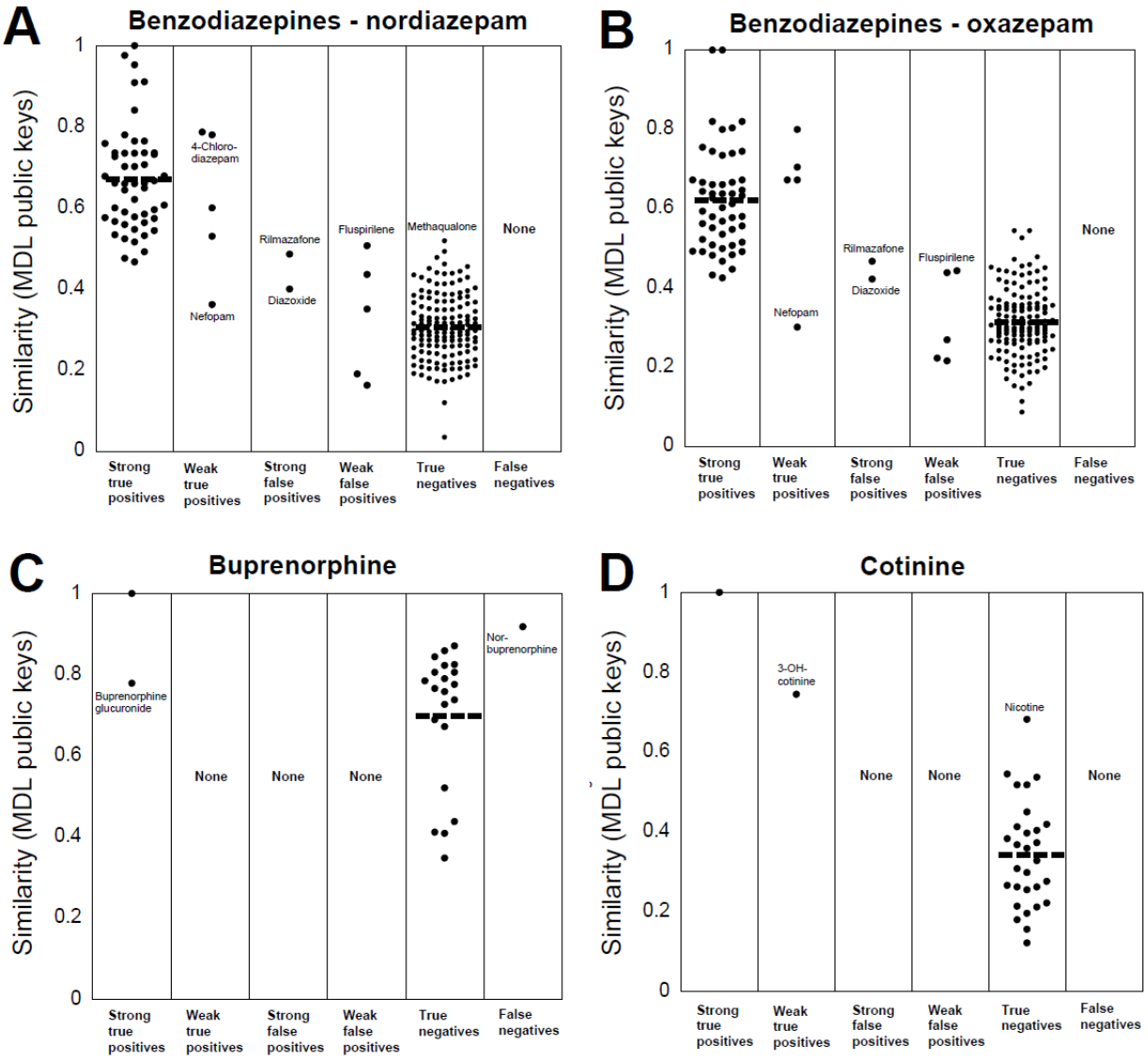
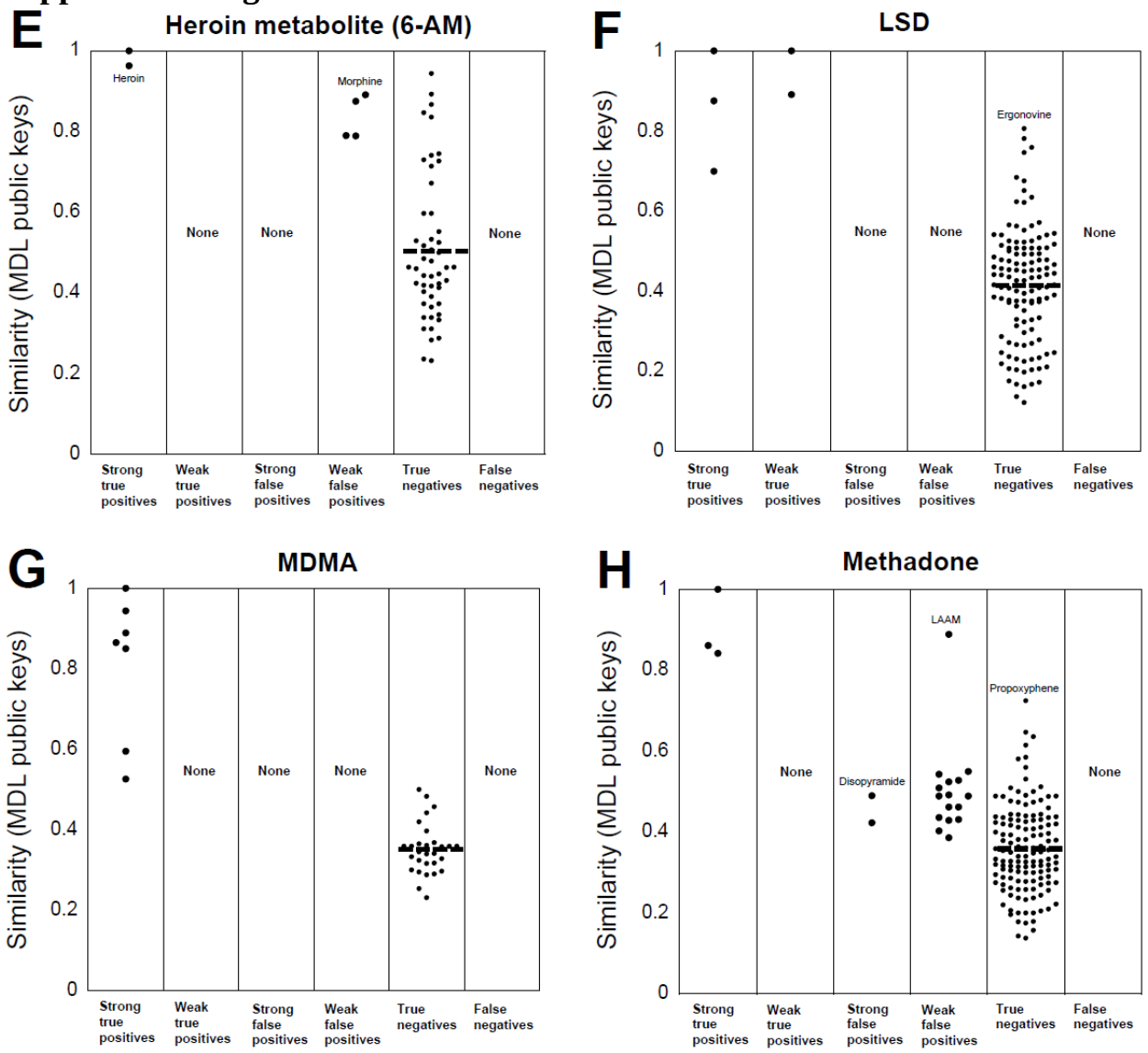
Data Supplement 2

