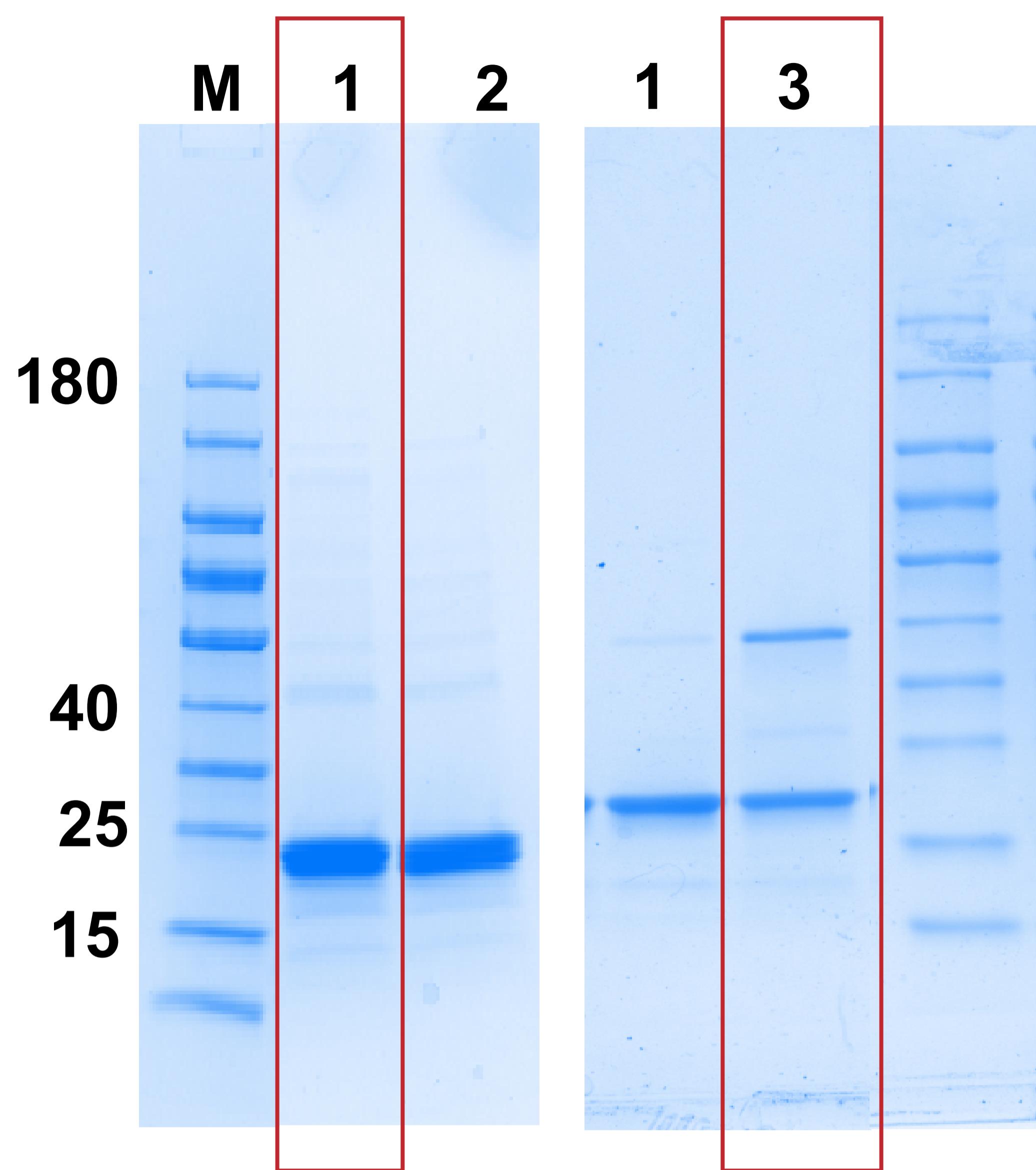
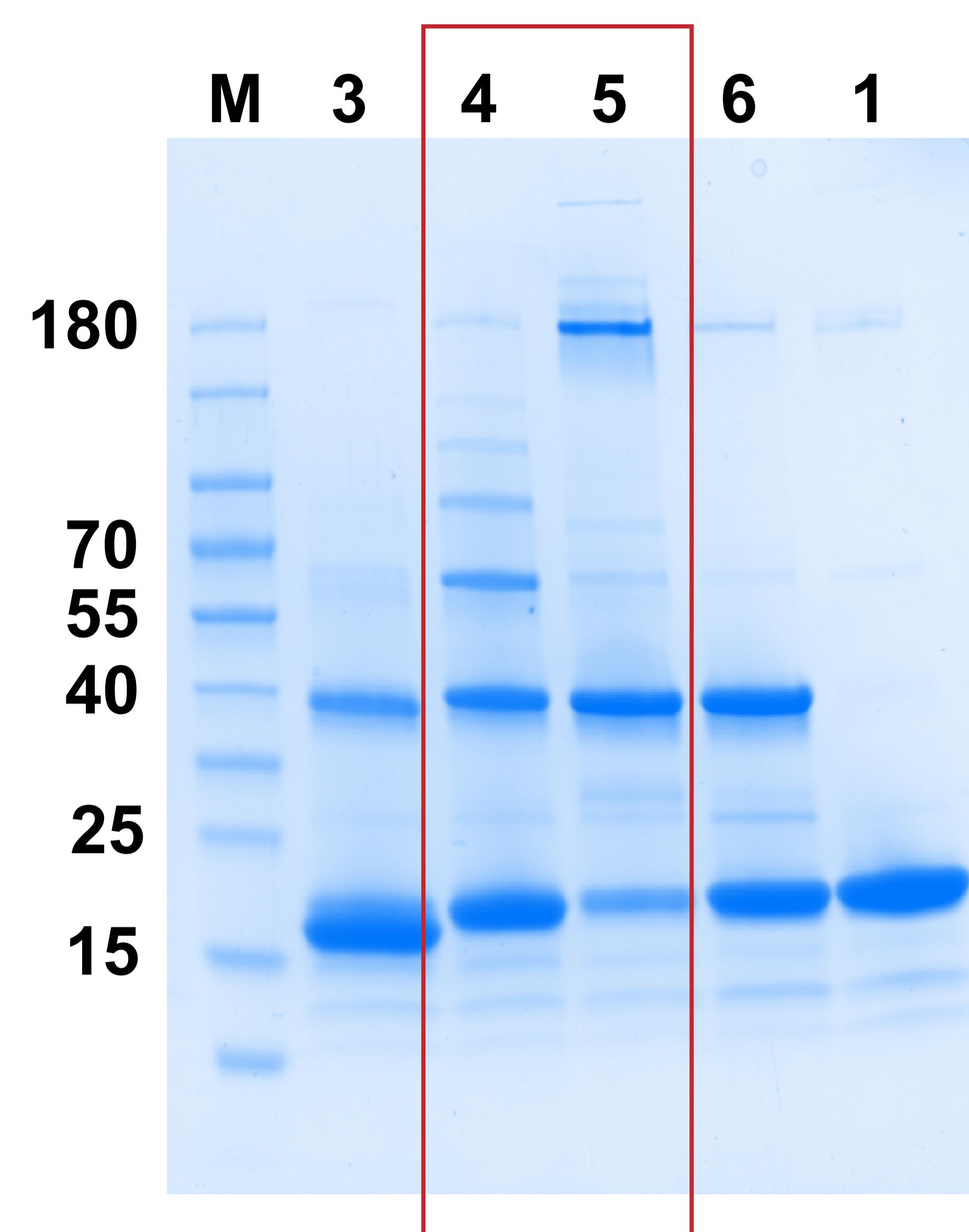
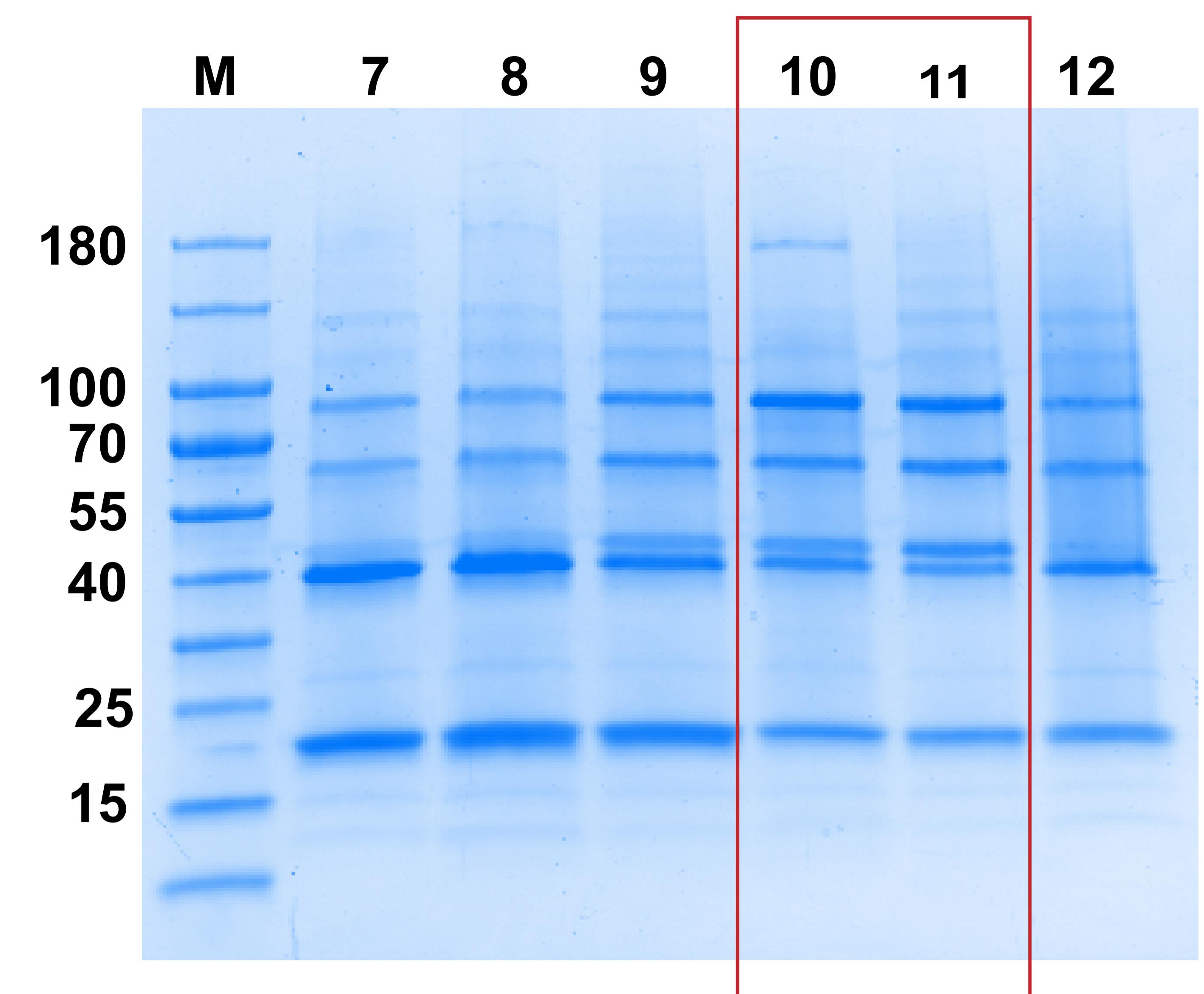
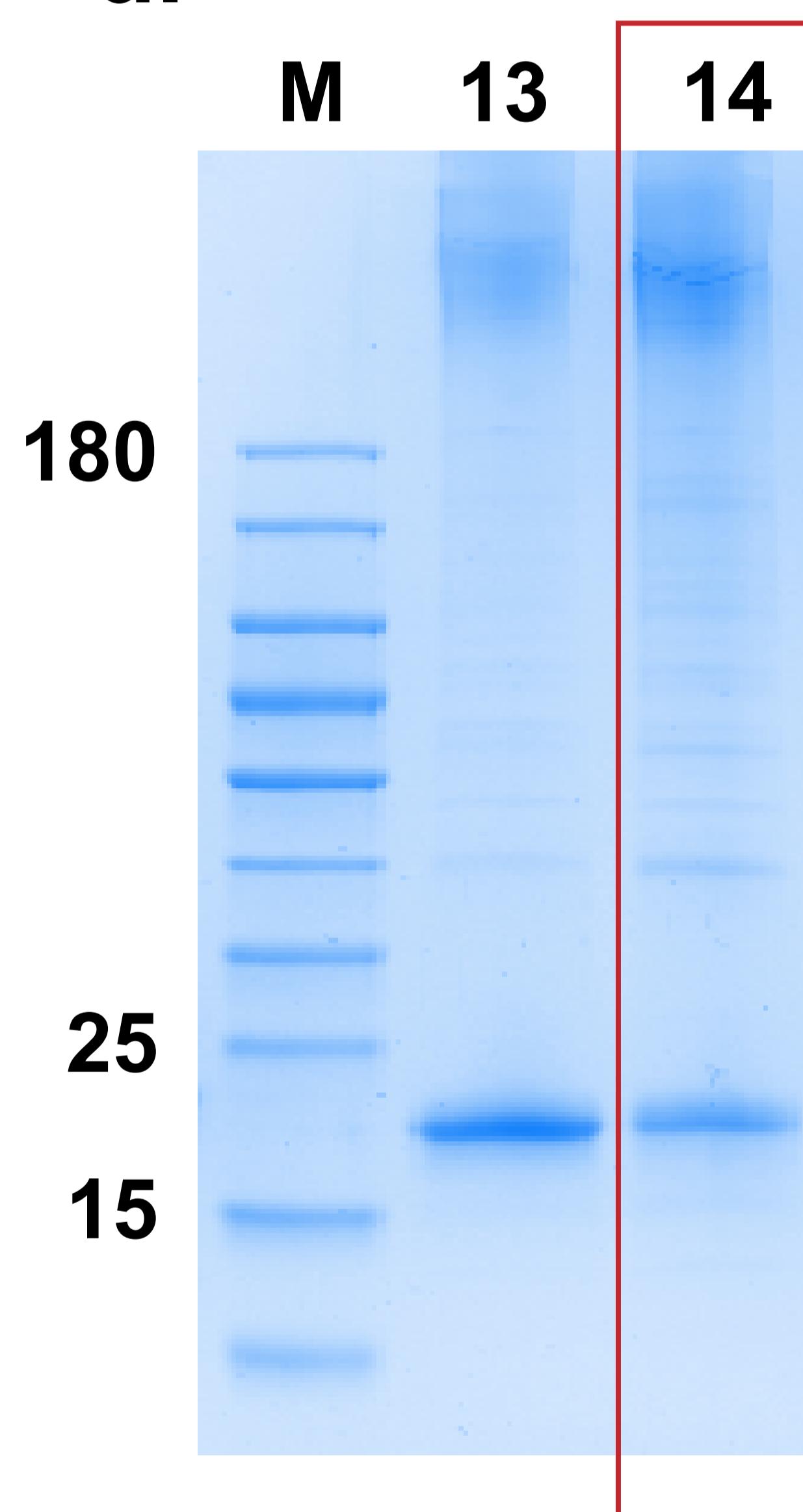


a.**b.****c.****d.**

- 1. tES
 - 2. tES R151C
 - 3. tES A152C
 - 4. tES A152C - L53C
 - 5. tES A152C - A74C
 - 6. tES A152C - G76C
 - 7. tES A152C - R66C
 - 8. tES A152C - L53C - R66C
 - 9. tES A152C - A74C - R66C
 - 10. tES A152C - G67C
 - 11. tES A152C - L53C - G67C
 - 12. tES A152C - A74C - G67C
 - 13. tES A152C - G67C - A117C - G37C
 - 14. tES A152C - L53C - G67C - A117C - G37C
- M. Marker

Figure S1. (a-d) Non-reducing SDS-PAGE for designed cysteine residue substitutions.

