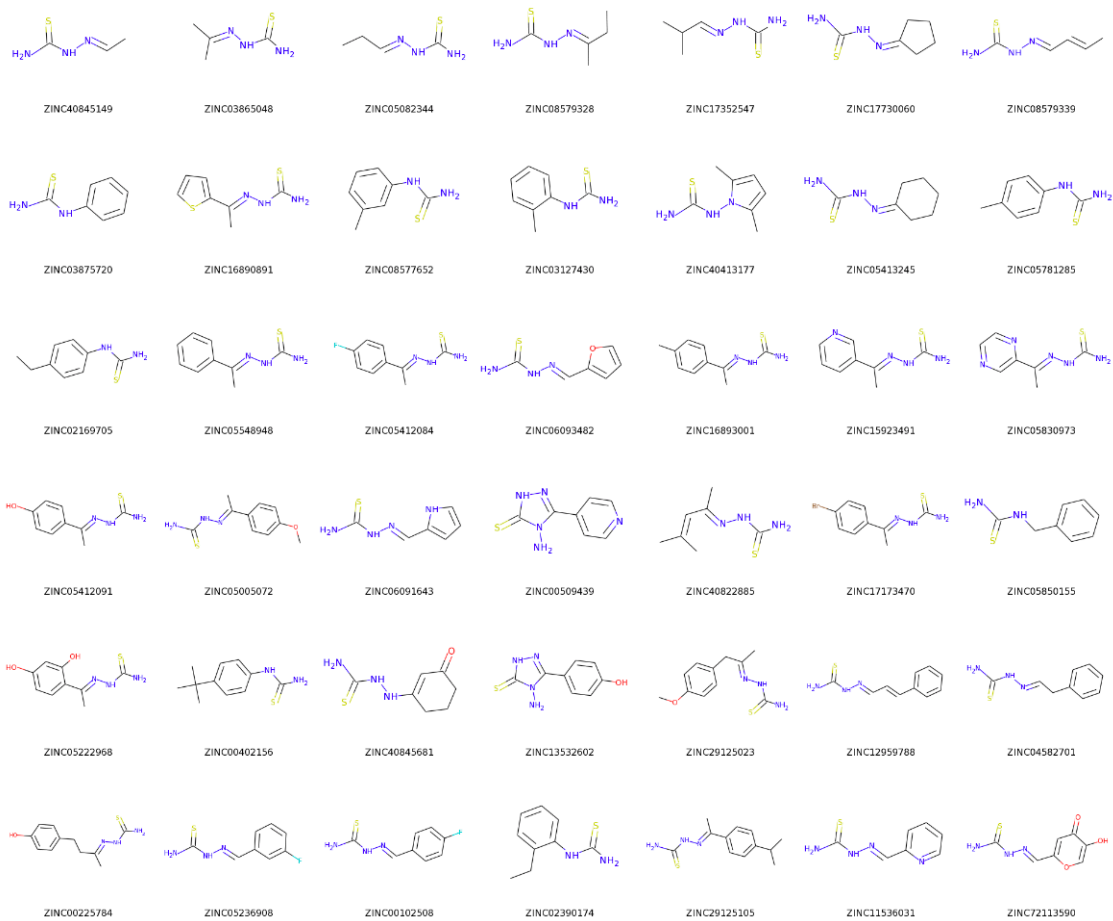


Supplementary Materials

Repositioning of Thiourea-Containing Drugs as Tyrosinase Inhibitors

Joonhyeok Choi and Jun-Goo Jee



