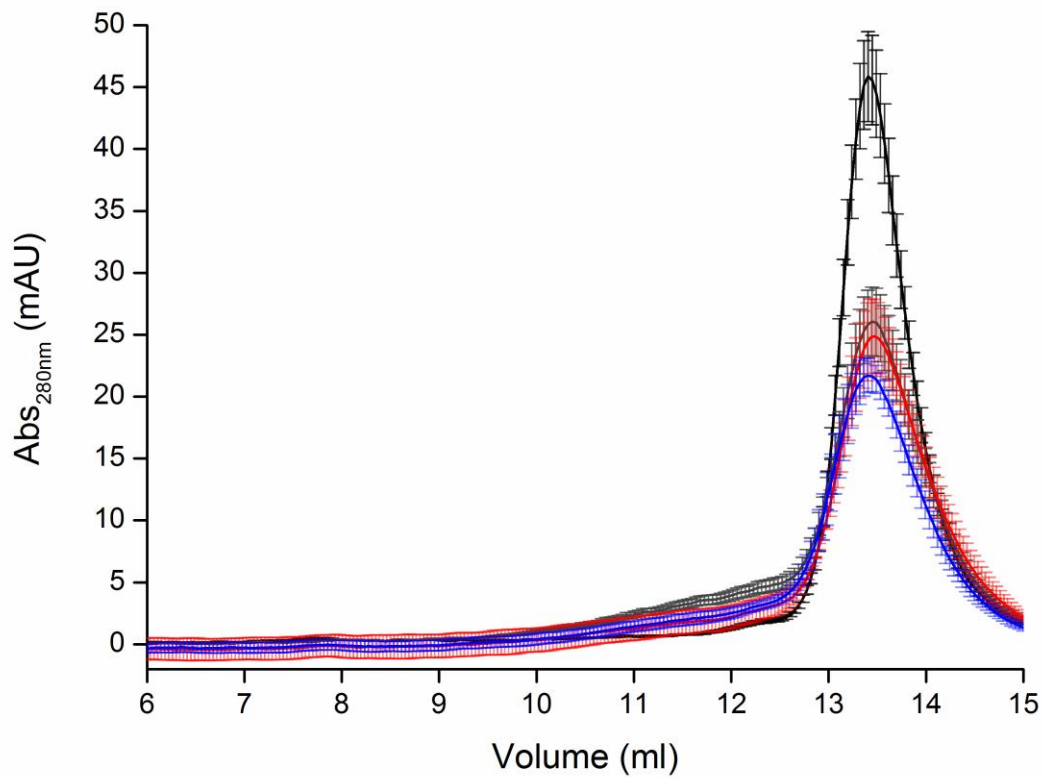
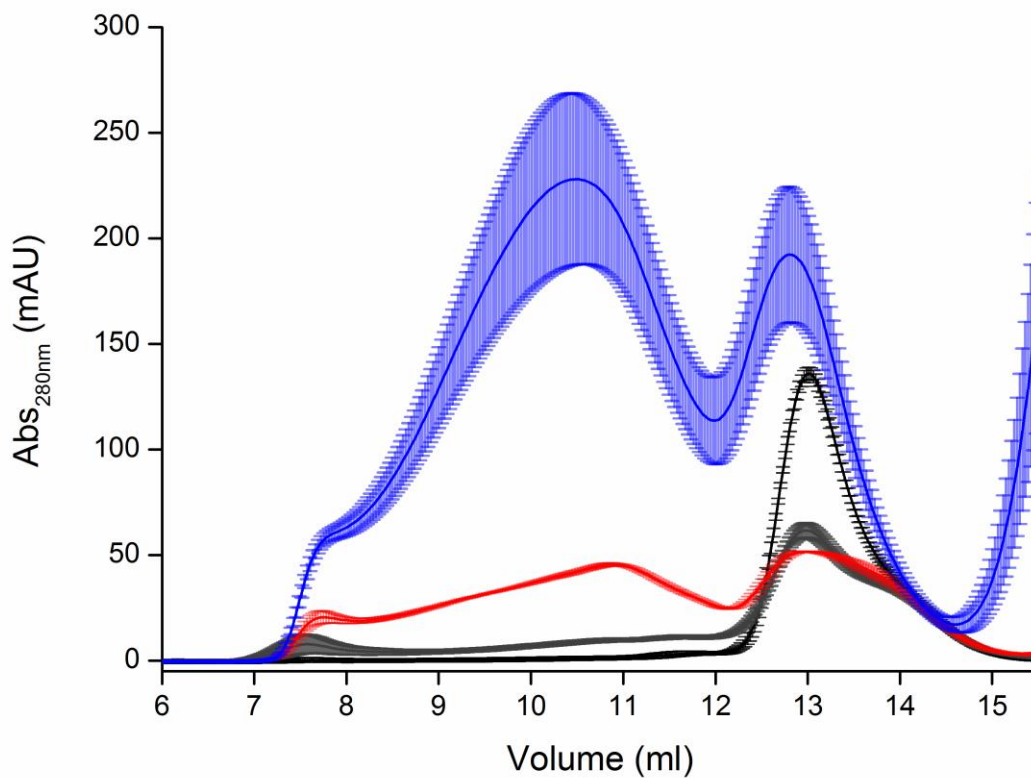


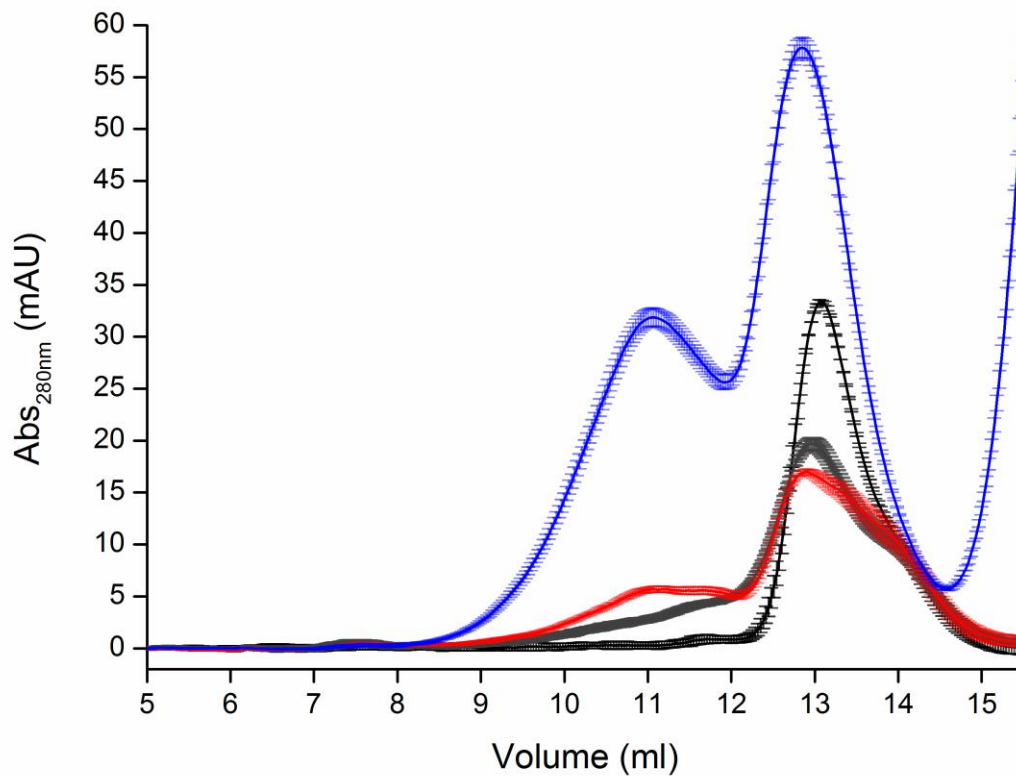
Supplementary Figure S1. Aggregation of 100 μM apo-I113T SOD1 in the presence of 5-fluorouridine. Size exclusion chromatograms of: Black – I113T SOD1, grey - I113T SOD1 after 48 hours incubation at 37°C, red – I113T SOD1 after 48 hours at 37°C with 300 μM 5-FUrd and, blue – I113T SOD1 after 48 hours at 37°C with 3 mM 5-FUrd. Each curve is the average of three separate aggregation reactions with error bars indicating standard deviation.