Supplemental Data Fig. 1 – MDL similarity analyses of individual DOA/Tox assays
As described in "Materials and Methods", cross-reactivity data for DOA/Tox assays were analyzed and the results used to sort tested compounds into one of six categories: "Strong True Positives", "Weak True Positives", "Strong True Positives", "Weak True Positives", "True Negatives", and "False Negatives". The similarity of each compound to the target molecule of the DOA/Tox assay using MDL public keys and the Tanimoto coefficient was plotted for the following assays: (A) benzodiazepines (using nordiazepam as the target), (B) benzodiazepines (using oxazepam as the target), (C) buprenorphine, (D) cotinine, (E) heroin metabolite (6-acetylmorphine), (F) LSD, (G) MDMA ('Ecstasy'), (H) methadone, (I) methadone metabolite (EDDP), (J) methaqualone, (K) oxycodone, (L) propoyxphene, (M) TCAs (using imipramine as the target).

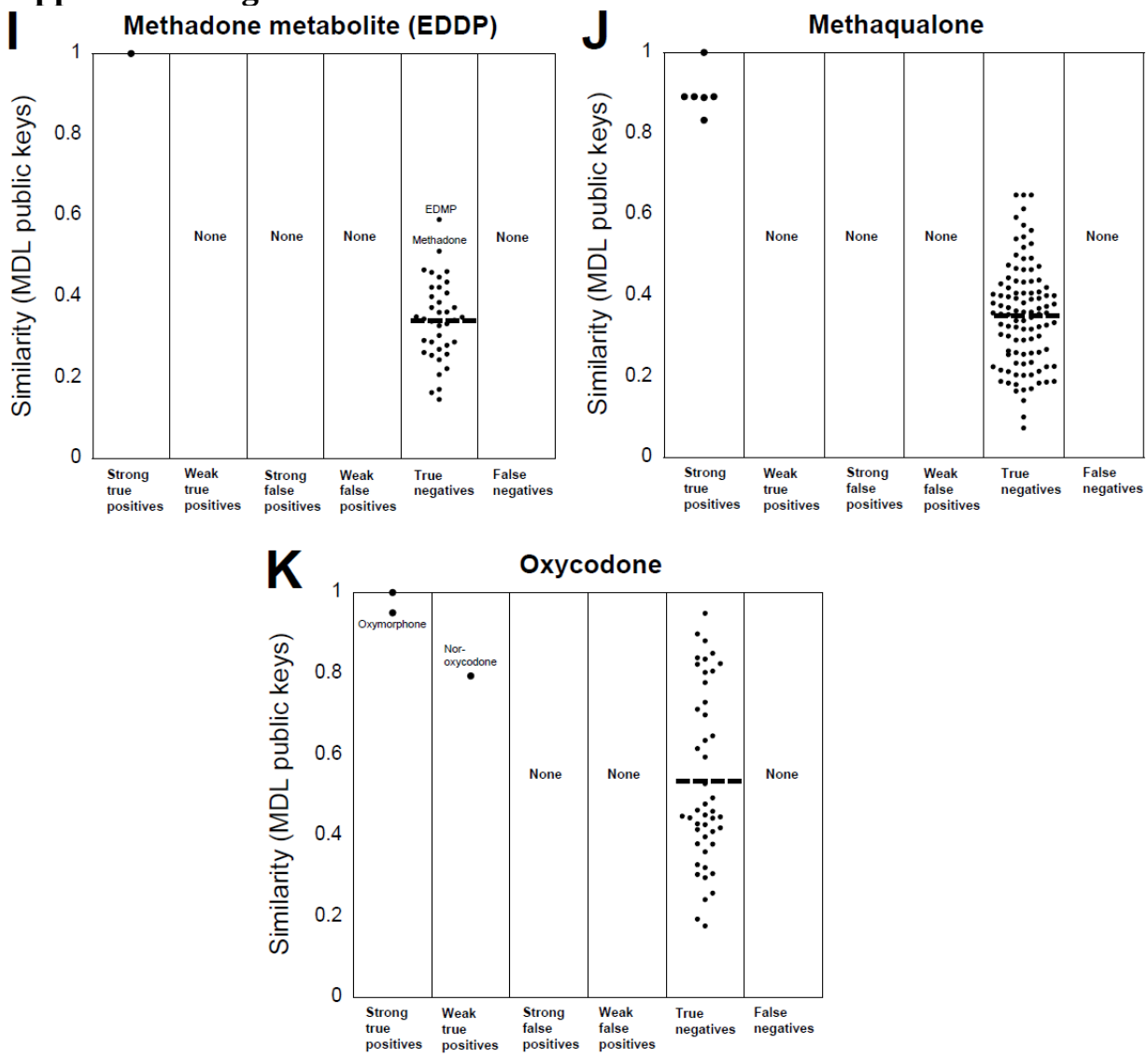
Supplemental Figure 1A-1D



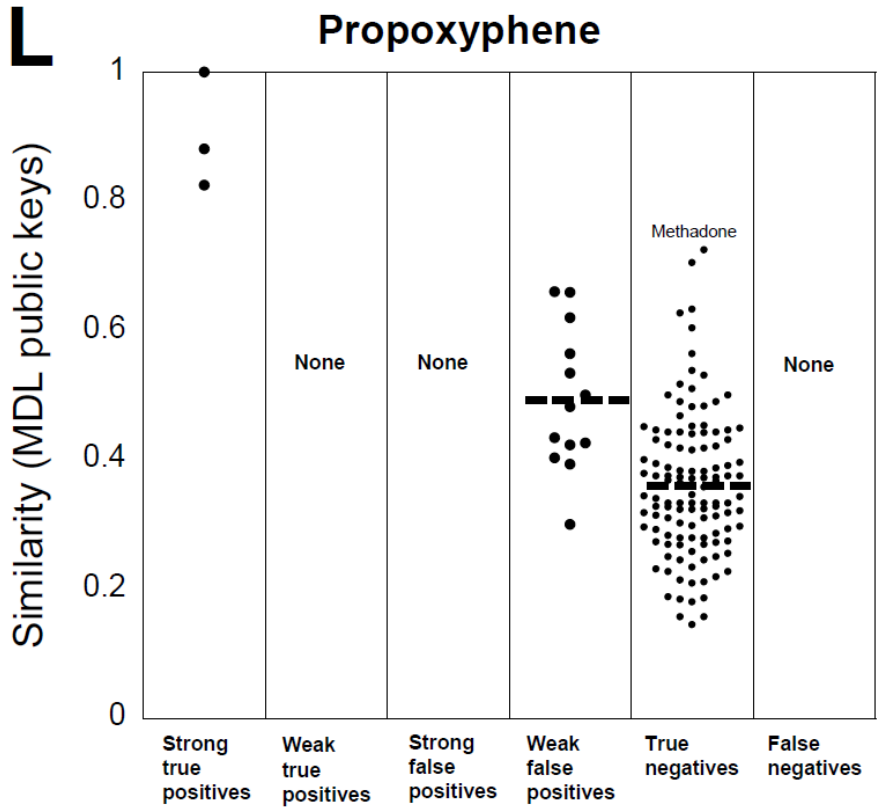
Supplemental Figure 1E-1H

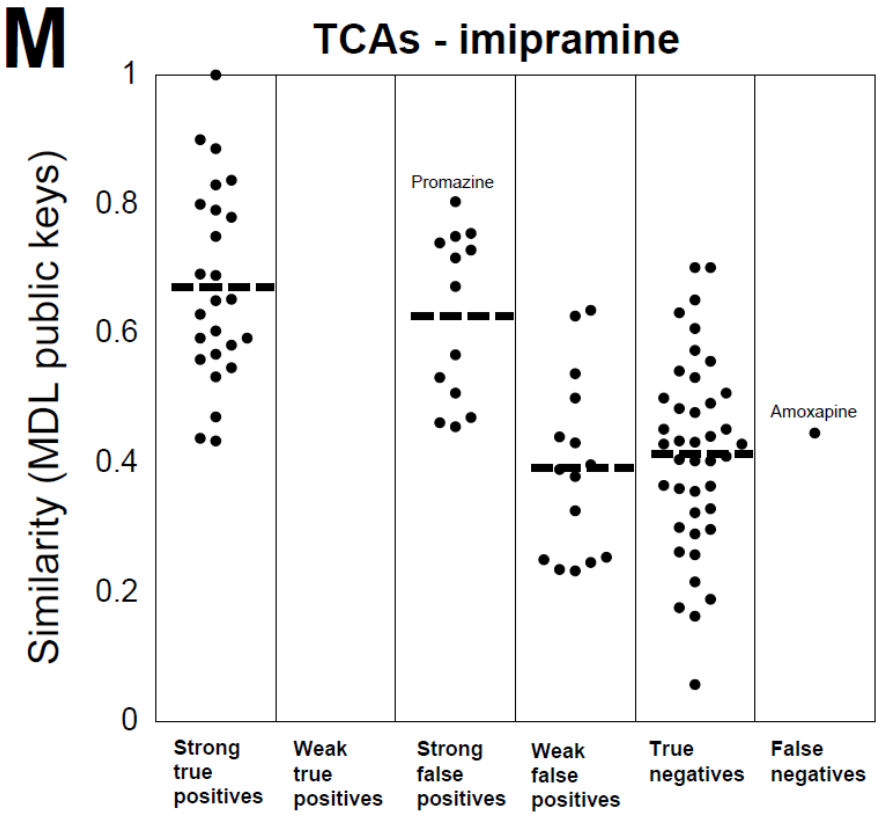


Supplemental Figure 1I-1K



Supplemental Figure 1L-1M

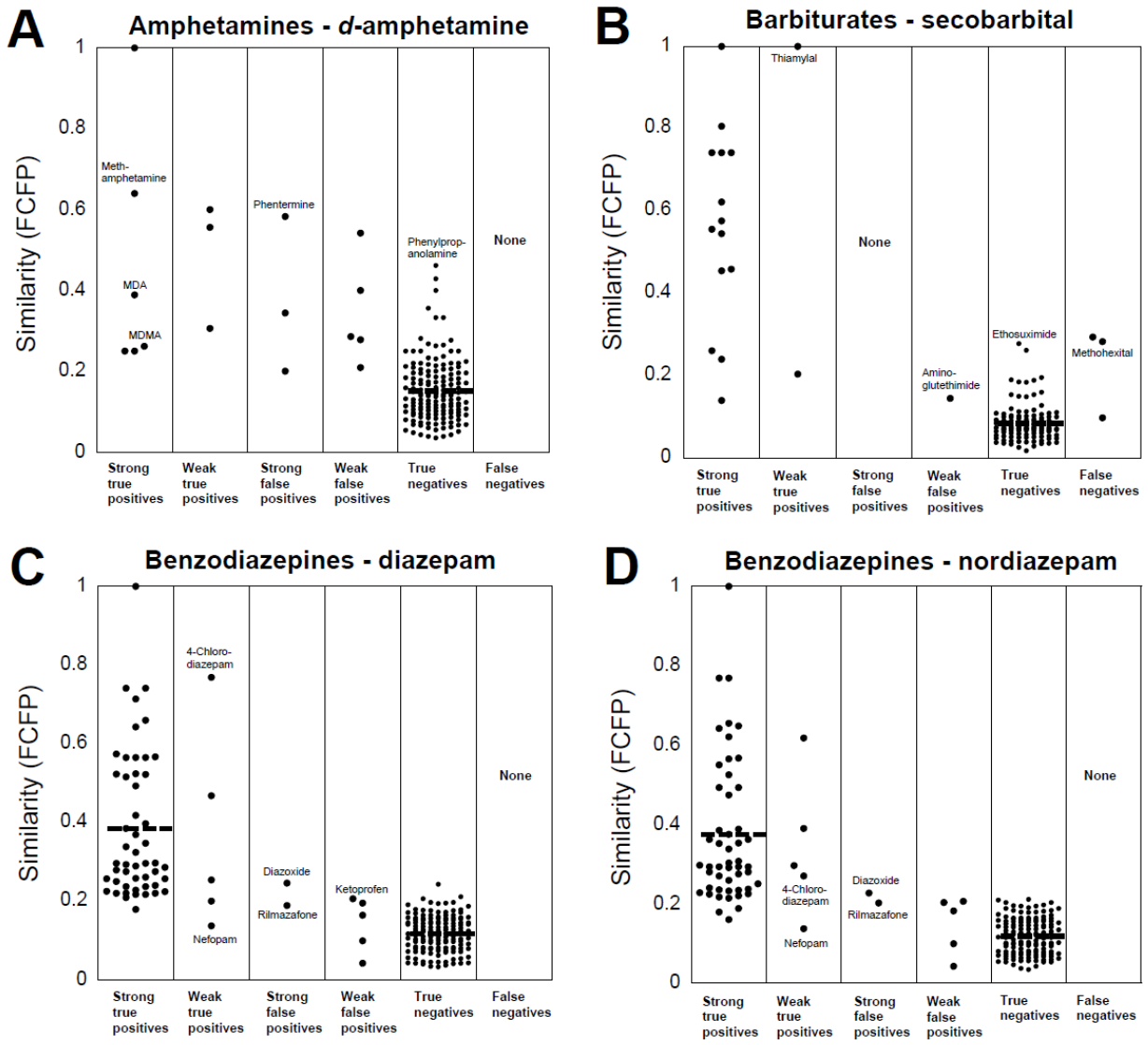




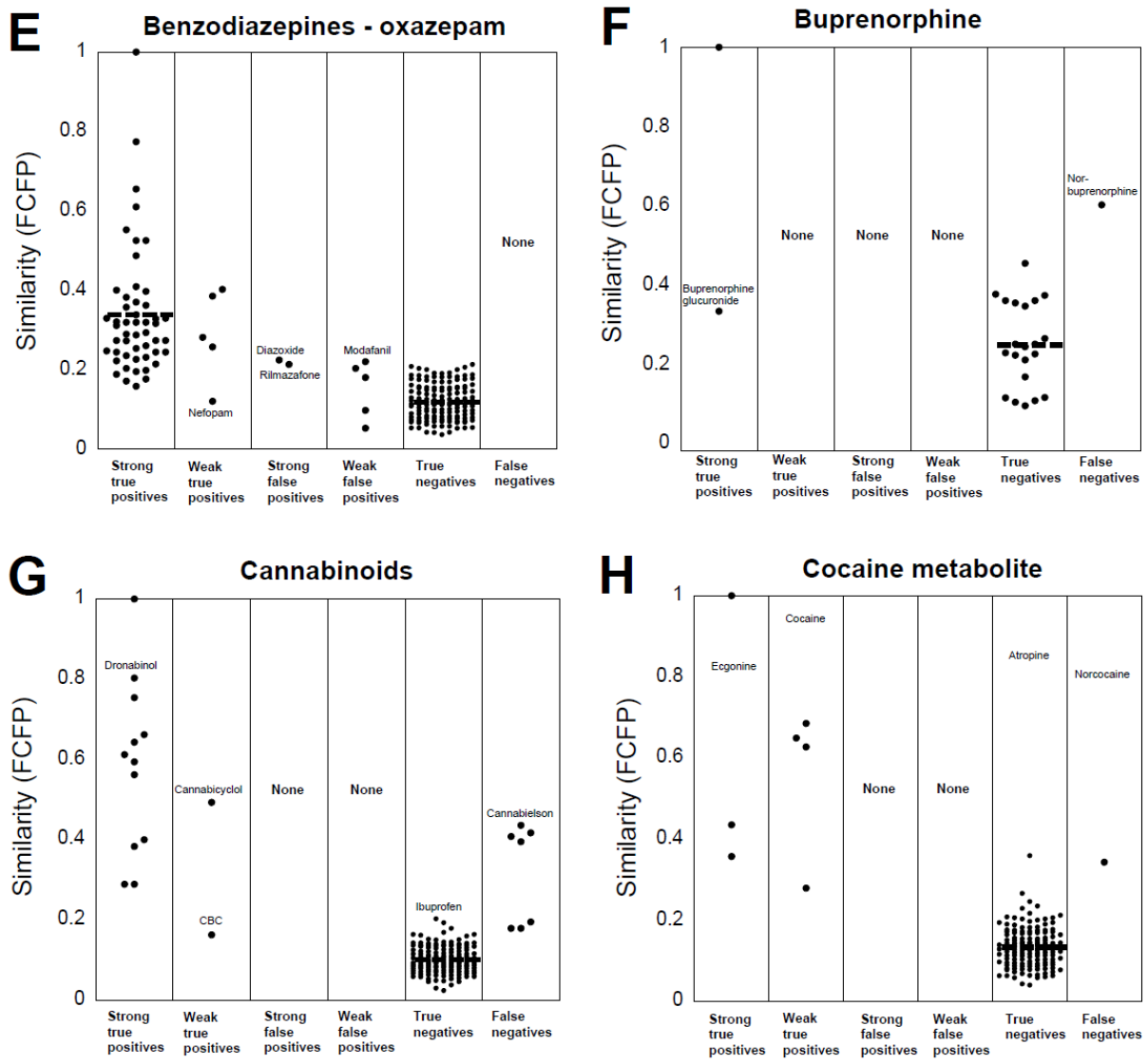
Supplemental Data Fig. 2 – FCFP_6 similarity analyses of individual DOA/Tox assays

