

## Supporting Information

### Structural and biochemical insights into the inhibition of human acetylcholinesterase by G-series nerve agents and subsequent reactivation by HI-6

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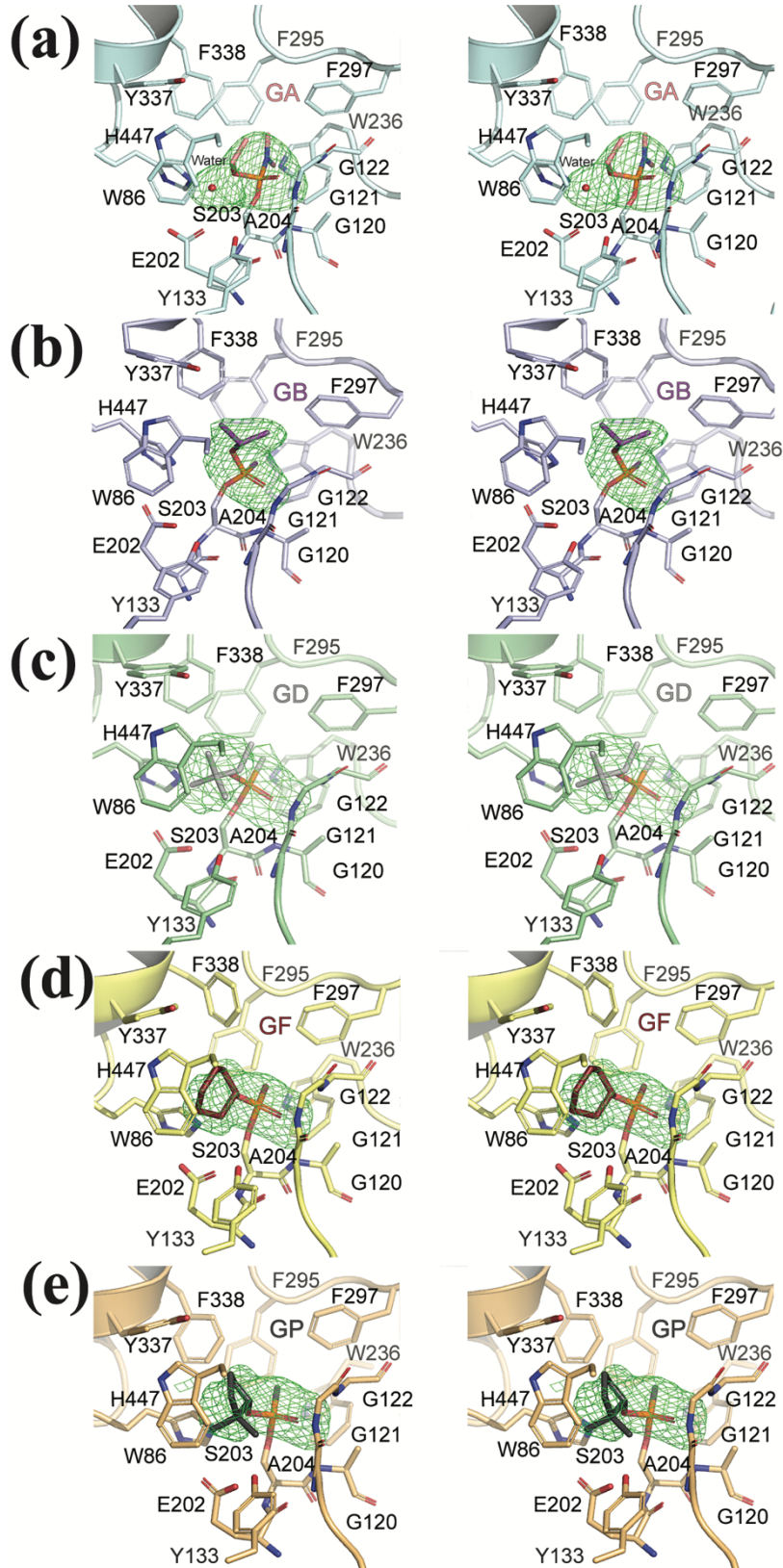
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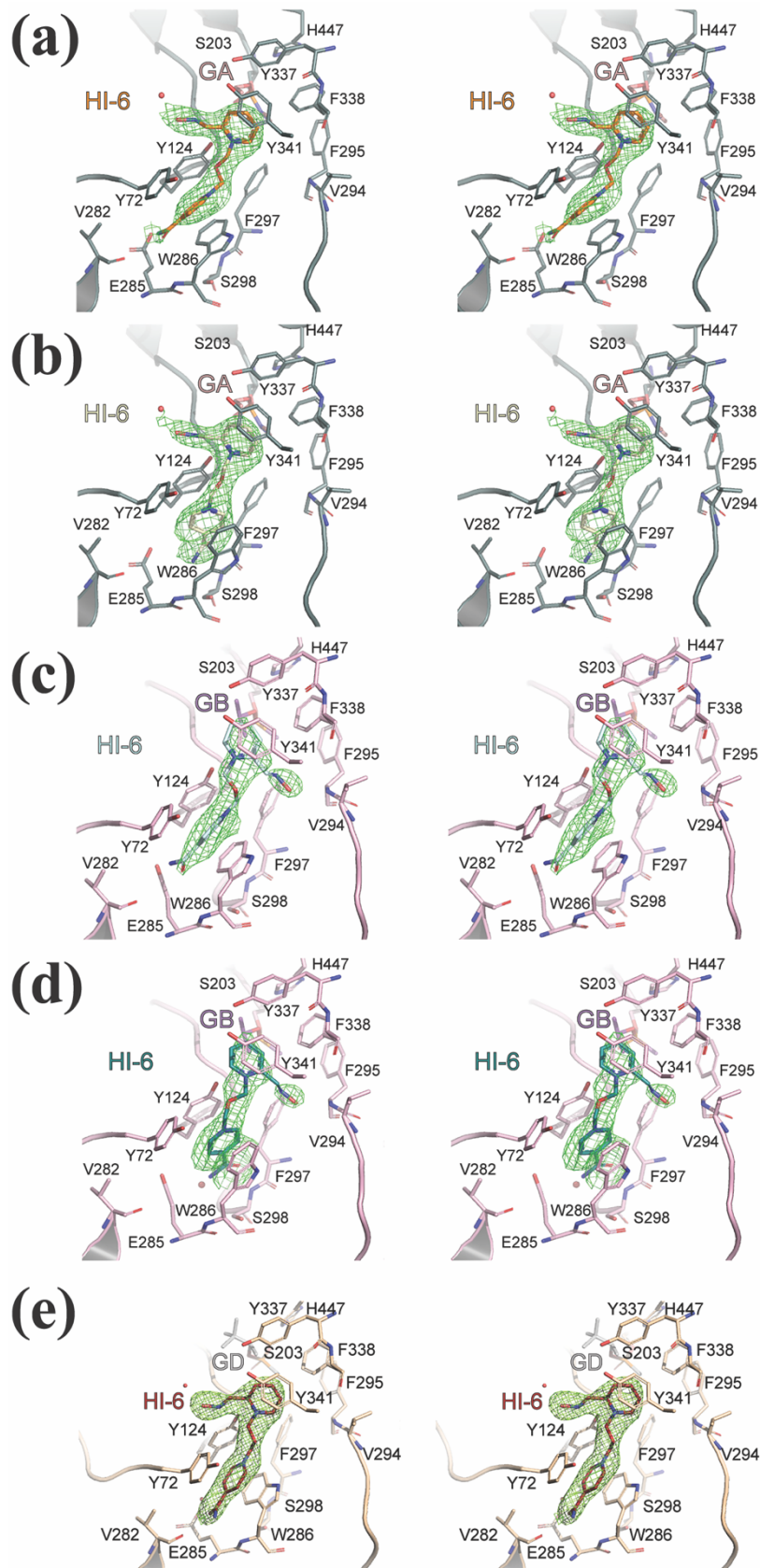
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**Figure S1.** Crystal structures of Human Acetylcholinesterase in complex with G-series nerve agent. (a) Wall-eyed stereoview of GA (salmon) bound to the active site of hAChE (pale cyan) with hAChE  $F_o - F_c$  density scaled to  $3\sigma$  (green mesh). (b) Wall-eyed stereoview of GB (dark violet) bound to the active site of hAChE (blue-grey) with hAChE  $F_o - F_c$  density scaled to  $3\sigma$  (green mesh). (c) Wall-eyed stereoview of GD (silver) bound to the active site of hAChE (wheat) with hAChE  $F_o - F_c$  density scaled to  $3\sigma$  (green mesh). (d) Wall-eyed stereoview of GF (dark red) bound to the active site of hAChE (light yellow) with hAChE  $F_o - F_c$  density scaled to  $3\sigma$  (green mesh). (e) Wall-eyed stereoview of GP (dark grey) bound to the active site of hAChE (light orange) with hAChE  $F_o - F_c$  density scaled to  $3\sigma$  (green mesh).



**Figure S2.** Crystal structures of HI-6 bound in the active site of hAChE. (a-b) Wall-eyed stereoview of the active site of hAChE (grey-green) bound to two conformations of HI-6 (orange and pale yellow).  $F_o - F_c$  density scaled to  $3\sigma$  (green mesh). (c-d) Wall-eyed stereoview of the active site of hAChE (light pink) bound to two conformations of HI-6 (light teal and dark teal).  $F_o - F_c$  density scaled to  $3\sigma$  (green mesh). (e) Wall-eyed stereoview of the active site of hAChE (wheat) bound to HI-6 (dark red).  $F_o - F_c$  density scaled to  $3\sigma$  (green mesh). Waters are shown as red spheres.