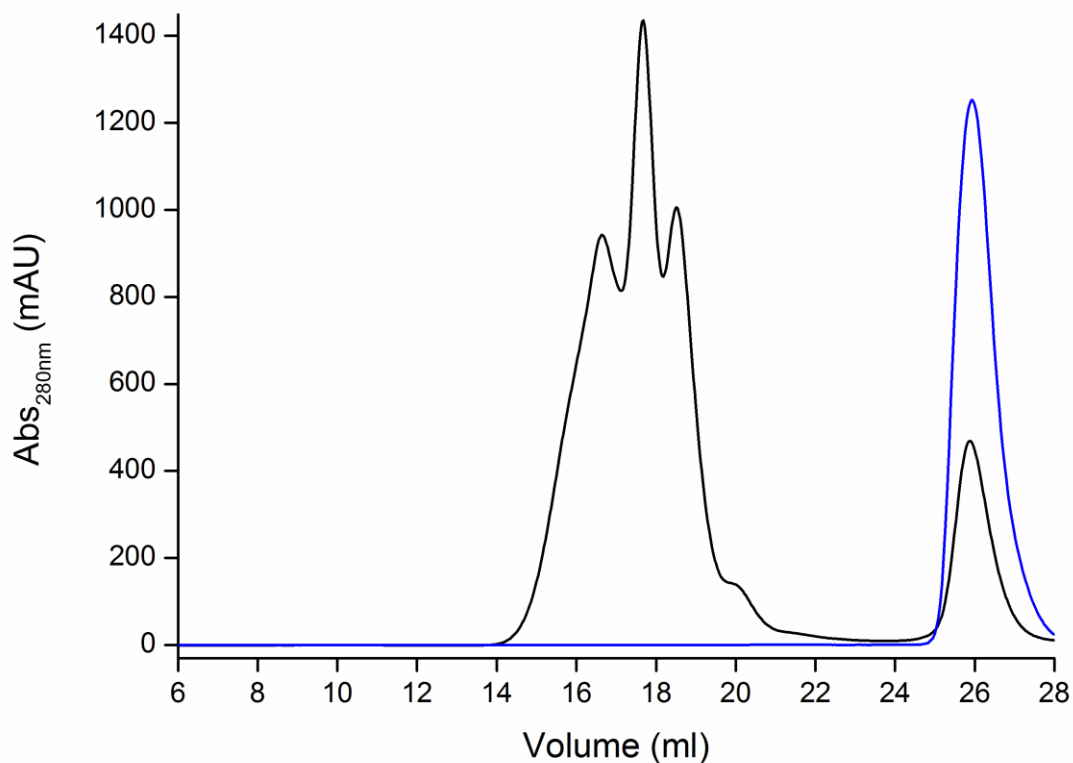
Supplementary Figure S2. Aggregation of 25 μ M apo-I113T SOD1 in the presence of 5-fluorouridine. Size exclusion chromatograms of: Black – I113T SOD1, grey - I113T SOD1 after 48 hours incubation at 37°C, red – I113T SOD1 after 48 hours at 37°C with 75 μ M 5-FUrd and, blue – I113T SOD1 after 48 hours at 37°C with 750 μ M 5-FUrd. Each curve is the average of three separate aggregation reactions with error bars indicating standard deviation.