As described in "Materials and Methods", cross-reactivity data for DOA/Tox assays were analyzed and the results used to sort tested compounds into one of six categories: "Strong True Positives", "Weak True Positives", "Strong True Positives", "Weak True Positives", "True Negatives", and "False Negatives". The similarity of each compound to the target molecule of the DOA/Tox assay using FCFP_6 similarity and the Tanimoto coefficient was plotted for the following assays: (A) amphetamines (using *d*-amphetamine as the target), (B) barbiturates (using secobarbital as the target), (C) benzodiazepines (using diazepam as the target), (D) benzodiazepines (using nordiazepam as the target), (E) benzodiazepines (using oxazepam as the target), (F) buprenorphine, (G) cannabinoids (using 9-carboxy-11-nor-Δ_9-tetrahydrocannabinol as the target compound), (H) cocaine metabolite (benzoylecgonine), (I) cotinine, (J) heroin metabolite (6-acetylmorphine), (K) LSD, (L) MDMA ('Ecstasy'), (M) methadone, (N) methadone metabolite (EDDP), (O) methaqualone, (P) opiates (using morphine as the target), (Q) oxycodone, (R) phencyclidine, (S) propoxyphene, (T) TCAs (using desipramine as the target), and (U) TCAs (using imipramine as the target).

