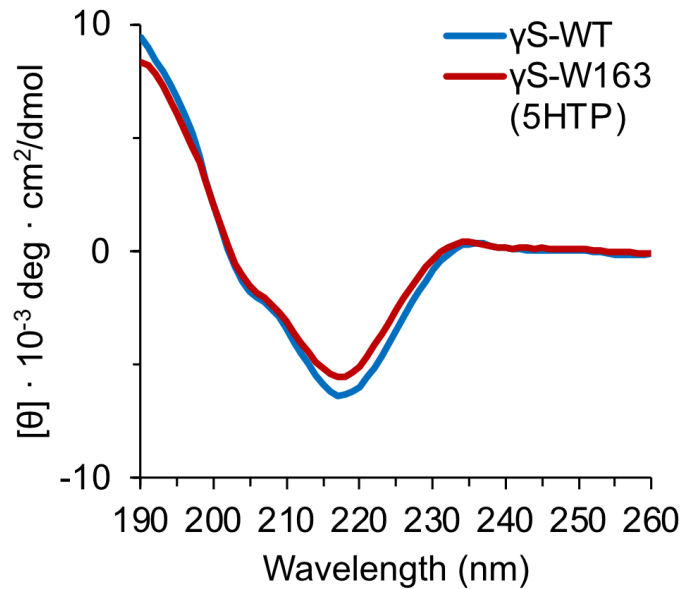
what are the structural and biophysical consequences of W163 oxidation?