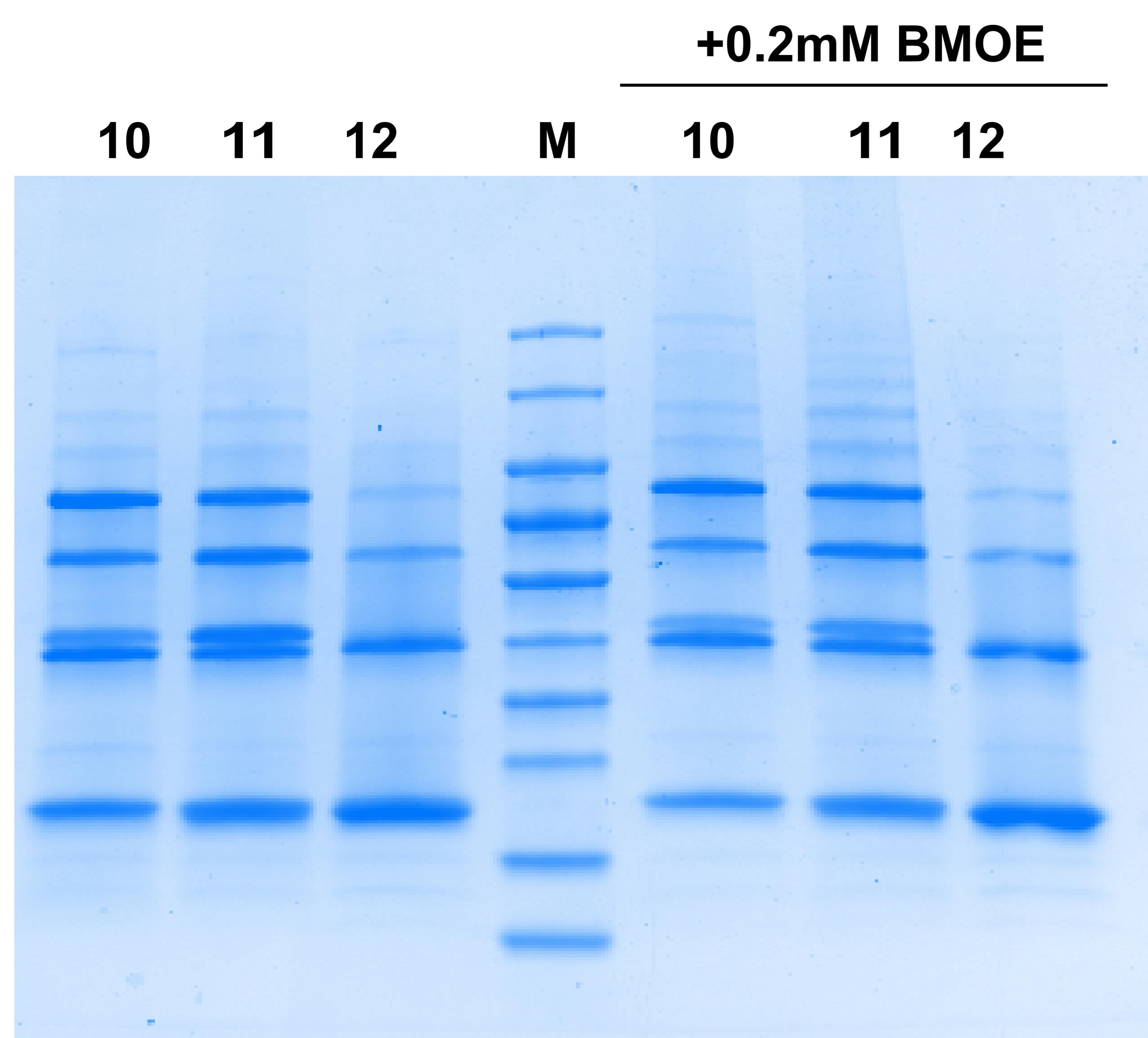
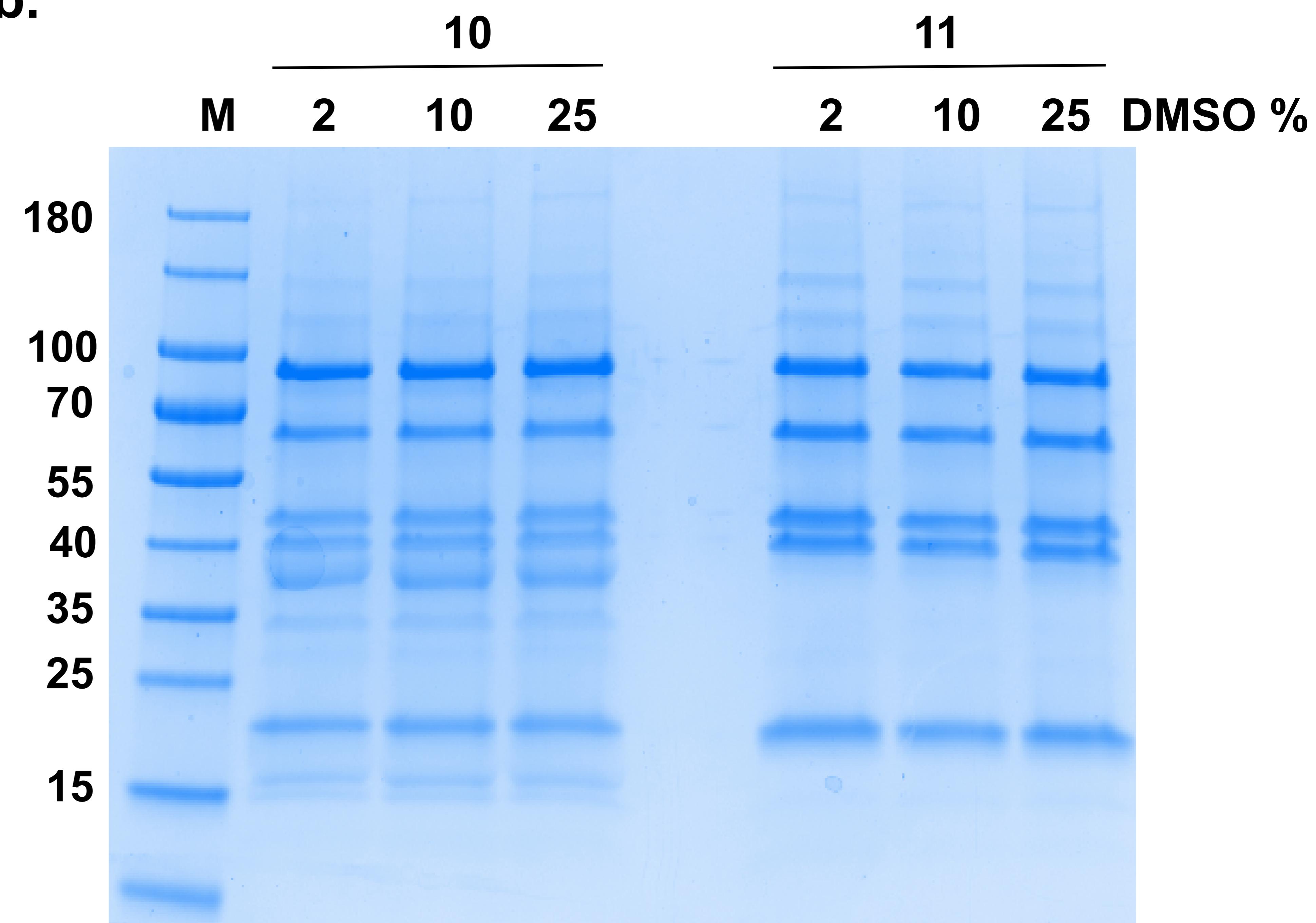
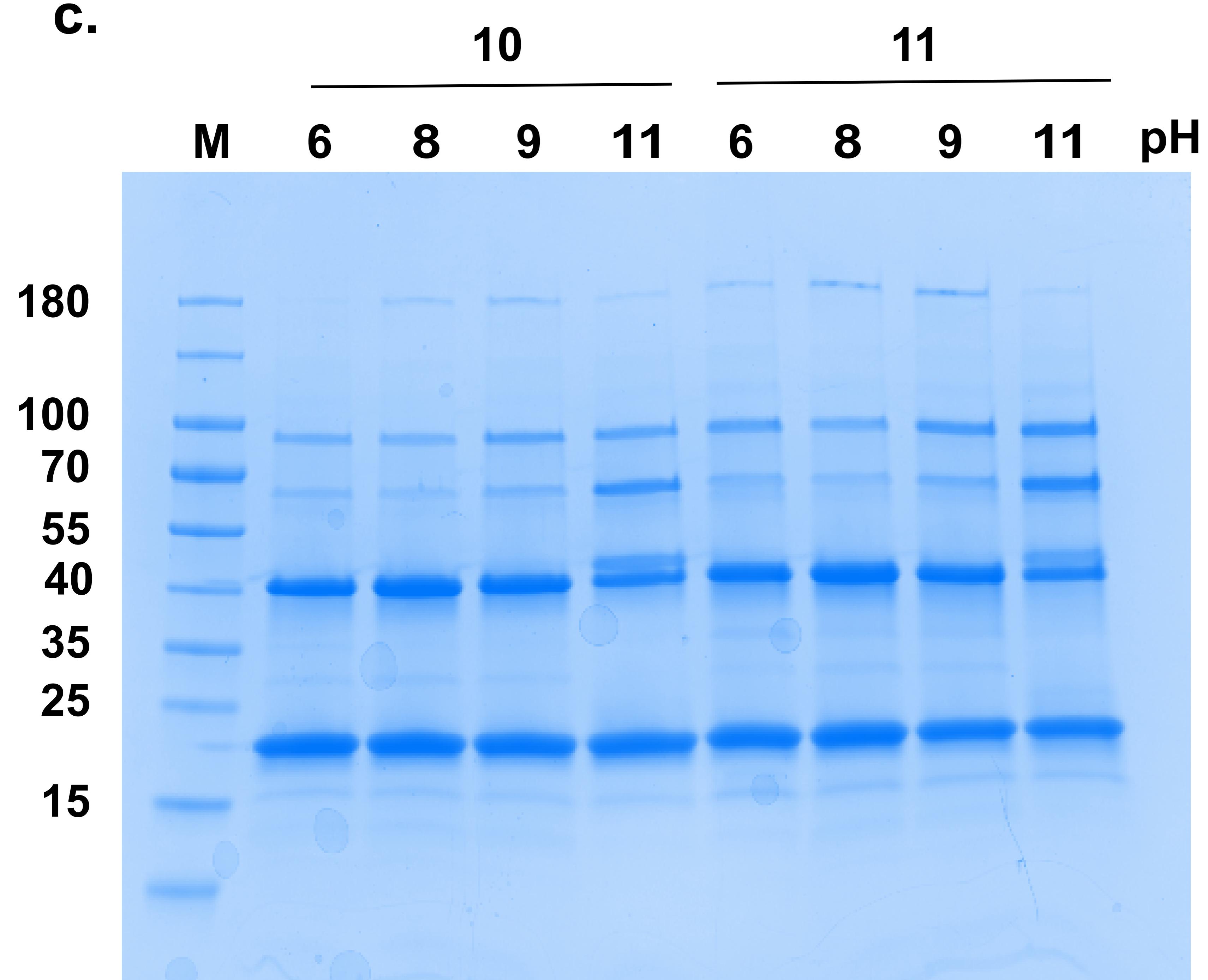
