

Supplementary Information for Fragment Screening of Human Kynurenine

Aminotransferase-II

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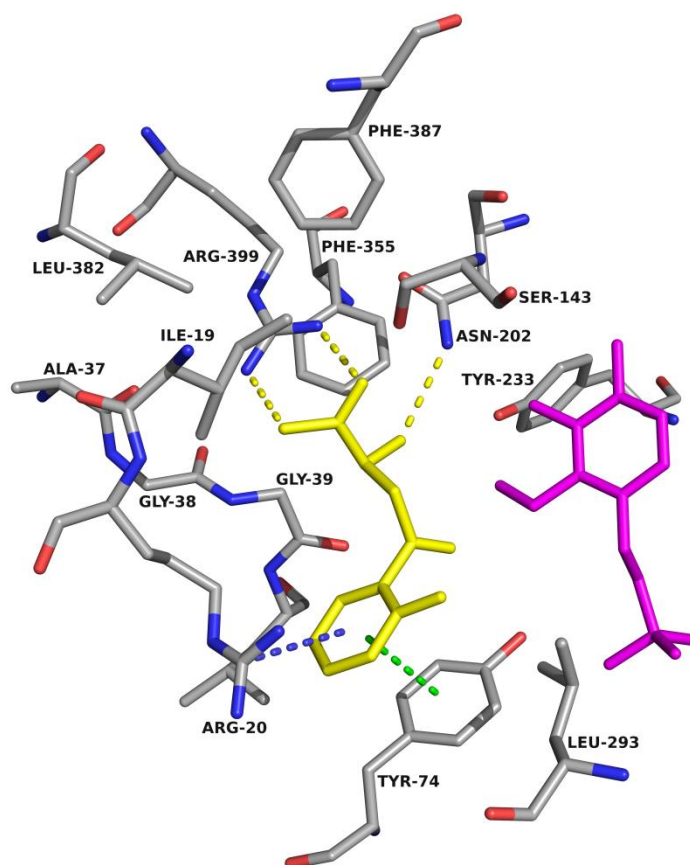
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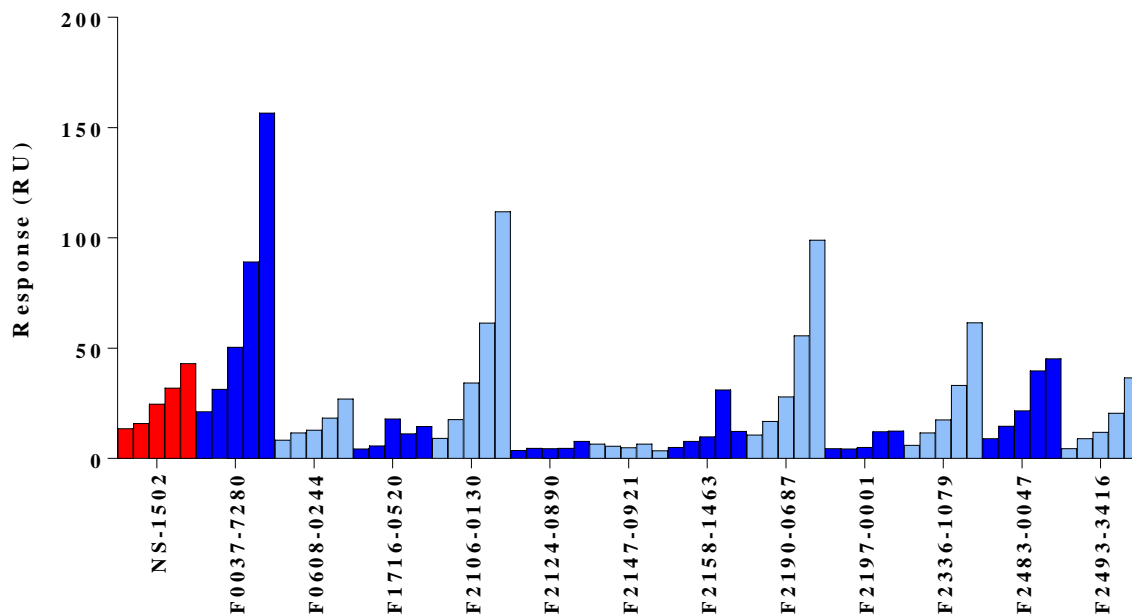
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Supplementary Table S1. The Inhibition Result for the Top 18 Fragments Selected from the SPR Screening.