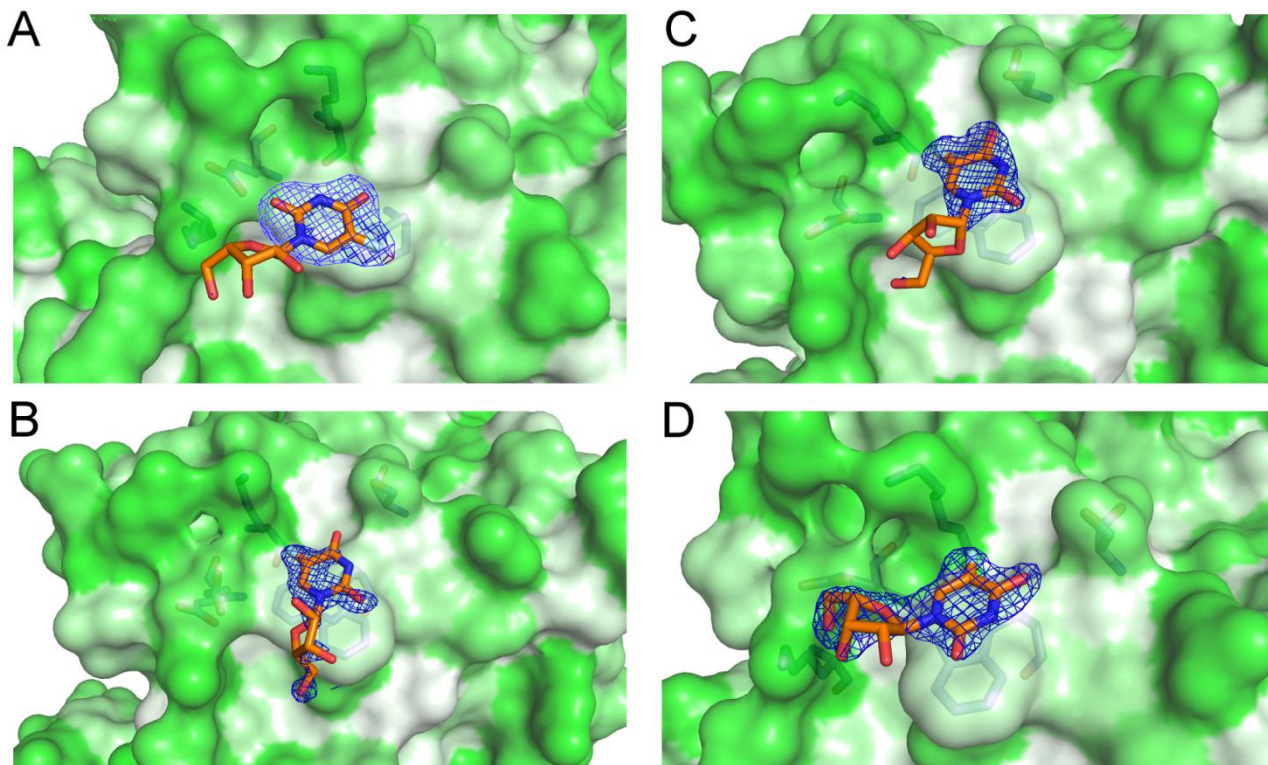
Supplementary Figure S3. Aggregation of 100 μ M apo-I113T SOD1 in the presence of isoproteranol. Size exclusion chromatograms of: Black – I113T SOD1, grey - I113T SOD1 after 48 hours incubation at 37°C, red – I113T SOD1 after 48 hours at 37°C with 300 μ M isoproteranol and, blue – I113T SOD1 after 48 hours at 37°C with 3 mM isoproteranol. Each curve is the average of three separate aggregation reactions with error bars indicating standard deviation.



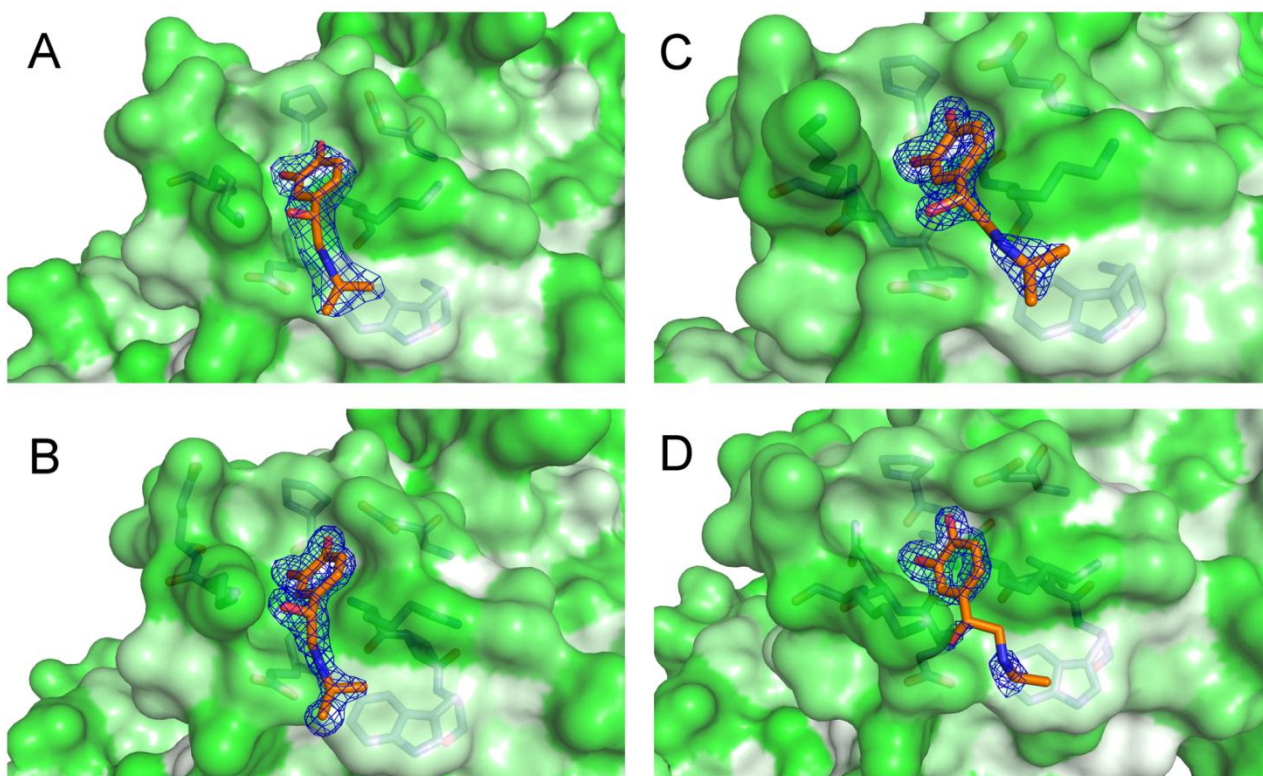
Supplementary Figure S4. Aggregation of 25 μM apo-I113T SOD1 in the presence of isoproteranol. Size exclusion chromatograms of: Black – I113T SOD1, grey - I113T SOD1 after 48 hours incubation at 37°C, red – I113T SOD1 after 48 hours at 37°C with 75 μM isoproteranol and, blue – I113T SOD1 after 48 hours at 37°C with 750 μM isoproteranol. Each curve is the average of three separate aggregation reactions with error bars indicating standard deviation.



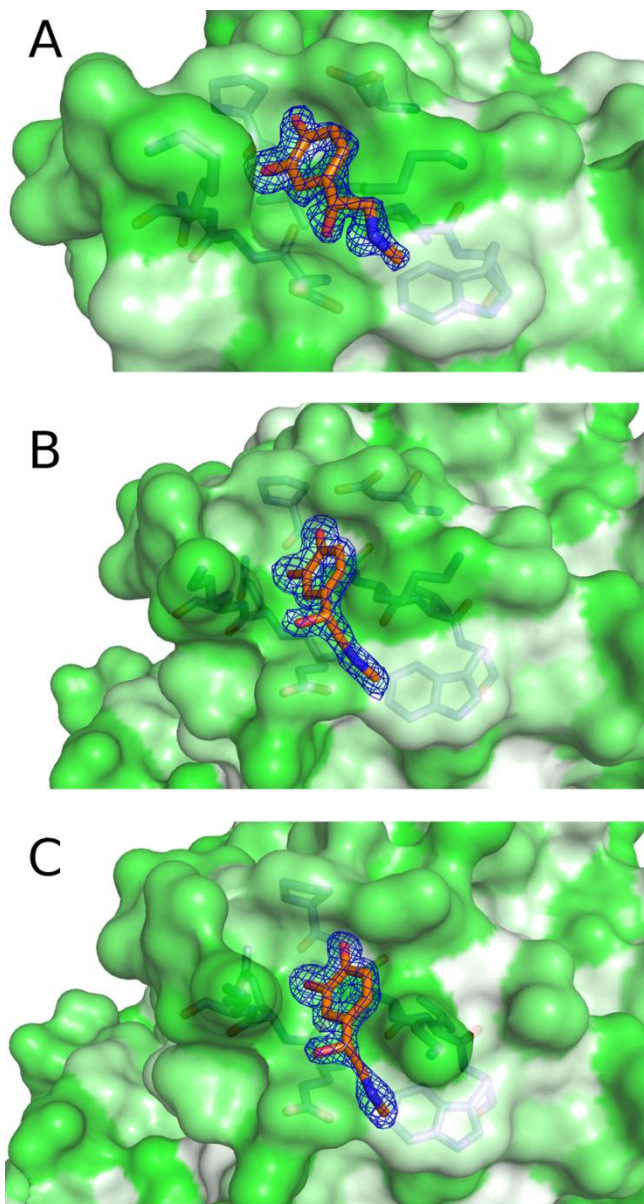
Supplementary Figure S5. Aggregation of isoproterenol. Size exclusion chromatogram of 3 mM isoproterenol before (blue) and after (black) incubation at 37°C for 48 hours. Fresh isoproterenol elutes from the Superpose 12 column as a single peak at approximately 1 column volume (26 ml) indicating a single, small molecule. After incubation under identical conditions to those used for SOD1 aggregation, the size of this peak is reduced and several new species are found to elute at 14 - 21 ml. The elution volume 7 – 14 ml used throughout this study to assess SOD1 aggregation is completely free of ligand.