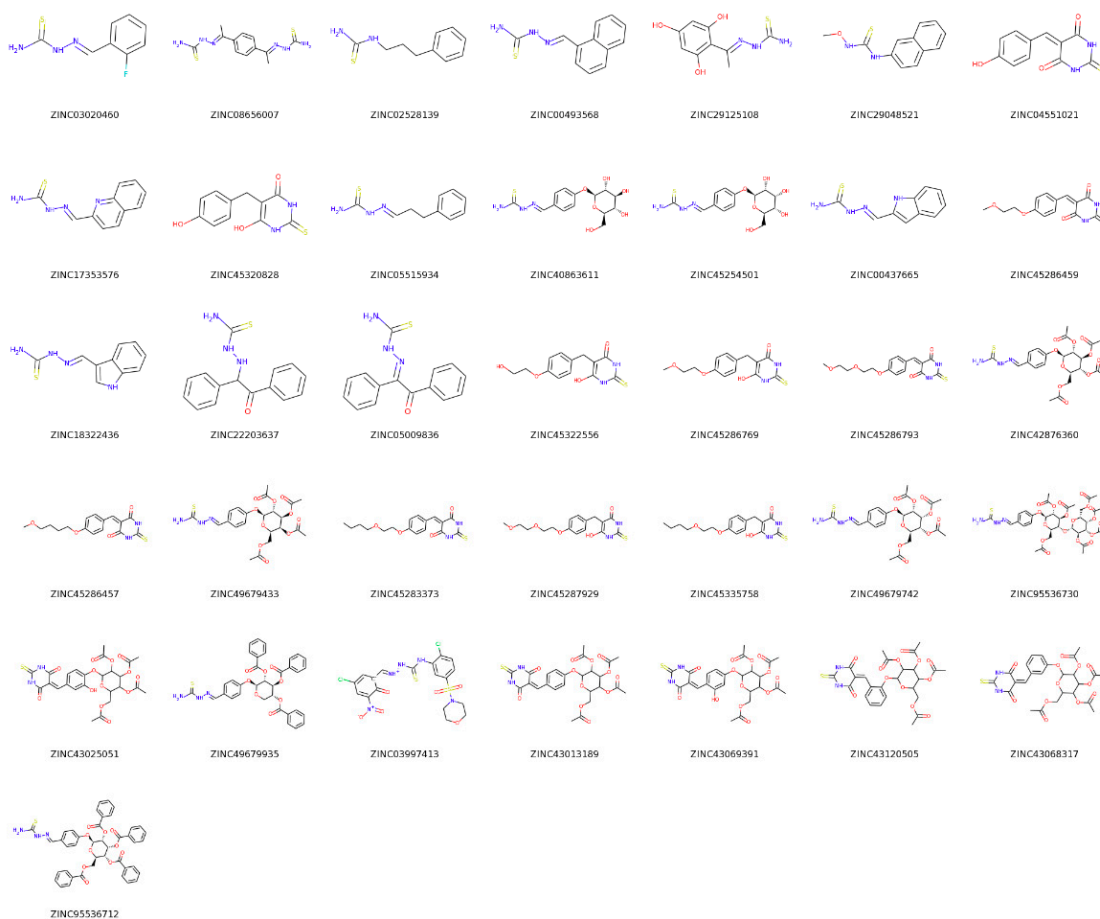


Figure S1. Seventy eight thiourea-containing compounds retrieved from the BindingDB database. ZINC ID of each compound is written beneath 2D structure.