Fragment	KAT-II Inhibition
F0037-7280	67%
F2106-0130	3%
F2190-0687	4%
F2336-1079	-
F2483-0047	-
F2493-3416	-
F3308-0230	-
F3358-0288	4%
F3371-0639	-
F3394-1274	-
F3412-0030	32%
F5847-0169	-
F5871-3538	4%
F6037-0164	15%
F6229-0348	-
F6230-0300	-
F6445-6917	-
F9995-0188	-

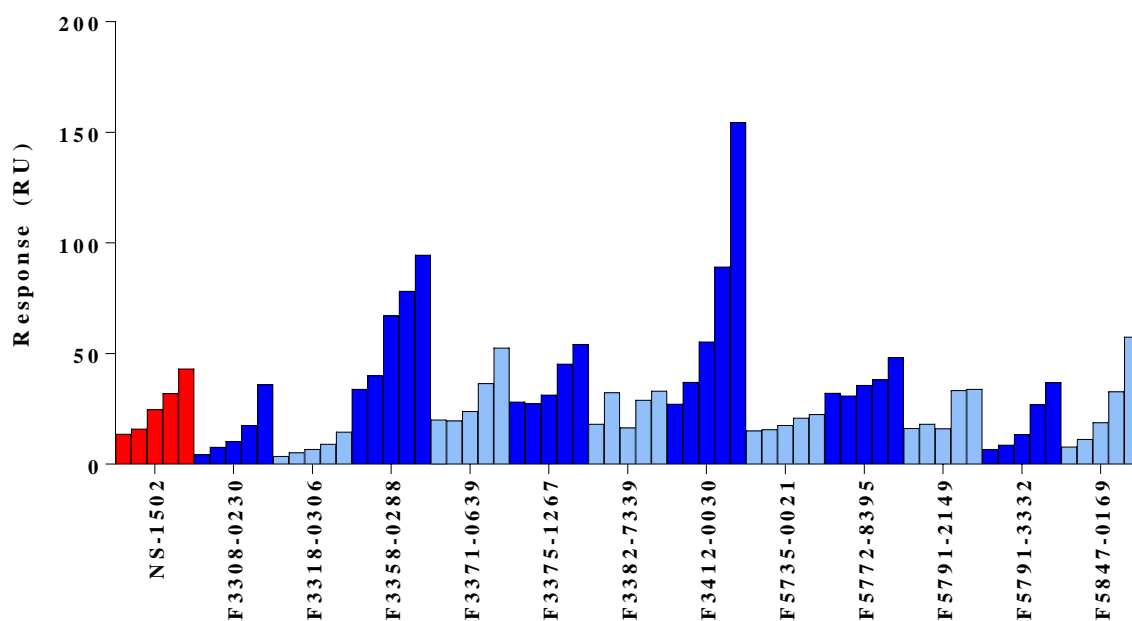


Supplementary Figure S1. The amino acids with an atom within 5.0 Å of kynurenine (yellow) in KAT-II were chosen for display, with PLP also depicted (magenta). Residue Tyr-142 was removed for clarity. The carboxyl moiety forms a salt bridge (yellow dashes) with Arg-399, and the amine group forms hydrogen bonds (yellow dashes) with Asn-202. The aromatic ring forms pi-pi interactions (green dashes) with Tyr-74, and pi-cation interactions (blue dashes) with Arg-20.