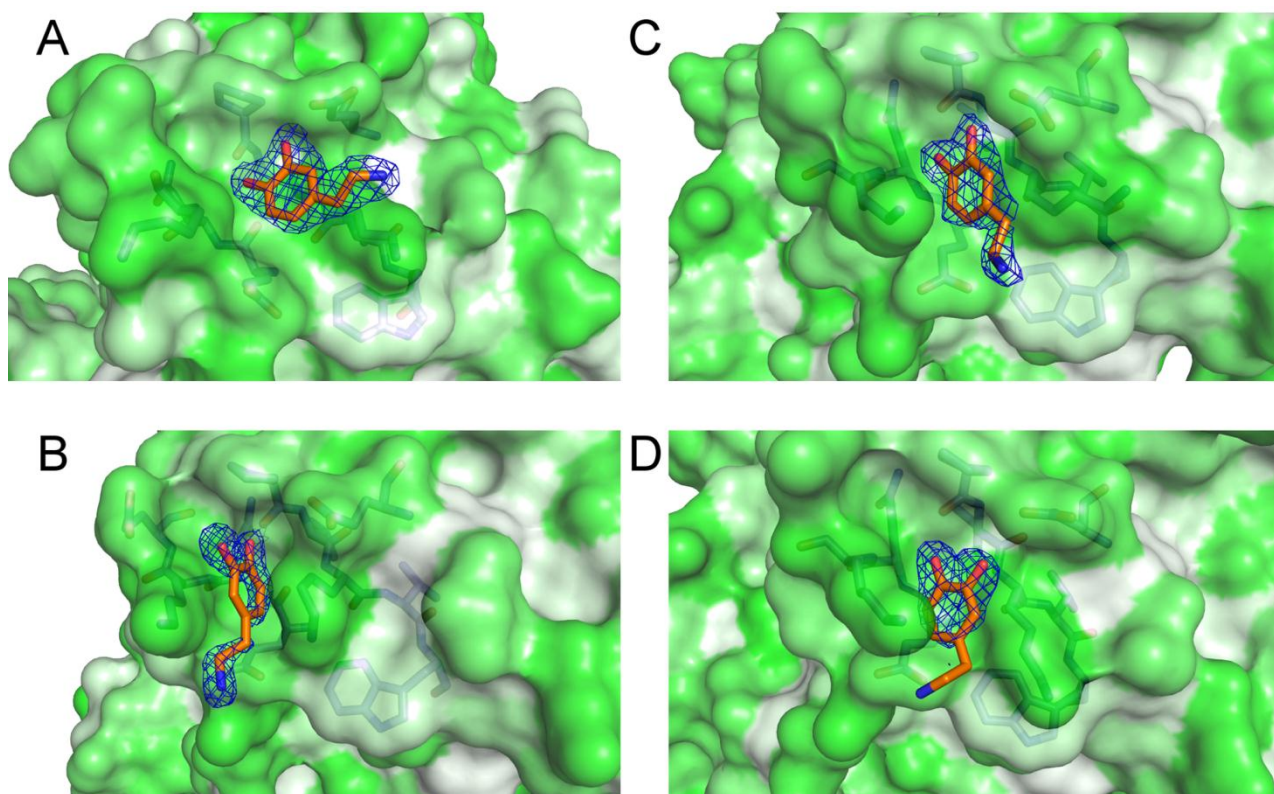
Supplementary Figure S6. 5-Fluorouridine bound to several SOD1 variants. $2F_o-F_c$ electron density maps contoured at 1σ of 5-FUrd bound at the Trp32 site in (A) I113T SOD1 pH 8 $c222_1$ crystal structure (B) L38V SOD1 in the $p2_12_12_1$ form, (C) wild-type SOD1 and (D) H48Q SOD1 grown at pH 5 in the $p2_1$ form.



