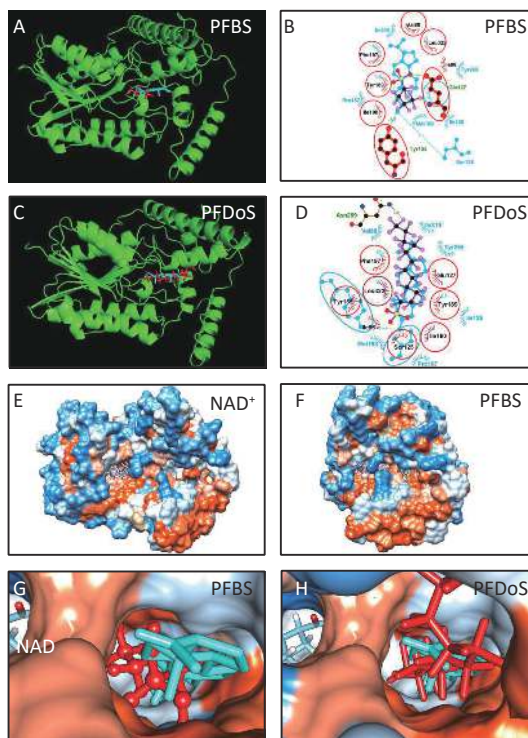


Supplementary Figure S1. *In silico* analysis of PFSA with *h3*-HSD1 A 3D model of *h3*-HSD1 (AF-P14060-F1-model_v4) has catalytic residue Ser125 and Tyr155 (cyan). (A, C, E, G) 3D structure of P5 (cyan), PFPS (red), PFHxS (red), 6:2FTS (red), and 8:2FTS (red), respectively; (B, D, F, H) superimposed images for PFPS (purple), PFHxS (purple), 6:2FTS (purple) and 8:2FTS (purple): hydrogen bonds (green line), overlapping residues (red circled), P5 (cyan) as background.



Supplementary Figure S2. *In silico* analysis of PFSA with *h3*-HSD1 A 3D model of *h3*-HSD1 (AF-P14060-F1-model_v4) has catalytic residue Ser125 and Tyr155 (cyan). (A, C) 3D structure of P5 (cyan), PFDS (red), PFDoS (red), respectively; (B, D) superimposed images for PFBS (purple), PFDoS (purple): hydrogen bonds (green line), overlapping residues (red circled), P5 (cyan) as background; (E, F) hydrophobicity surface structure of *h3*-HSD1 with NAD⁺ (pink structure) binding cavity, and with NAD⁺ (pink structure) and P5 (cyan) binding cavity, respectively; (G, H), P5 (cyan) binding cavity contains PFBS (red) showing that PFBS partially occupies P5 binding site and PFDoS (red) showing that PFDoS stretches its P5 binding site.