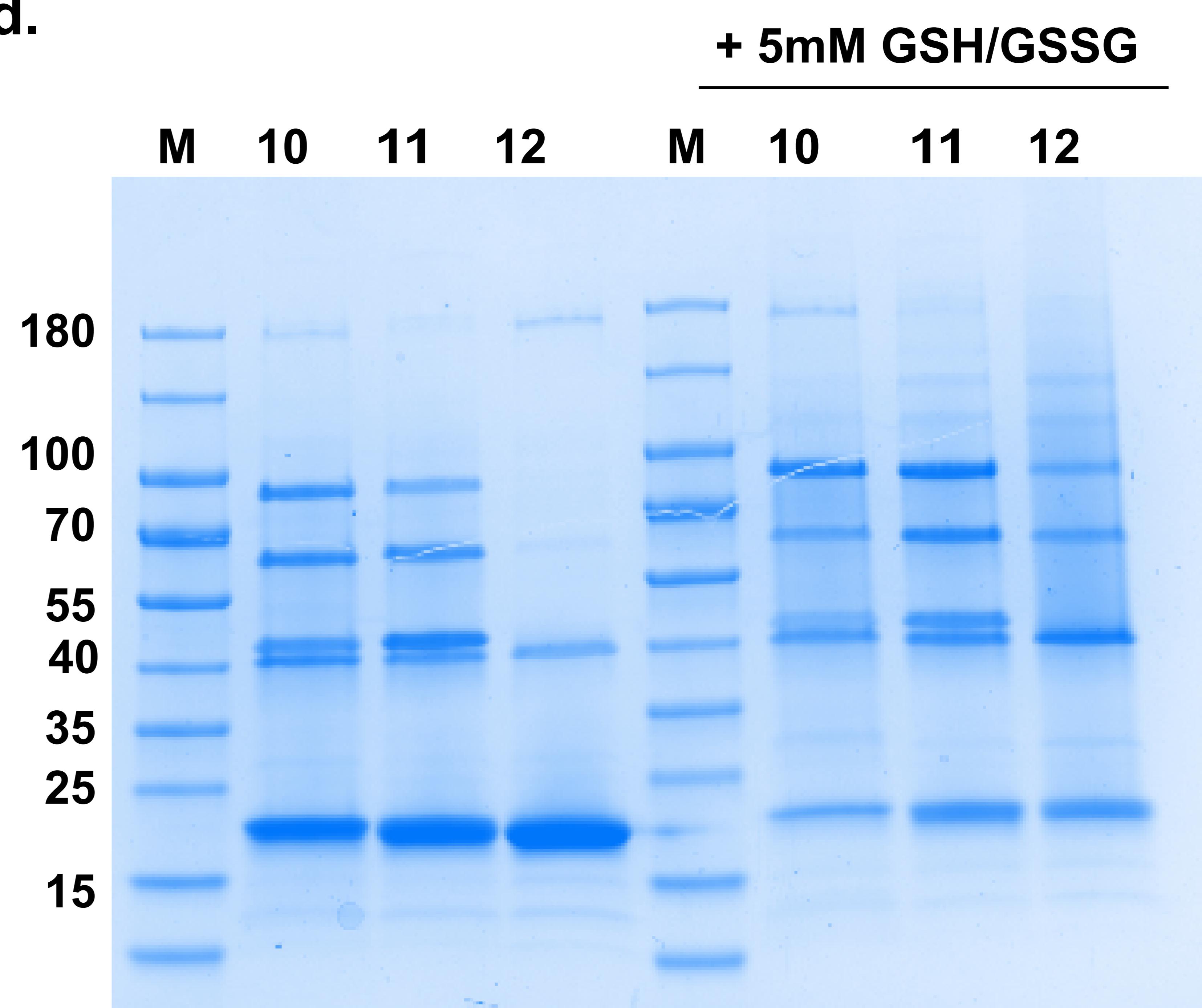
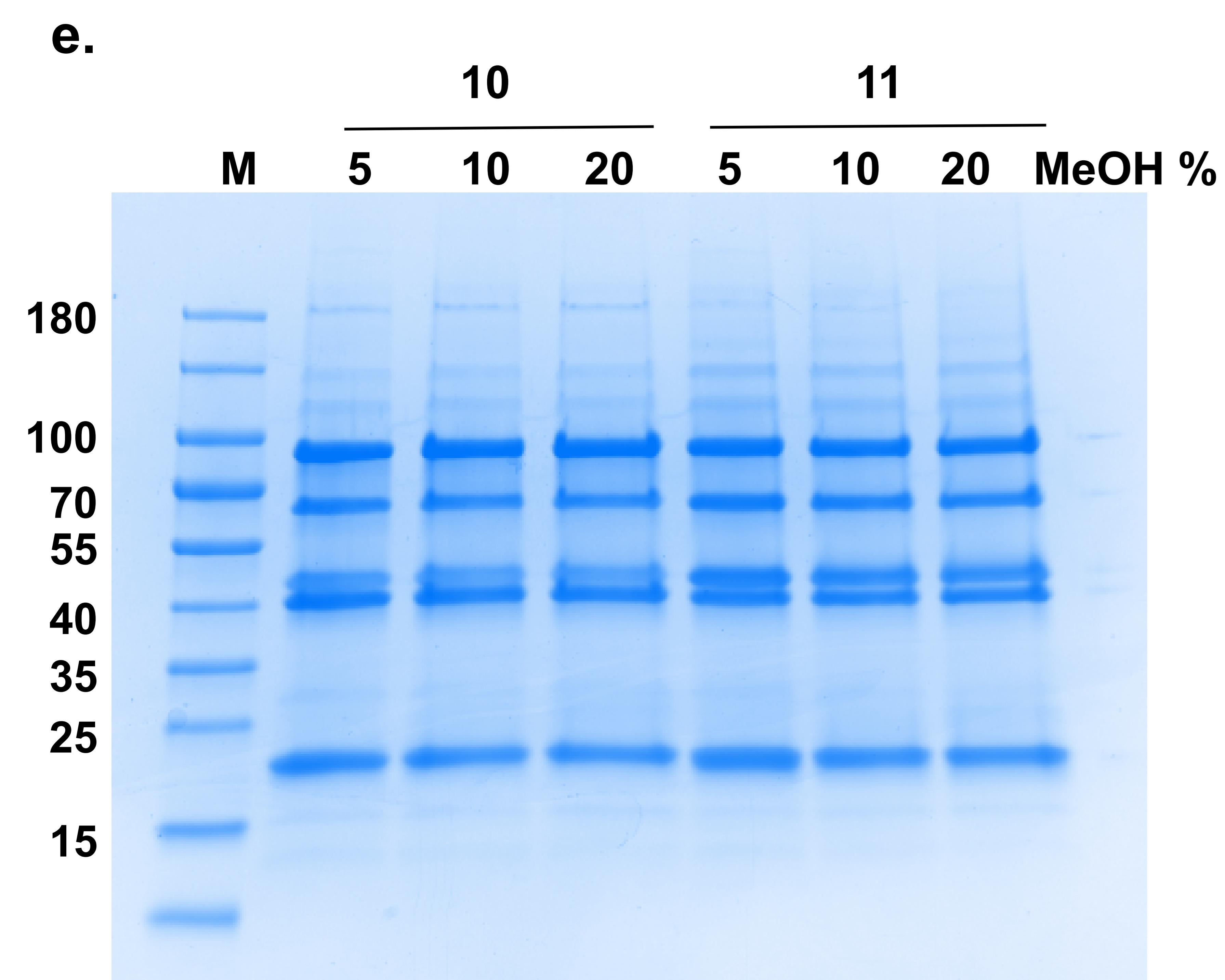
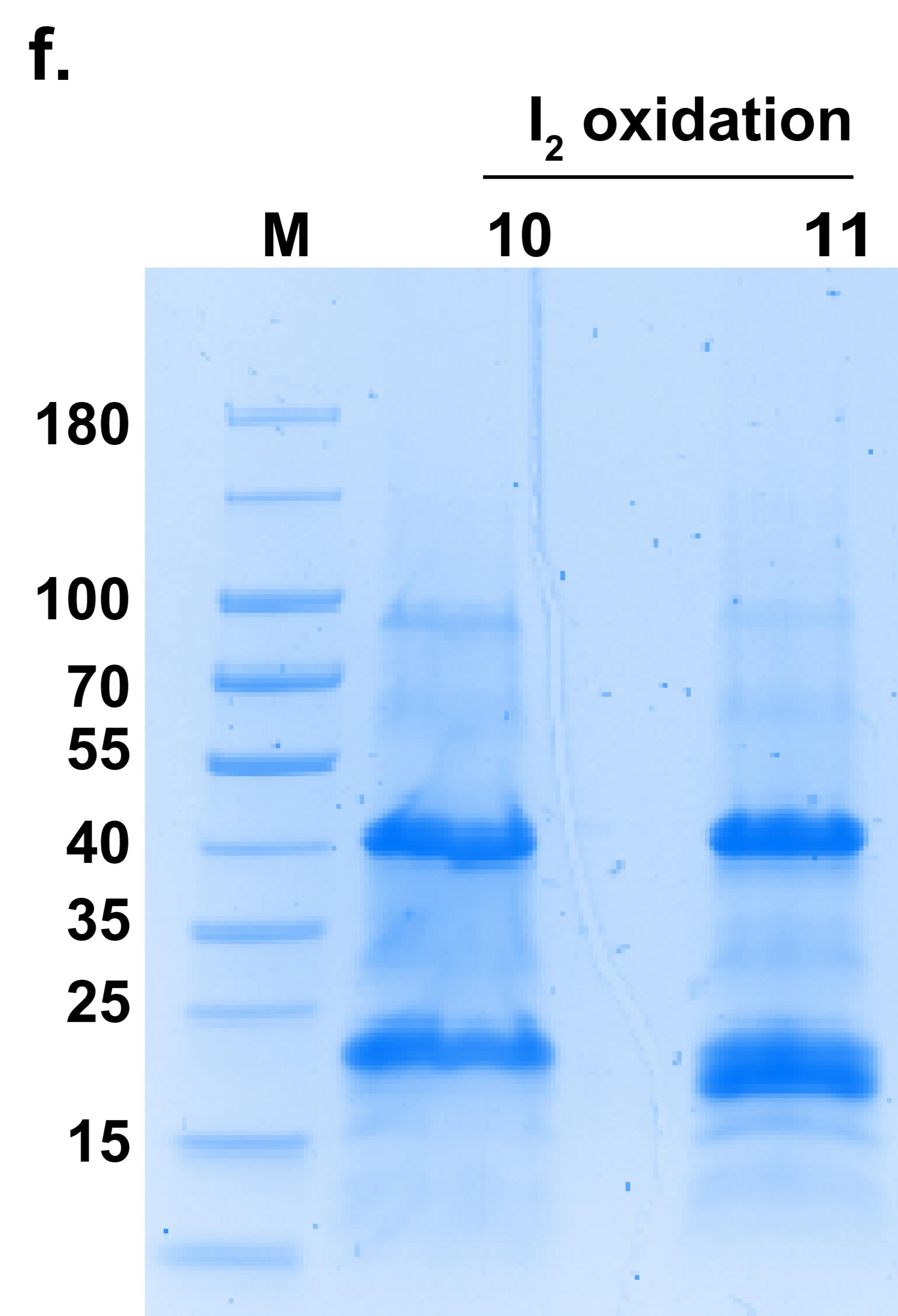