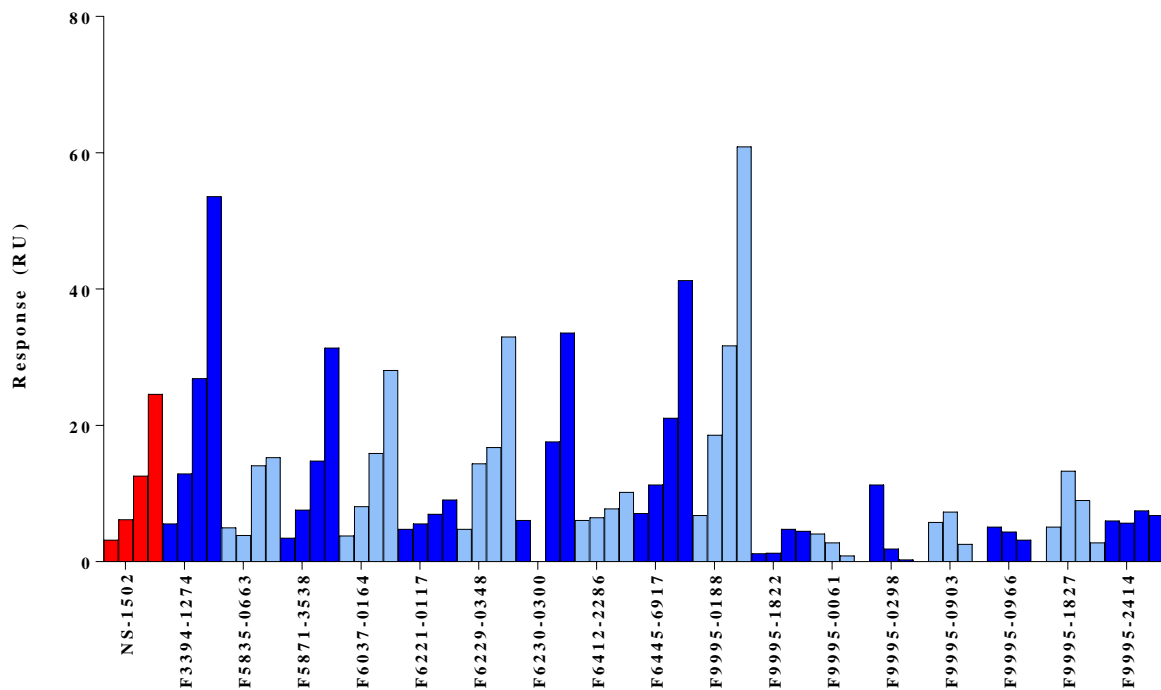
Supplementary Figure S2A. Evaluation of the best hits from the initial SPR screen. Positive control (NS-1502) is in red. Fragments are in alternating dark and light blue colours.

Displayed is the response (RU) of each fragment for increasing concentrations (ranging 6.25 – 100 μM).



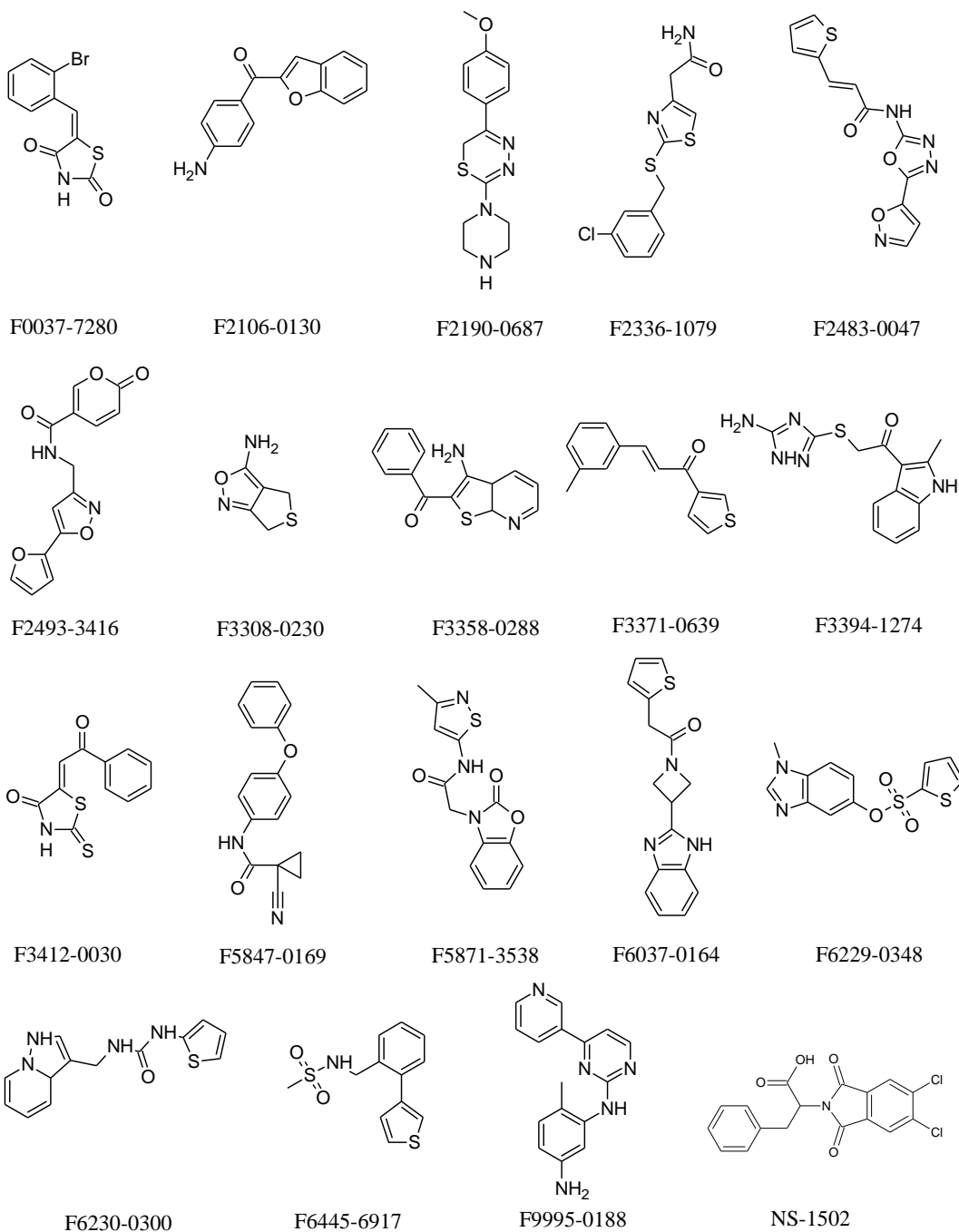
Supplementary Figure S2B. Evaluation of the best hits from the initial SPR screen. Positive control (NS-1502) is in red. Fragments are in alternating dark and light blue colours.

