

**Table S9:** The accuracy and ROC-AUC value of five major CYP Isoforms from PubChem Data Set II. ImageMol\_NonPretrained and ImageMol indicate that ImageMol is not pre-trained and ImageMol is pre-trained on 10M molecular images. "MACCS-" represents the method based on MACCS molecular fingerprint, "FP4-" represents the method based on FP4 molecular fingerprint. "CC-" represents combined algorithm (ensemble learning). For details on other methods, see [1]. ImageMol\_NonPretrained and ImageMol are fine-tuned on PubChem Data Set I and evaluated on PubChem Data Set II. The best and second best result for each dataset is bolded and underlined, respectively. The methods in blue background represent image-based methods. The "3 times" represents the mean  $\pm$  standard deviation of 3 runs with different random seeds.

ValidationSet										
methods	accuracy					ROC-AUC				
	1A2	2C9	2C19	2D6	3A4	1A2	2C9	2C19	2D6	3A4
MACCS-SVM	68.0	<u>86.6</u>	80.3	<u>87.8</u>	74.9	0.814	0.854	0.841	0.88	0.783
MACCS-C4.5 DT	68.3	78.1	77.5	82.6	70.6	-	-	-	-	-
MACCS-k-NN	69.0	81.5	80.7	84.5	70.4	-	-	-	-	-
MACCS-NB	61.0	69.4	70.5	80.6	69.3	-	-	-	-	-
MACCS-CC-I	71.3	86.5	80.6	87.5	75.1	0.809	0.857	0.838	0.88	0.78
MACCS-CC-II	72.0	<b>86.7</b>	80.8	87.5	74.9	0.806	<u>0.861</u>	0.842	0.88	0.777
MACCS-CC-III	72.3	86.3	80.5	87.5	74.6	0.814	0.85	0.839	0.872	0.775
MACCS-CC-IV	<u>73.1</u>	86.4	80.4	87.6	75.0	0.815	0.853	0.829	0.886	0.785
MACCS-CC-V	69.9	83.6	80.4	86.2	74.2	0.776	0.837	0.829	0.86	0.754
MACCS-Mean	68.1	84.0	76.6	87.2	73.6	0.801	0.845	0.756	<u>0.881</u>	0.778
MACCS-Maximum	67.0	81.5	79.7	86.0	72.8	0.789	0.813	0.67	0.874	0.765
MACCS-Multiply	67.1	82.7	79.5	86.8	73.7	0.795	0.829	0.704	0.879	0.772
FP4-SVM	67.6	84.2	80.5	86.4	75.6	0.803	0.832	0.82	0.848	0.785
FP4-C4.5 DT	65.8	78.8	77.2	78.5	72.0	-	-	-	-	-
FP4-k-NN	69.7	78.4	77.9	81.1	66.3	-	-	-	-	-
FP4-NB	59.7	75.4	73.5	80.2	70.9	-	-	-	-	-
FP4-CC-I	70.7	84.5	80.2	85.6	<u>75.8</u>	0.805	0.842	0.798	0.86	0.79
FP4-CC-II	71.2	84.6	81.0	86.1	<u>75.8</u>	0.798	0.85	0.815	0.86	0.783
FP4-CC-III	70.8	84.6	80.7	85.8	<b>76.0</b>	0.794	0.827	0.812	0.839	0.787
FP4-CC-IV	71.7	84.1	80.7	85.6	75.4	0.805	0.837	0.793	0.842	0.792
FP4-CC-V	70.2	83.2	79.0	84.5	75.0	0.764	0.844	0.819	0.841	0.777
FP4-Mean	67.2	81.9	77.5	85.6	74.8	0.782	0.848	0.774	0.856	<u>0.79</u>
FP4-Maximum	66.5	80.0	78.1	83.9	74.0	0.772	0.836	0.674	0.843	0.784
FP4-Multiply	67.3	81.1	77.9	85.2	73.9	0.778	0.842	0.729	0.851	0.788
Chemception	65.1	66.7	67.1	68.1	69.3	0.699	0.733	0.738	0.753	0.763
ADMET-CNN	62.5	73.3	76.4	81.0	70.5	0.556	0.697	0.616	0.559	0.654
QSAR-CNN	55.6	64.1	60.1	82.1	60.0	0.712	0.736	0.752	0.761	0.734
ImageMol_NonPretrained	<b>73.3</b>	84.3	<u>82.2</u>	85.7	74.2	<u>0.837</u>	0.841	<u>0.848</u>	0.83	0.763
ImageMol	71.9	85.0	<b>82.9</b>	<b>88.3</b>	74.6	<b>0.852</b>	<b>0.870</b>	<b>0.871</b>	<b>0.893</b>	<b>0.799</b>
Chemception (3 times)	64.8 $\pm$ 0.4	67.1 $\pm$ 0.4	65.9 $\pm$ 1.2	67.5 $\pm$ 0.7	69.2 $\pm$ 0.2	0.690 $\pm$ 0.010	0.727 $\pm$ 0.005	0.728 $\pm$ 0.007	0.744 $\pm$ 0.09	0.761 $\pm$ 0.002
ADMET-CNN (3 times)	62.2 $\pm$ 0.4	76.4 $\pm$ 0.0	73.3 $\pm$ 0.0	81.1 $\pm$ 0.1	70.5 $\pm$ 0.0	0.546 $\pm$ 0.008	0.668 $\pm$ 0.020	0.603 $\pm$ 0.009	0.565 $\pm$ 0.005	0.652 $\pm$ 0.003
QSAR-CNN (3 times)	55.9 $\pm$ 2.0	64.1 $\pm$ 0.1	59.9 $\pm$ 0.4	81.6 $\pm$ 0.8	58.8 $\pm$ 1.7	0.710 $\pm$ 0.003	0.734 $\pm$ 0.009	0.735 $\pm$ 0.007	0.759 $\pm$ 0.008	0.734 $\pm$ 0.003
ImageMol (3 times)	<b>74.0<math>\pm</math>0.8</b>	<b>84.7<math>\pm</math>0.4</b>	<b>83.1<math>\pm</math>0.2</b>	<b>88.3<math>\pm</math>0.03</b>	<b>75.6<math>\pm</math>0.3</b>	<b>0.845<math>\pm</math>0.001</b>	<b>0.874<math>\pm</math>0.004</b>	<b>0.868<math>\pm</math>0.003</b>	<b>0.890<math>\pm</math>0.003</b>	<b>0.796<math>\pm</math>0.001</b>

[1] Cheng F, Yu Y, Shen J, et al. Classification of cytochrome P450 inhibitors and noninhibitors using combined classifiers[J]. Journal of chemical information and modeling, 2011, 51(5): 996-1011.