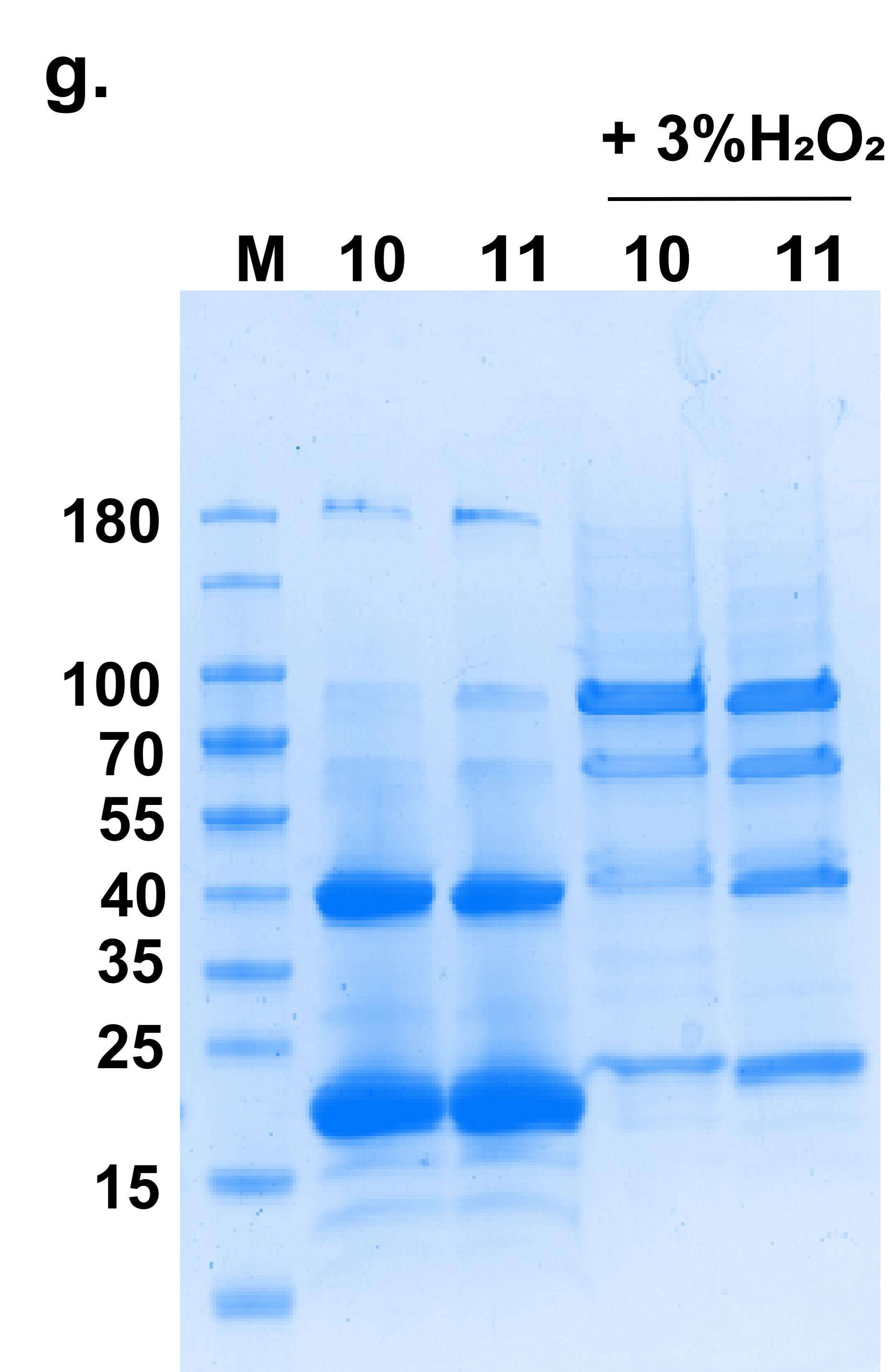
a.**b.****c.****d.****e.****f.****g.****9. tES A152C - A74C - R66C****10. tES A152C - G67C****11. tES A152C - L53C - G67C****M. Marker**

Figure S2. (a-g) Non-reducing SDS-PAGE to increase disulfide formation in 9,10, and 11 constructs.