Displayed is the response (RU) of each fragment for increasing concentrations (ranging 6.25 – 100 μM).



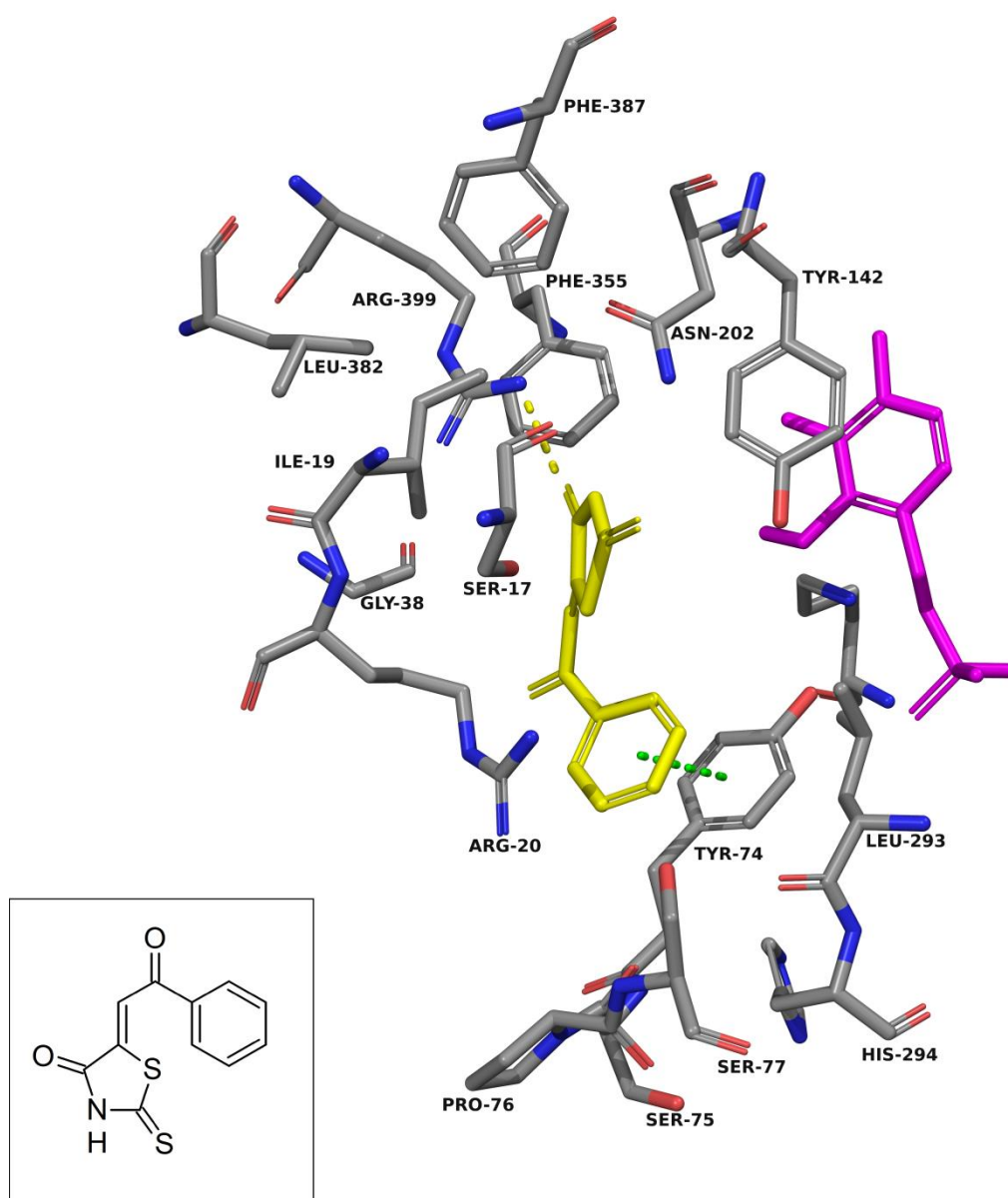
Supplementary Figure S2C. Evaluation of the best hits from the initial SPR screen. Positive control (NS-1502) is in red. Fragments are in alternating dark and light blue colours.