Chatterjee's GCE platform enabled site-specific oxidation

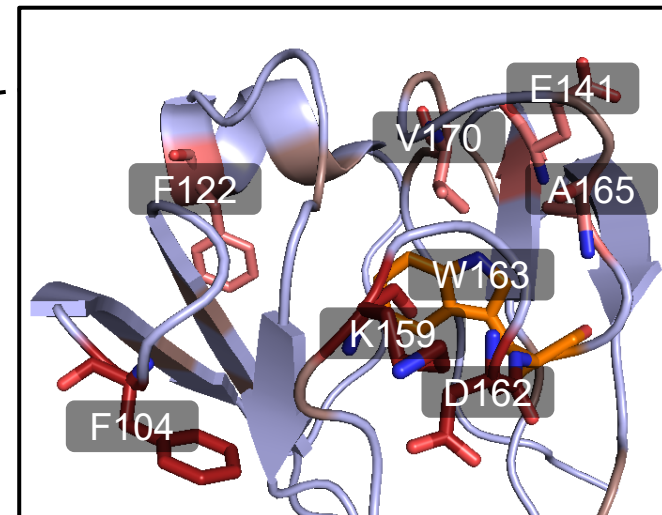
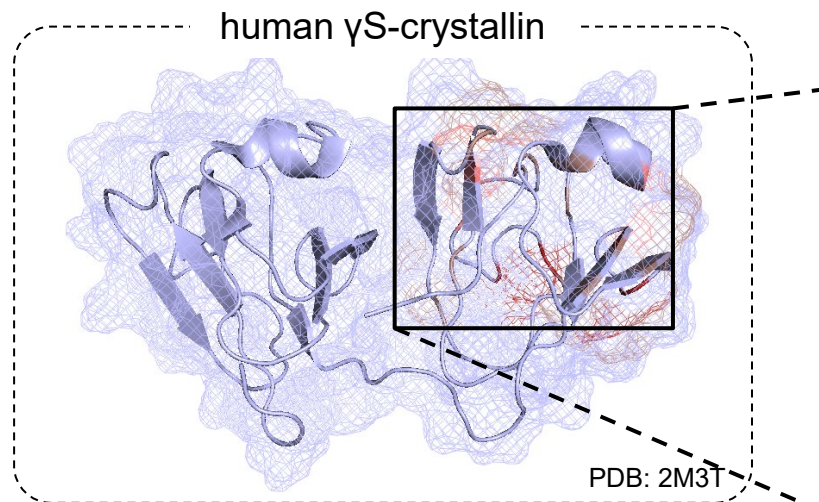
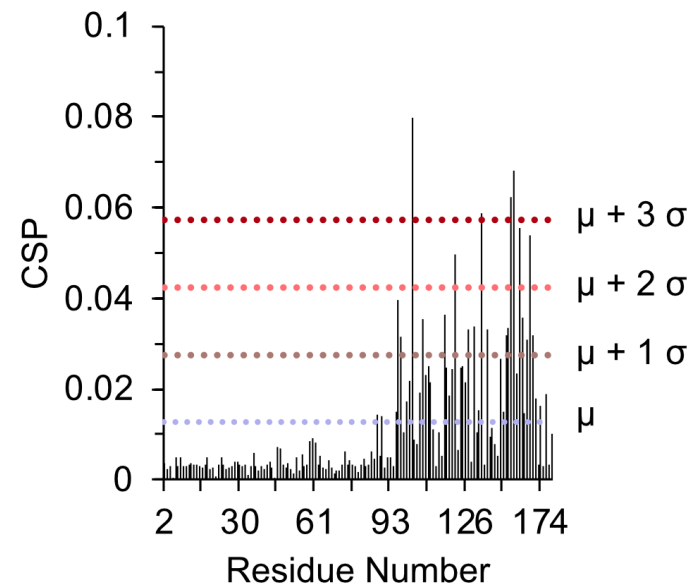
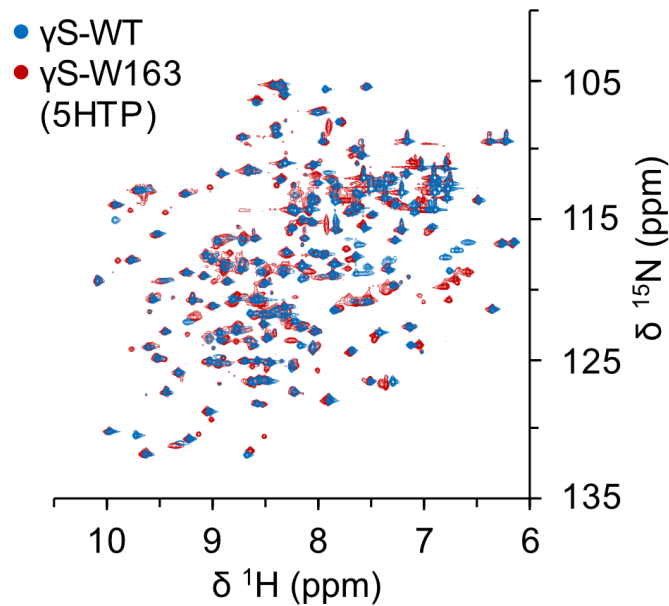


Seo, Y., et al. Martin, R. W. *Biophys. Rep.* **2026**, in press
Chatterjee, A. et al. *Angew. Chem. Int. Ed.* **2013**, 52, 5106
Italia, J., et al. Chatterjee, A. *Nat. Chem. Biol.* **2017**, 13, 446
Ficaretta, E. D., et al. Chatterjee, A. *J. Mol. Biol.* **2022**, 434, 167304