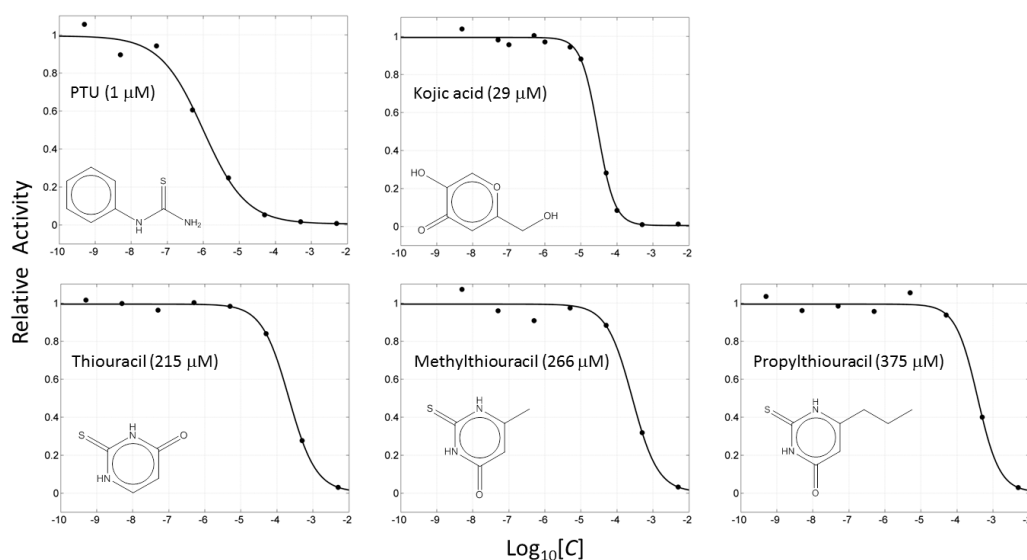


Figure S2. Concentration-dependent inhibitory activities of the compounds in this study. Activity is normalized to come under the values in the range of 0 to 1. The values in parentheses indicate IC_{50} .