Displayed is the response (RU) of each fragment for increasing concentrations (ranging 6.25 – 100 μM).

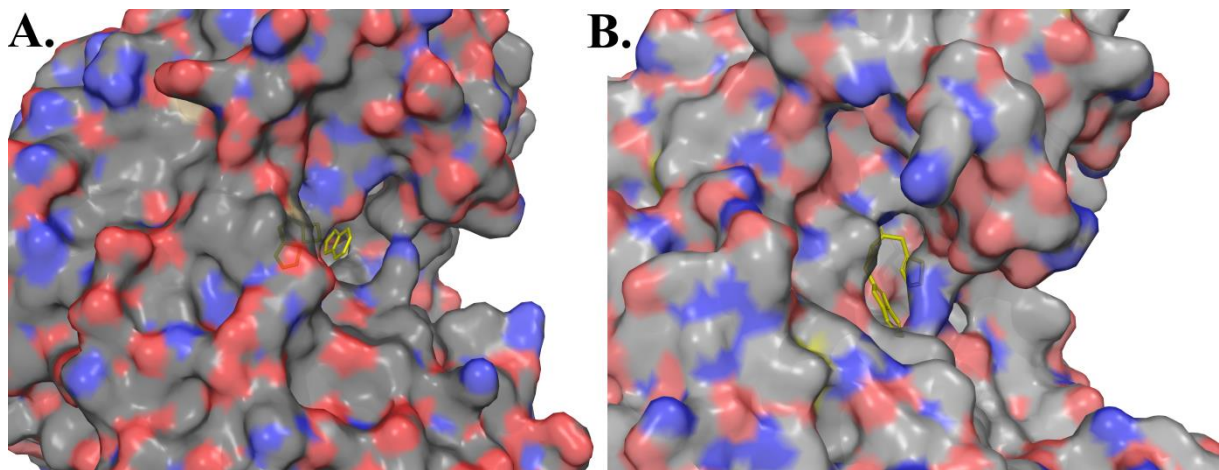


Supplementary Figure S3

The top 18 fragments selected from the SPR screening, and NS-1502. The structural similarity of an aromatic ring fused to a five membered ring can be seen in F2106-0130, F3308-0230, F3358-0288, F3394-1274, F5871-3538, F6037-0164, F6229-0348, and F6230-0300.



Supplementary Figure S4. The amino acids with an atom within 5.0 Å of F3412-0030 (yellow) were chosen for display. F0037-7280 is docked into 2R2N with PLP (magenta) present. Residues Gly-39, Leu-40, Ser-143, Gly-144 removed for clarity. The carbonyl on the succinimide-like ring forms a hydrogen bond (yellow dashes) with Arg-399. The aromatic ring forms pi-pi interactions (green dashes) with Tyr-74.



Supplementary Figure S5. (A) F6037-0164 is docked into 3FVU (yellow). (B) F6037-0164 is docked into 2R2N (yellow). The surface view of the protein shows that the fragment is close to accessing the exterior of KAT-I (A), but sits in the active site cavity in KAT-II (B).