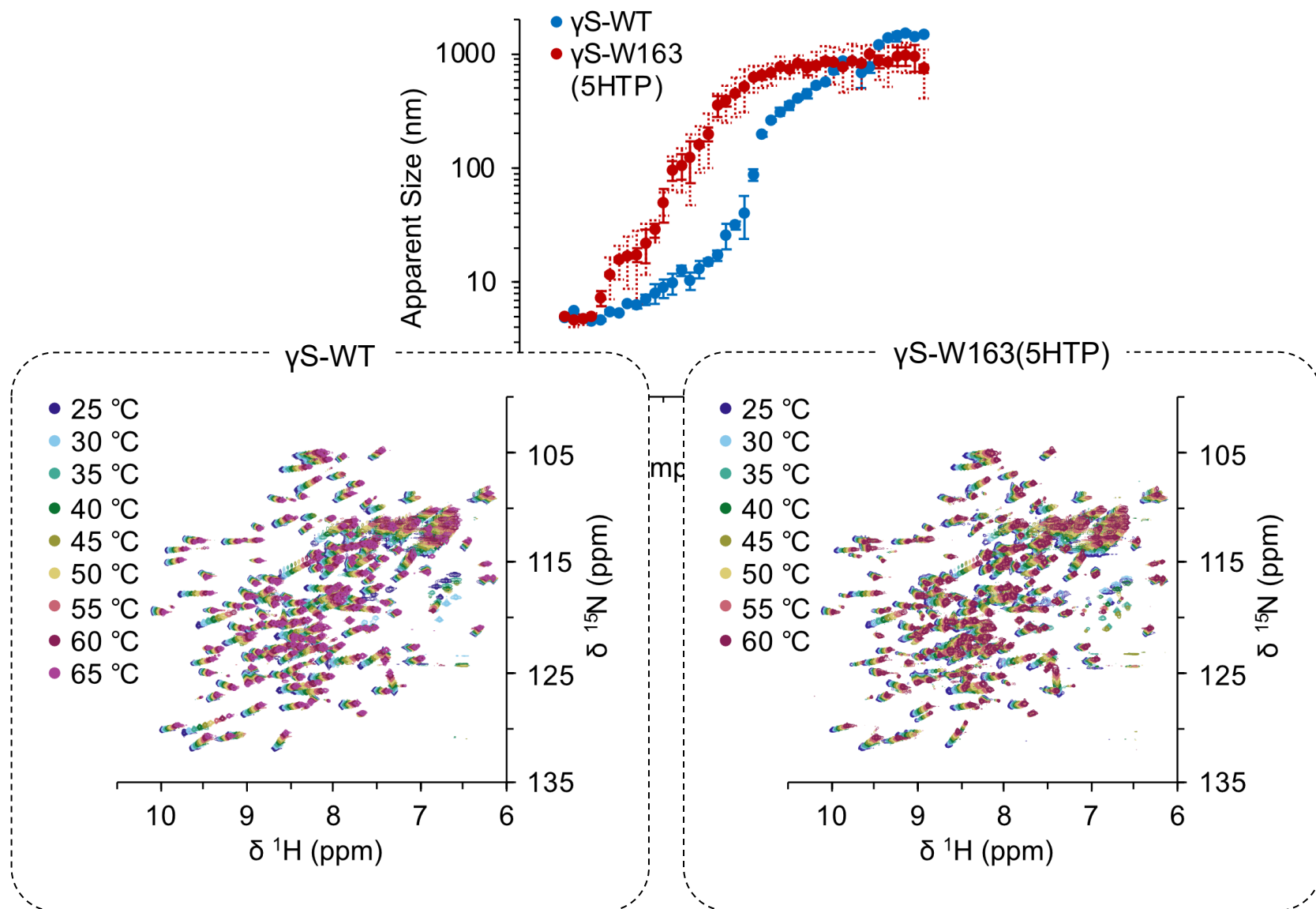
W163 oxidation caused small structural changes