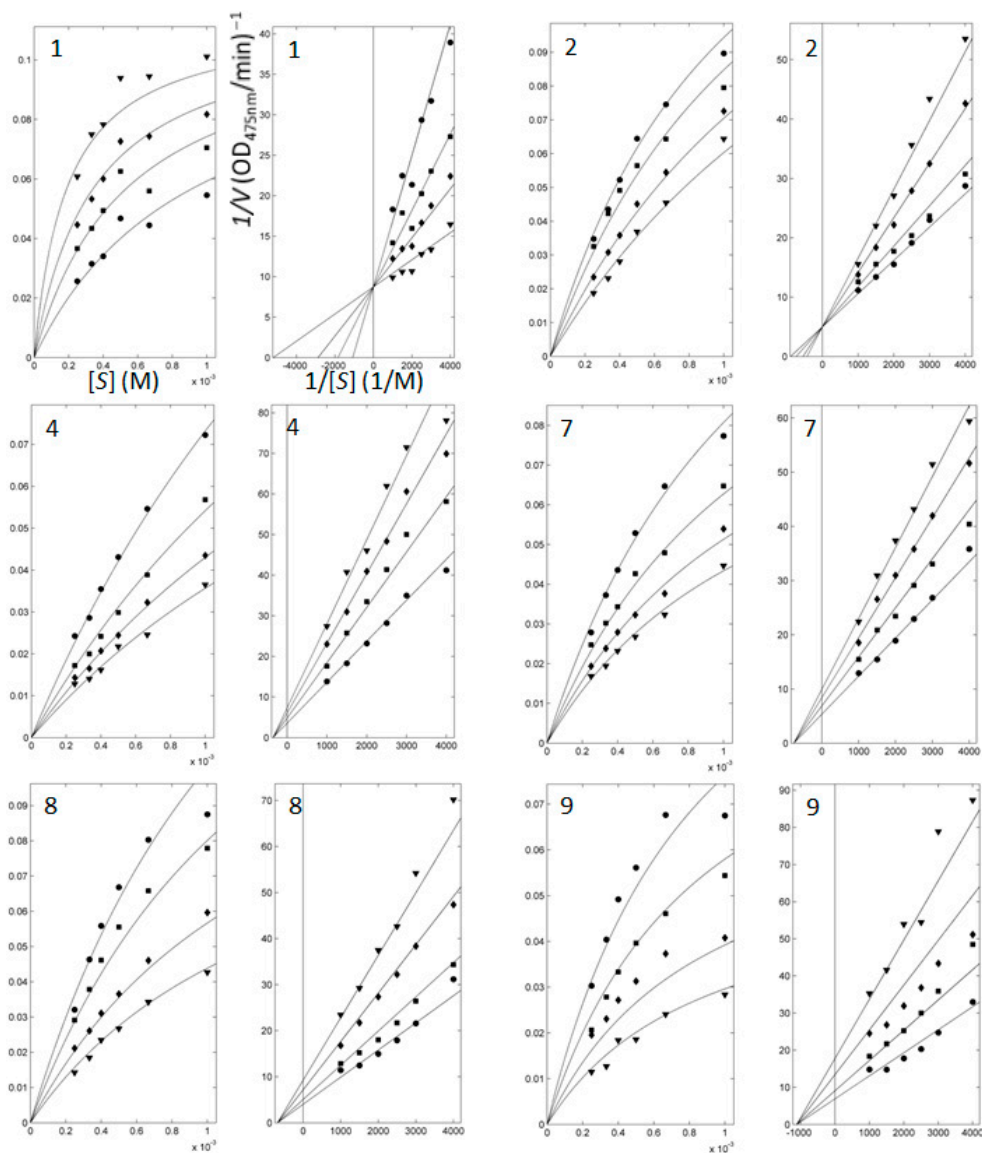


Figure S3. Profiles of inhibitory enzyme kinetics. (1) phenylthiourea (PTU); (2) kojic acid; (4) ambazone; (7) thiouracil; (8) methylthiouracil; and (9) propylthiouracil are drawn. Left and right figures in each compound represent Michaelis-Menten and Lineweaver-Burk plots, respectively.

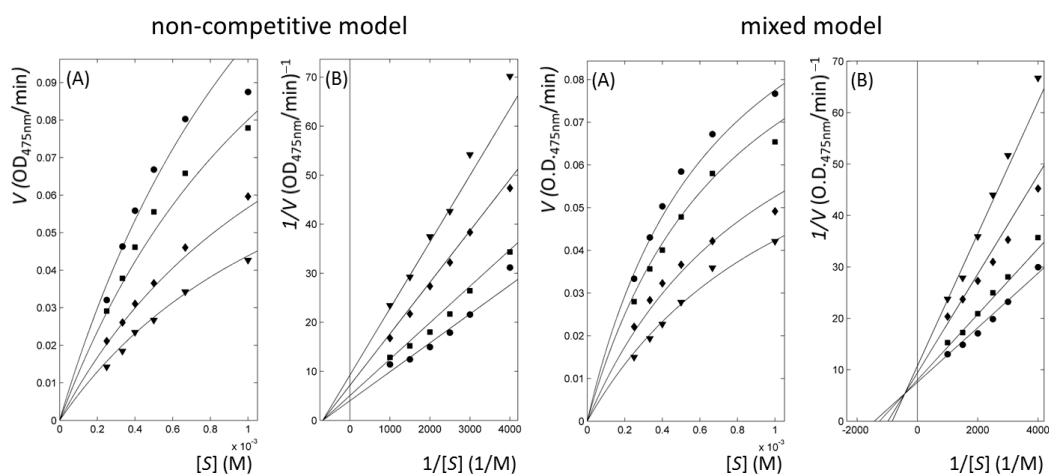


Figure S4. Profile of inhibitory enzyme kinetics with methimazole. The identical data were nonlinearly fitted with non-competitive and mixed models. (A,B) correspond to Michaelis-Menten and Lineweaver-Burk plots, respectively.