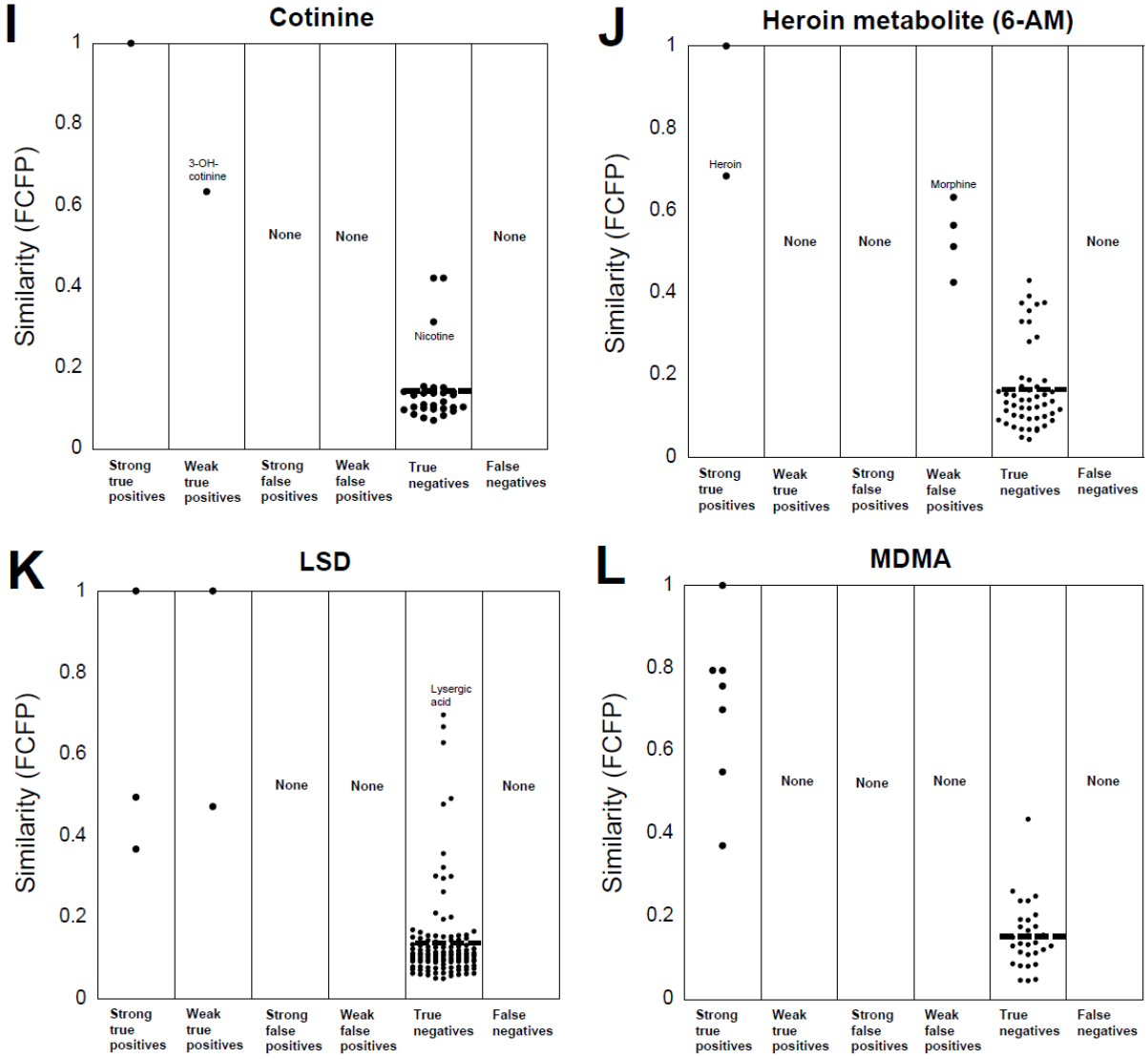
Supplemental Figure 2A-2D



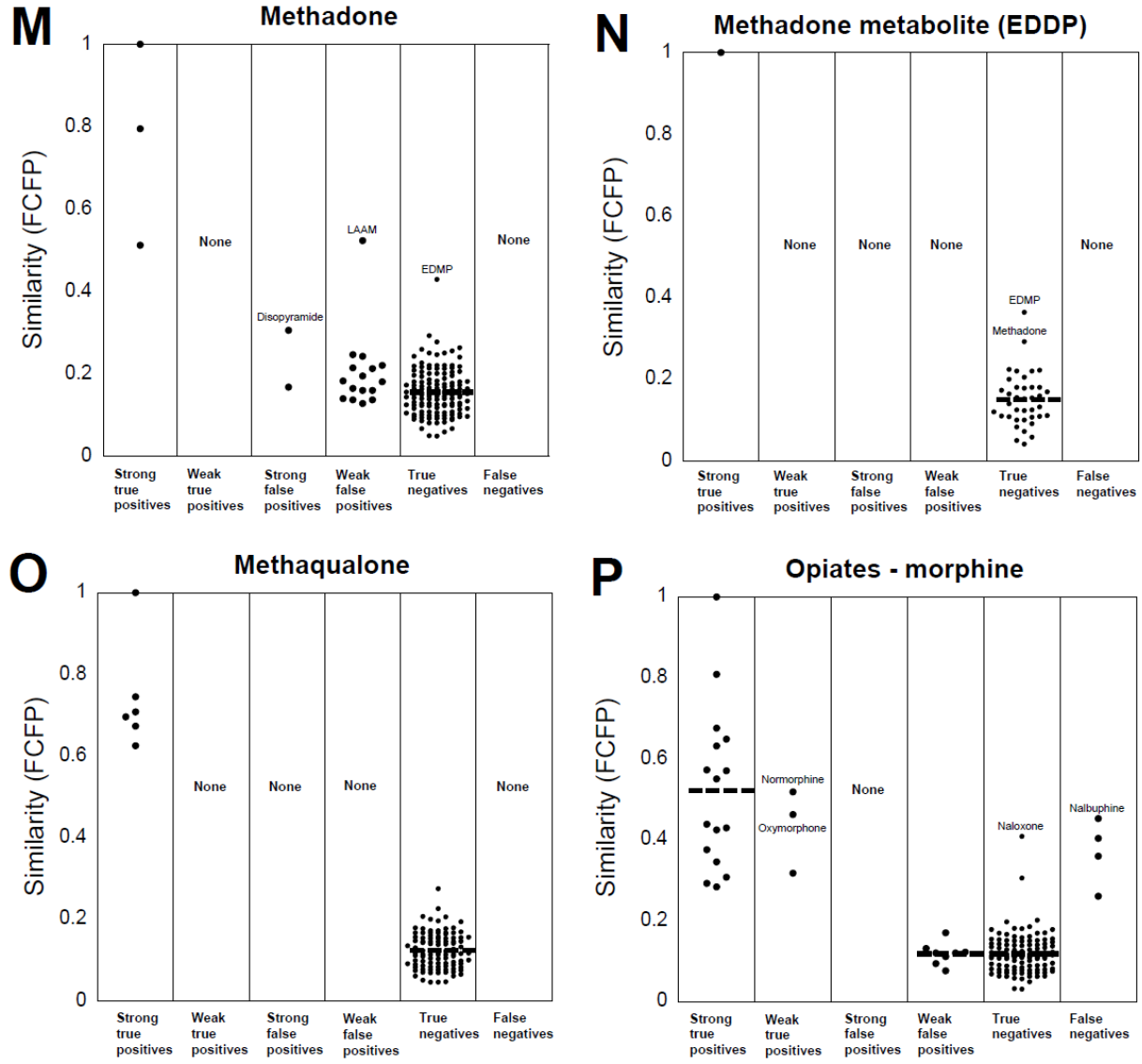
Supplemental Figure 2E-2H



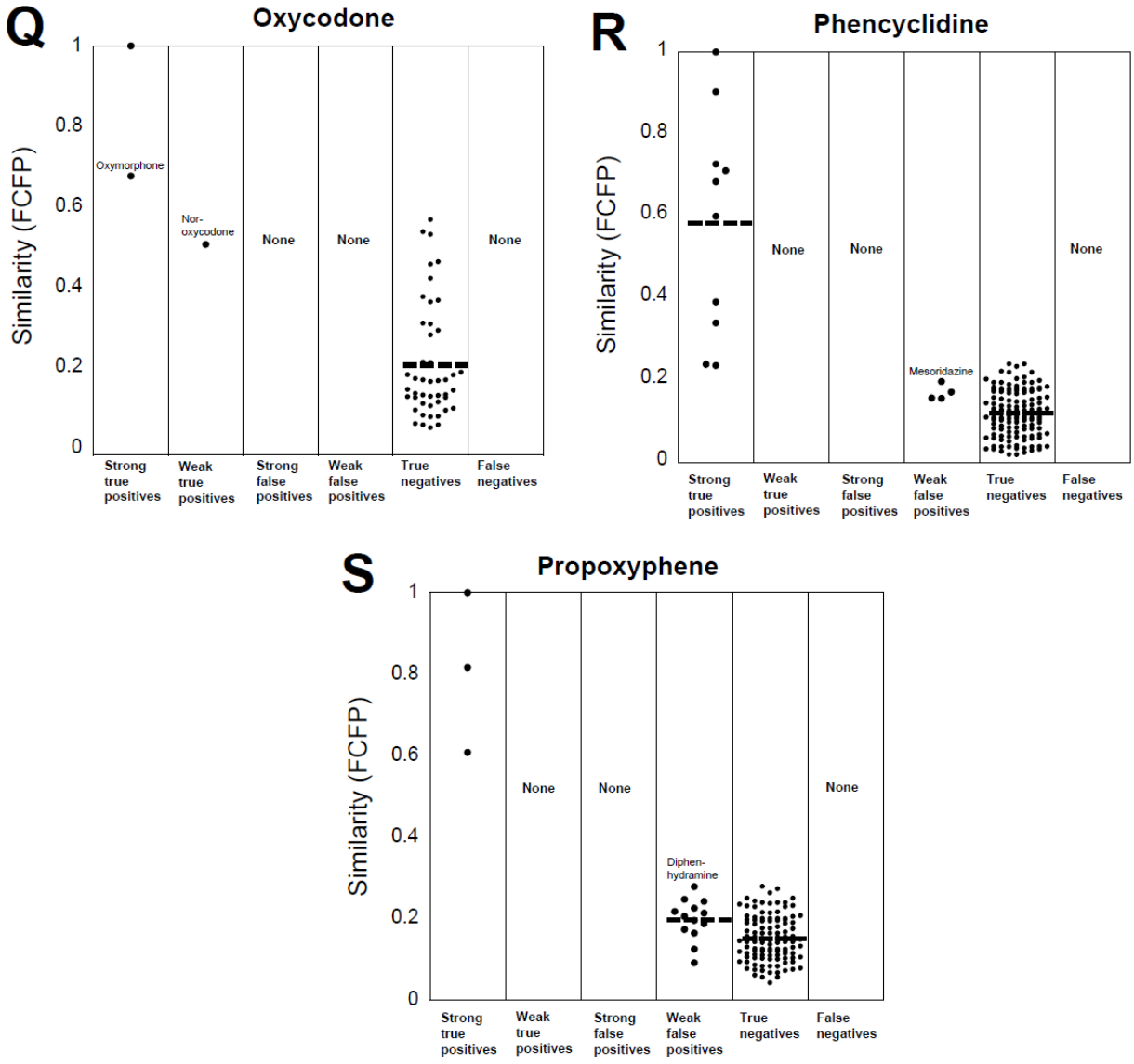
Supplemental Figure 2I-2L



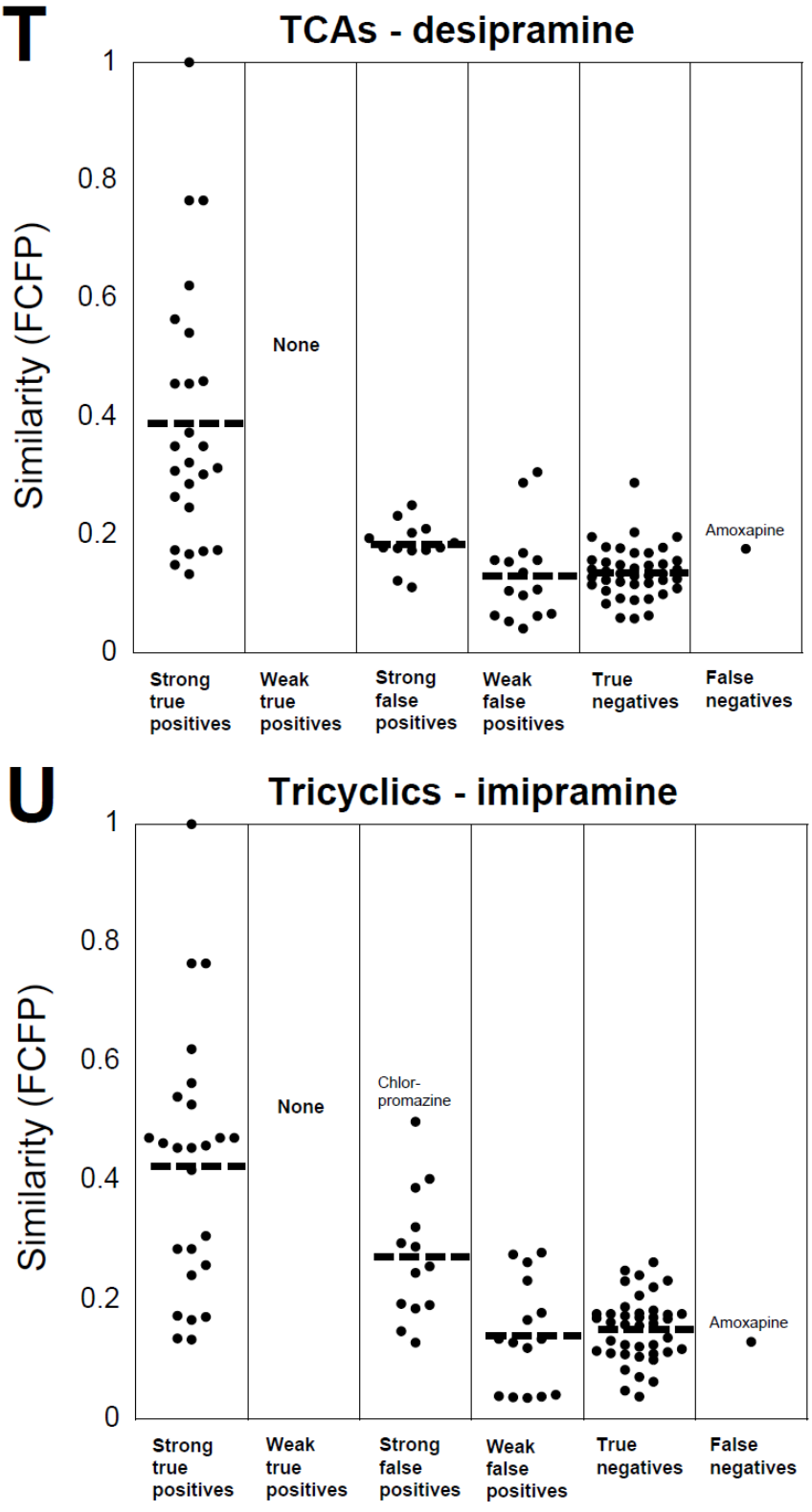
Supplemental Figure 2M-2P



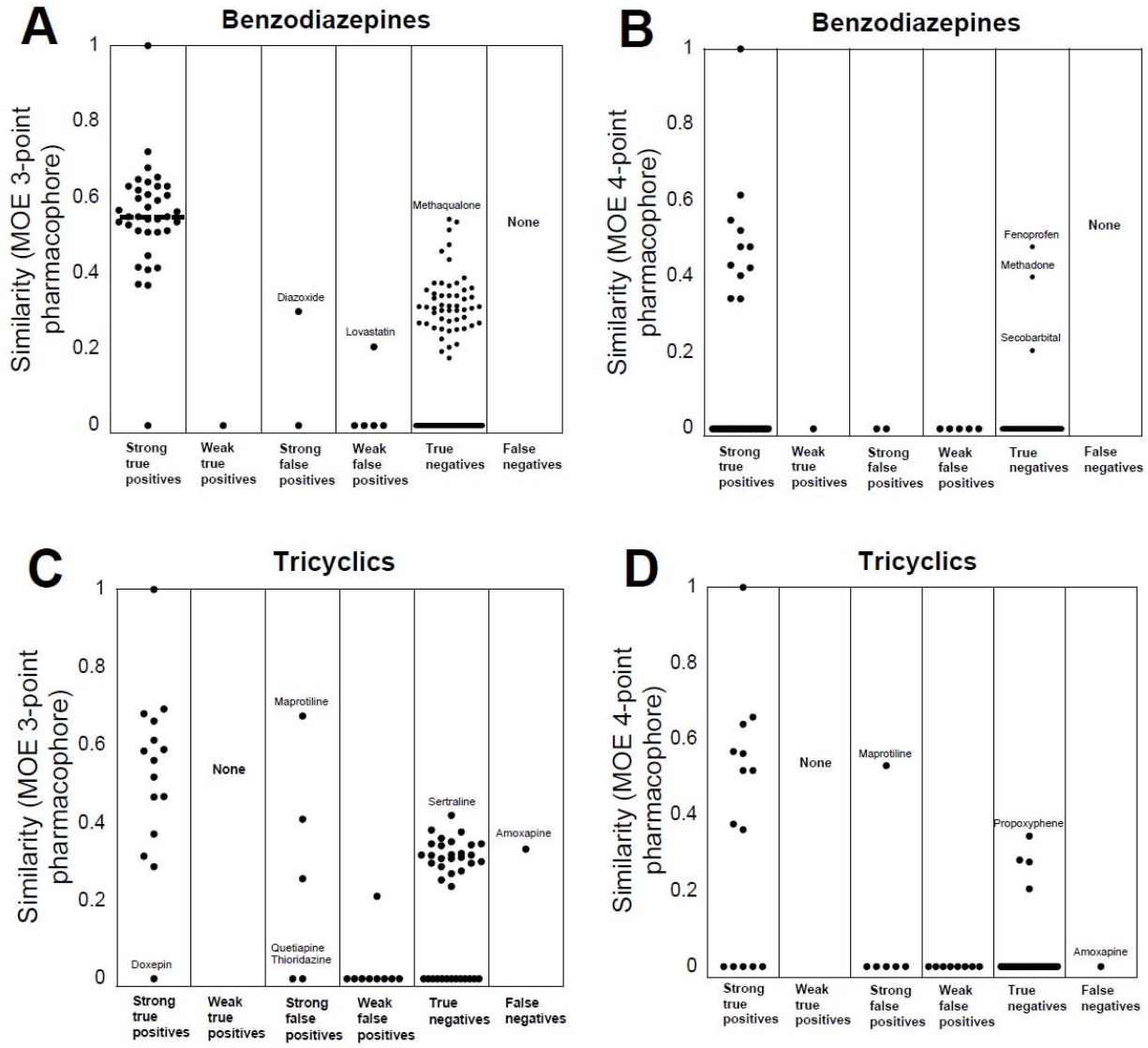
Supplemental Figure 2Q-2S



Supplemental Figure 2T-2U



Supplemental Data Fig. 3 – MOE pharmacophore analyses of individual DOA/Tox assays
As described in "Materials and Methods", cross-reactivity data for two DOA/Tox assays (benzodiazepines and TCAs) were analyzed and the results used to sort tested compounds into one of six categories: "Strong True Positives", "Weak True Positives", "Strong True Positives", "Weak True Positives", "True Negatives", and "False Negatives". The similarity of each compound relative to diazepam (benzodiazepine assay) or desipramine (TCA assay) using (A,C) MOE three-point pharmacophore fingerprints and (B,D) MOE four-point pharmacophore fingerprints were plotted.



Supplemental Data Fig. 4 – Similarity of untested compounds

For the eighteen DOA/Tox screening assays, compounds in the Expanded SCUT database for which cross-reactivity data is unavailable were determined. The similarity of these compounds to the respective target molecules using MDL public keys and the Tanimoto coefficient were plotted. The solid horizontal lines indicate the lowest similarity coefficient for a strongly cross-reactive compound (Strong True Positives or Strong False Positives) for these assays. (A) Data for amphetamines (AMPH), barbiturates (BARB), benzodiazepines (BENZ), buprenorphine (BUPN), cannabinoids (CANN), cocaine metabolite (COC). (B) Data for cotinine (COT), methadone metabolite (EDDP), heroin metabolite (6-acetylmorphine, 6-AM), LSD, MDMA, methadone (MTD). (C) Data for methaqualone (MTQ), opiates (OPIA), oxycodone (OXYC), phencyclidine (PCP), propoxyphene (PPX), tricyclic antidepressants (TCA).

Supplemental Figure 4