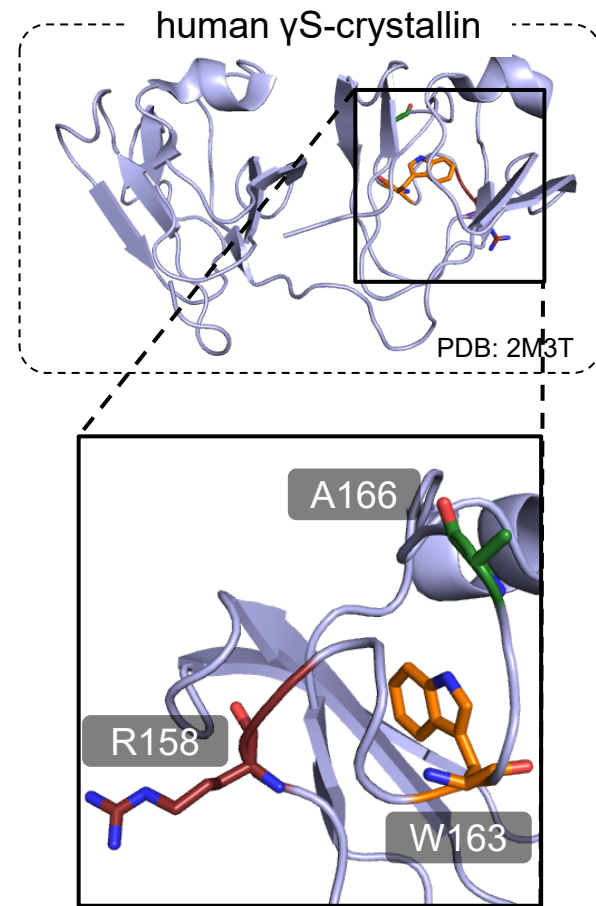
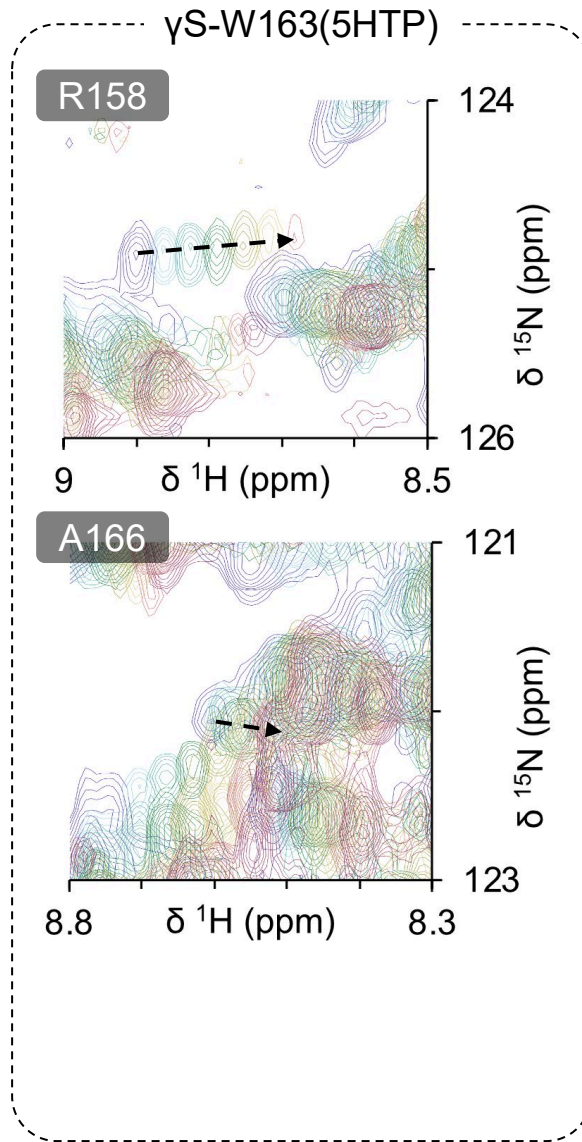
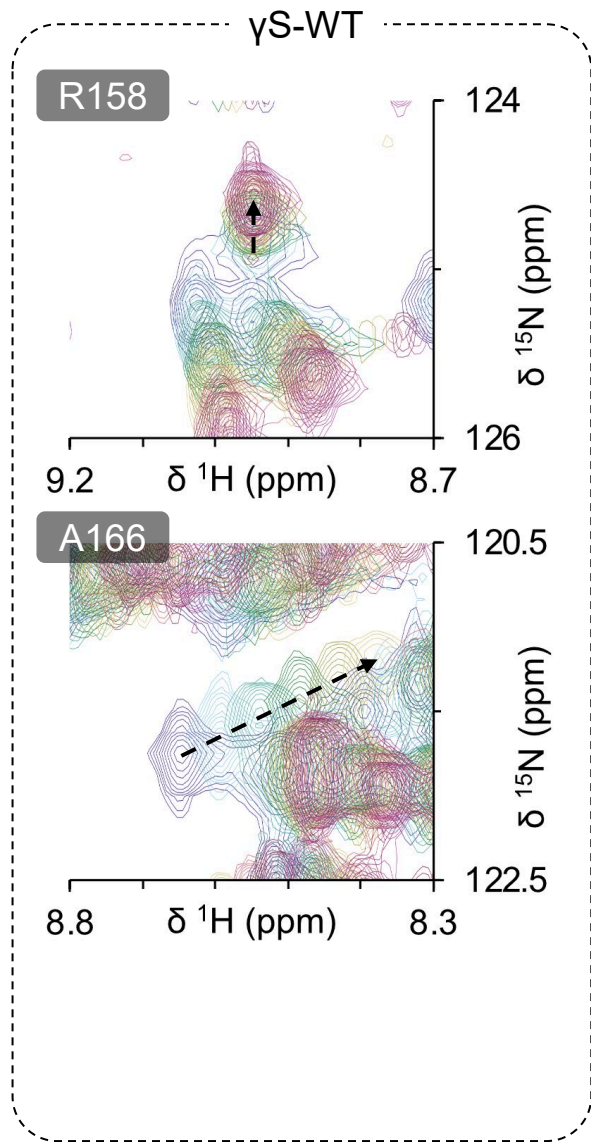
Structural changes were localized in the C-terminal domain