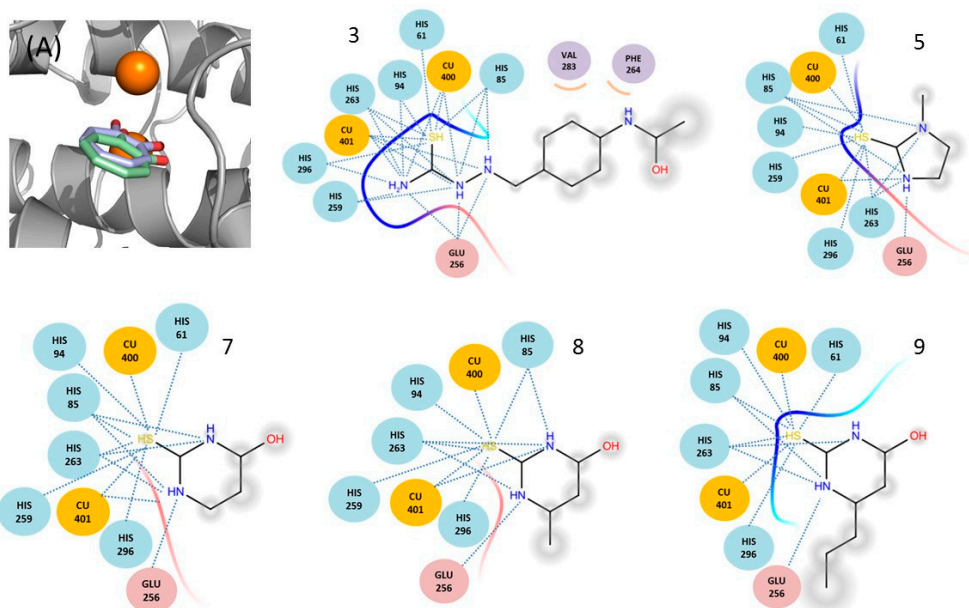


Figure S5. Predicted binding modes of the inhibitory compounds by docking simulation. (A) contains the overlaid tropolone conformations from X-ray (green) and docked (blue) structures, where orange spheres indicate copper ions. The figures of 3, 5, 7, 8, and 9 correspond to thioacetazone, methimazole, thiourasil, methylthiourasil, and propylthiourasil, respectively. Residues in tyrosinase are drawn in circle. Residues for hydrophilic and hydrophobic interactions are coloured in pink and purple, respectively. Dashed lines correspond to hydrophilic interactions, whereas curves indicate hydrophobic contacts. Atoms exposed to solvent exposure are shaded.

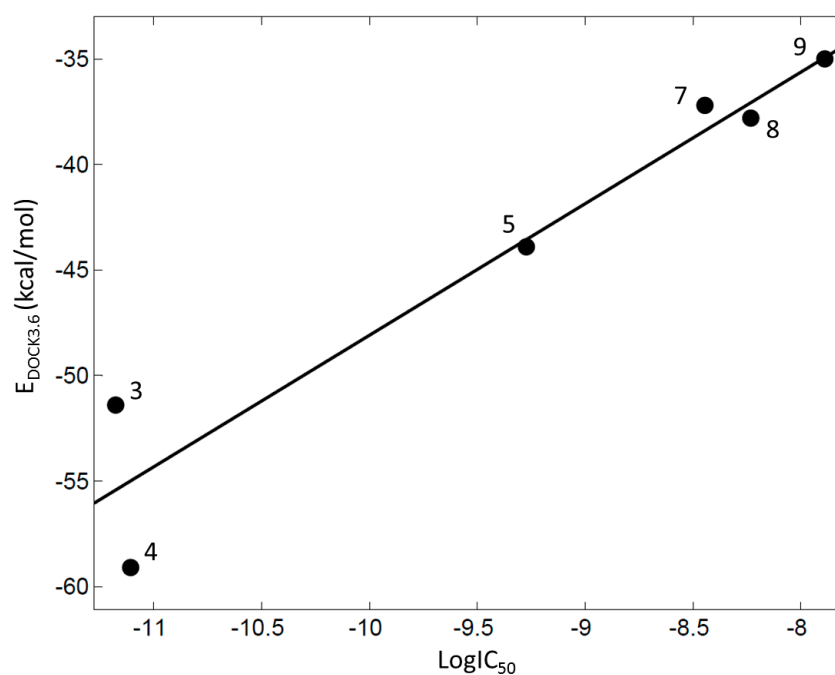


Figure S6. Correlation between experimental IC₅₀ values and simulated docking energies. The logarithmically scaled IC₅₀ values (X-axis) and the DOCK3.6-derived energies (Y-axis) in thiourea-containing drugs revealed the Pearson correlation coefficient (*R*) of 0.960 with $y = 6.234x + 14.241$. The points labeled with 3, 4, 5, 7, 8, and 9 correspond to thioacetazone, ambazone, methimazole, thiourasil, methylthiourasil, and propylthiourasil, respectively.