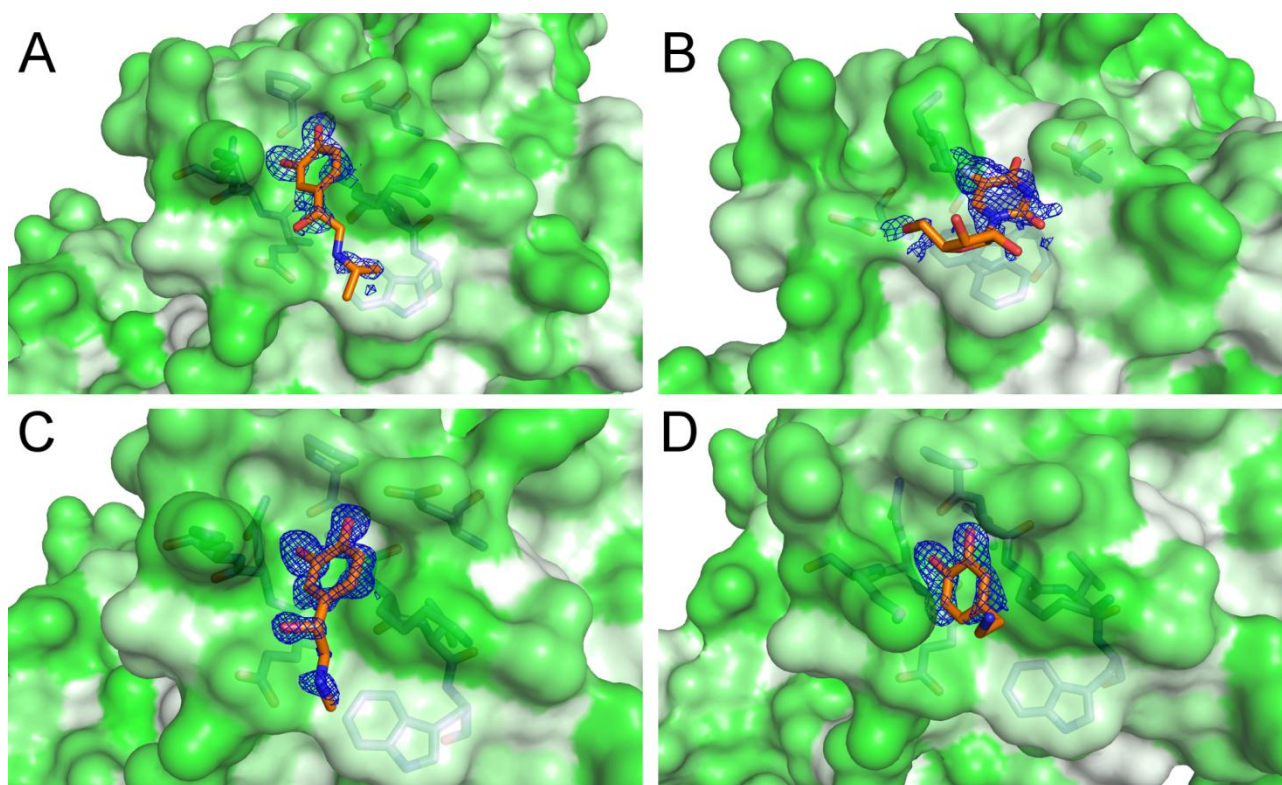
Supplementary Figure S7. Isoproterenol bound to several SOD1 variants. $2F_o-F_c$ electron density maps contoured at 1σ of isoproterenol bound at the Trp32 site in (A) I113T SOD1 pH 8 $c222_1$ crystal structure (B) L38V SOD1, (C) wild-type SOD1 and (D) H48Q SOD1 grown at pH 5 in the $p2_1$ form.