Thermal aggregation was exacerbated with W163 oxidation

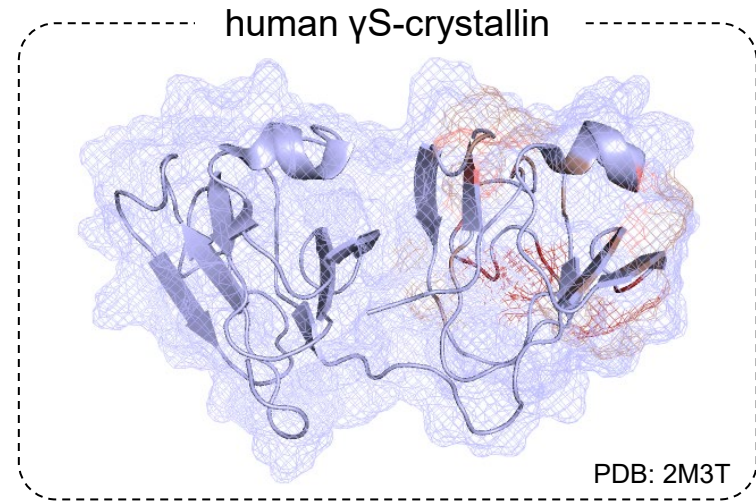
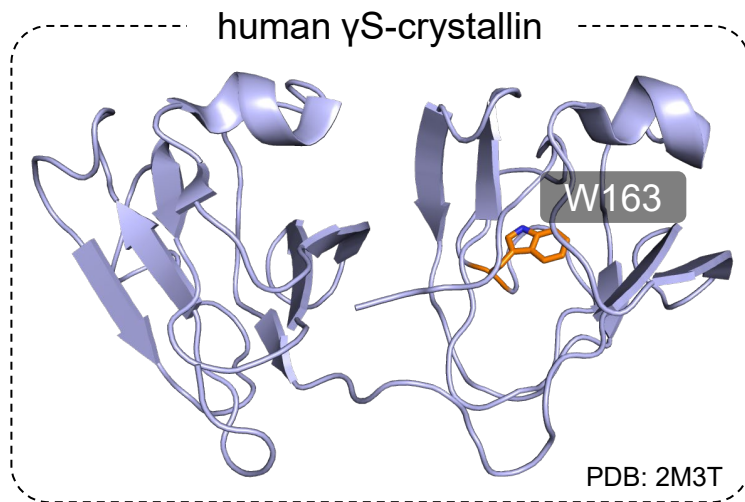


Local hydrogen bonds were displaced by W163 oxidation



W163 oxidation compromised resilience against stress

- site-specific oxidation of human γ S-crystallin at W163 was achieved using GCE
- oxidized variant exhibited premature aggregation under thermal stress
- thermal aggregation studied by ^1H - ^{15}N HSQC revealed disrupted H-bond network



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Dr. Felix Grün
Benjamin Katz
Dr. Suvrajit Sengupta



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