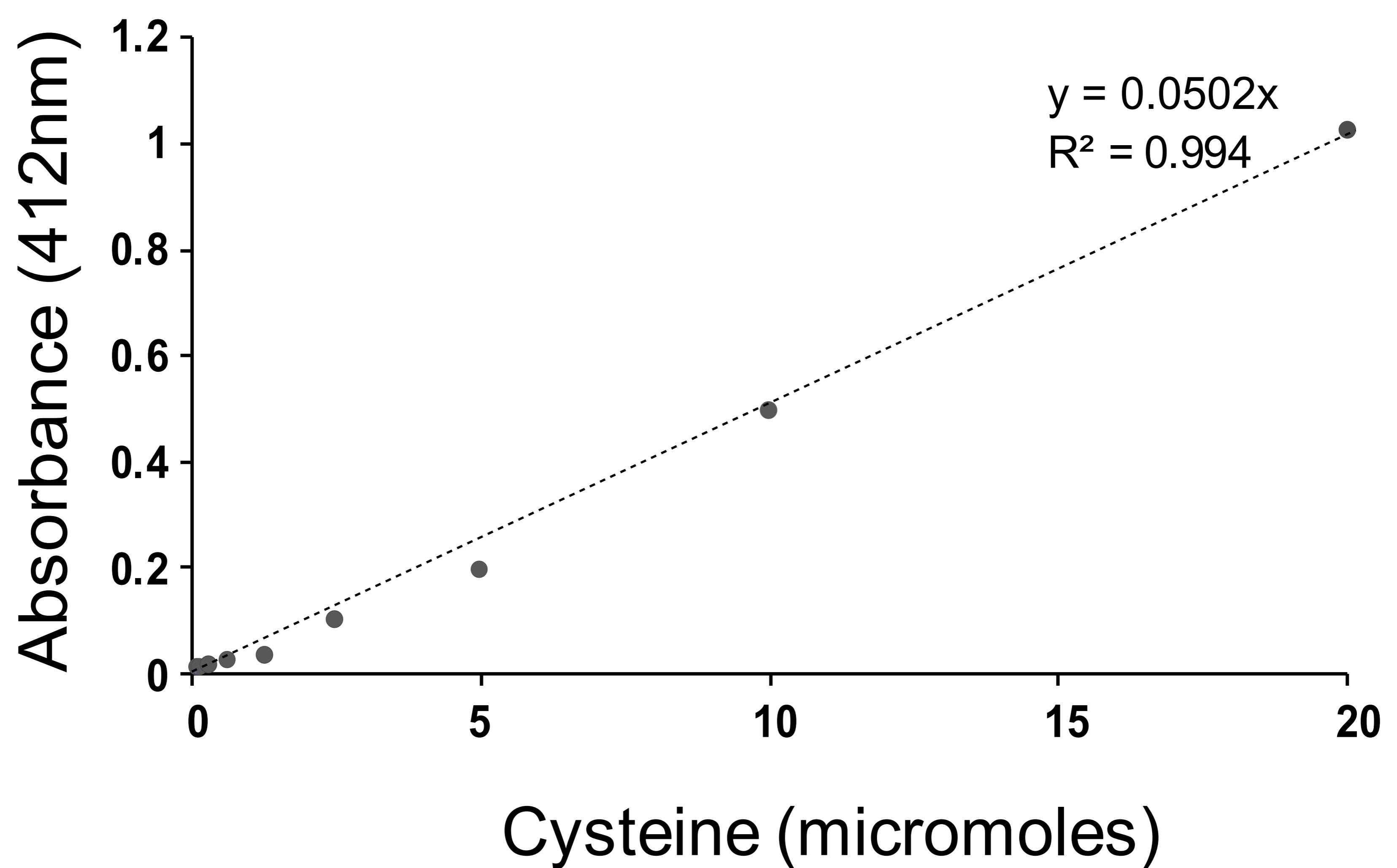


Figure S3. Ellman's Assay Standard Curve.

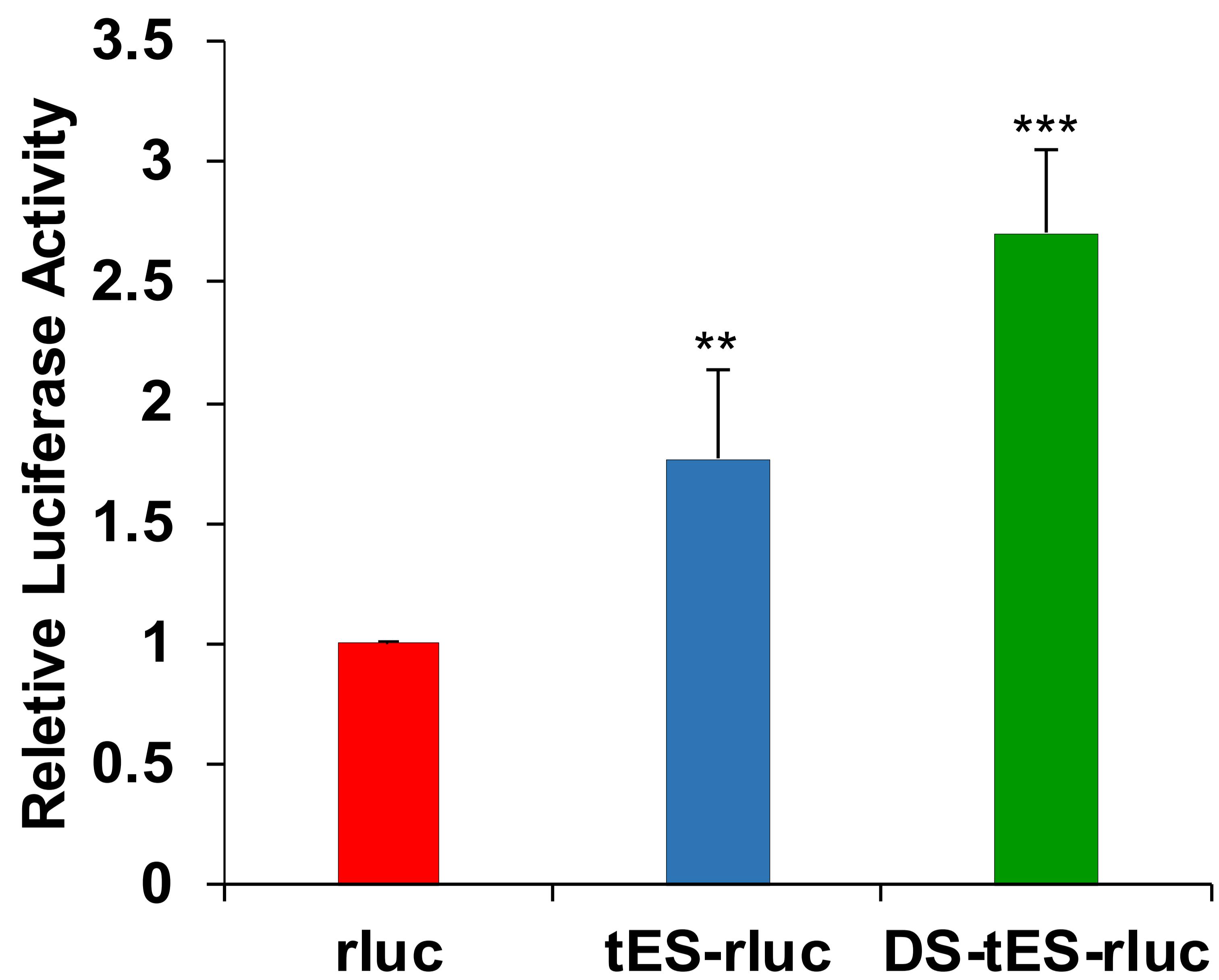


Figure S4. Permeability assay in Caco2 monolayers shows that both tES and DS-tES can permeabilize through intestinal epithelium. (Data are shown as mean ± SEM, n = 3. *** P < 0.001. and ** P< 0.01)

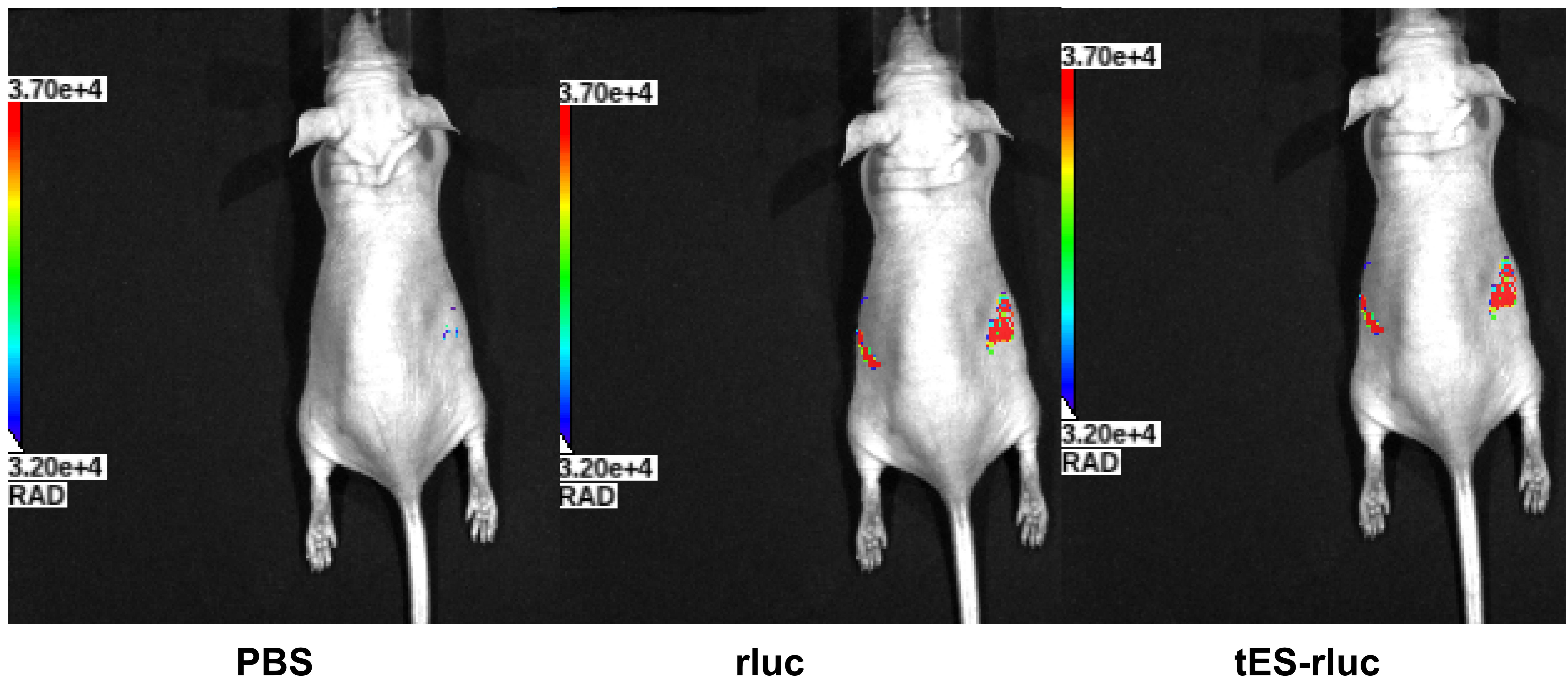
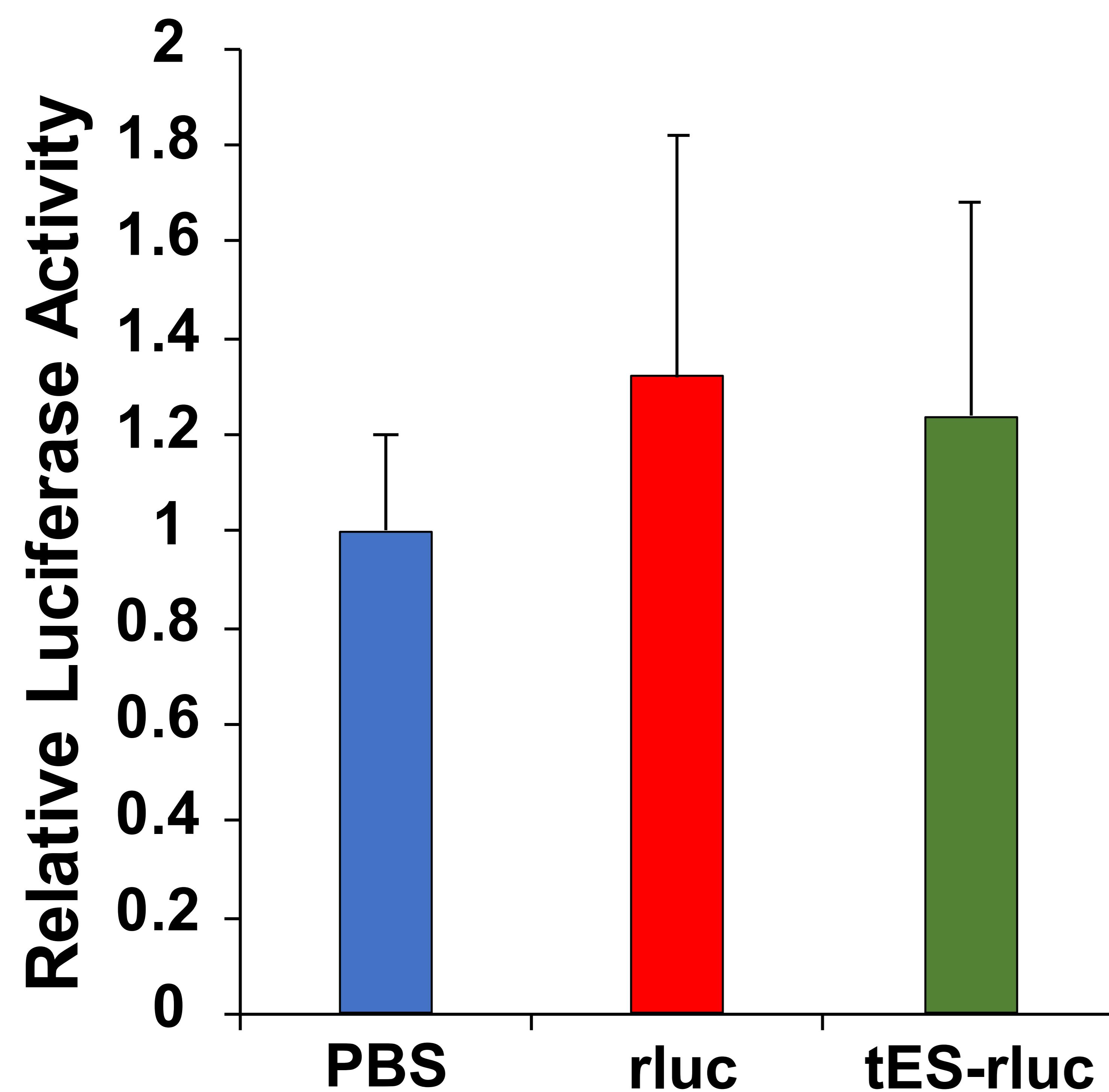
a.**PBS****rluc****tES-rluc****b.**

Figure S5.(a,b) Bioluminescence emitted from mice administered with tES-rluc/rluc in 3 h.

Features	DS-tES	tES
Number of cysteine per subunit	5	0
Non-reducing SDS-PAGE	Majorly oxidized Shell	Subunits
Molecular diameter	~13 nm	~13 nm
Stable at acidic pH (~4)	Yes	No
Against pepsin digestion at acidic pH	Highly stable	Not stable
Permeable through Caco2 monolayer	High	High

Table S1. Comparative analysis of DS-tES and tES