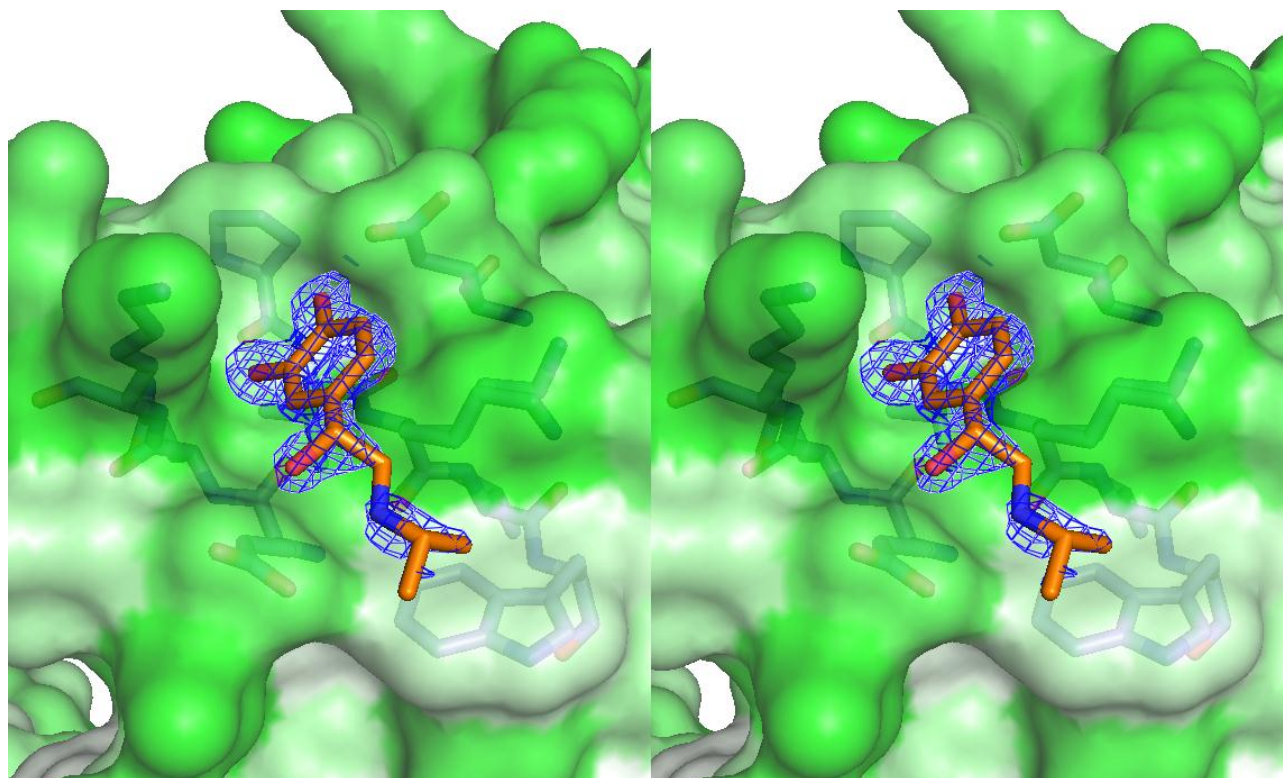
Supplementary Figure S8. Epinephrine bound to several SOD1 variants. $2F_o-F_c$ electron density maps contoured at 1σ of epinephrine bound at the Trp32 site in (A) L38V SOD1, (B) wild-type SOD1 and (C) H48Q SOD1 grown at pH 5 in the $p2_1$ form.



Supplementary Figure S9. Dopamine bound to several SOD1 variants. $2F_o - F_c$ electron density maps contoured at 1σ of dopamine bound at the Trp32 site in (A) I113T SOD1 pH 8 $c222_1$ crystal structure (B) L38V SOD1, (C) wild-type SOD1 and (D) H48Q SOD1 grown at pH 5 in the $p2_1$ form.



Supplementary Figure S10. Omit maps of ligands bound to SOD1. Omit electron density maps contoured at 2.5σ of (A) I113T SOD1 with isoproteranol, (B) I113T SOD1 with 5-fluorouridine, (C) I113T SOD1 with epinephrine and (D) I113T SOD1 with dopamine.



Supplementary Figure S11. $2F_o-F_c$ stereo electron density map contoured at 1σ of isoproteranol bound at the Trp32 site.