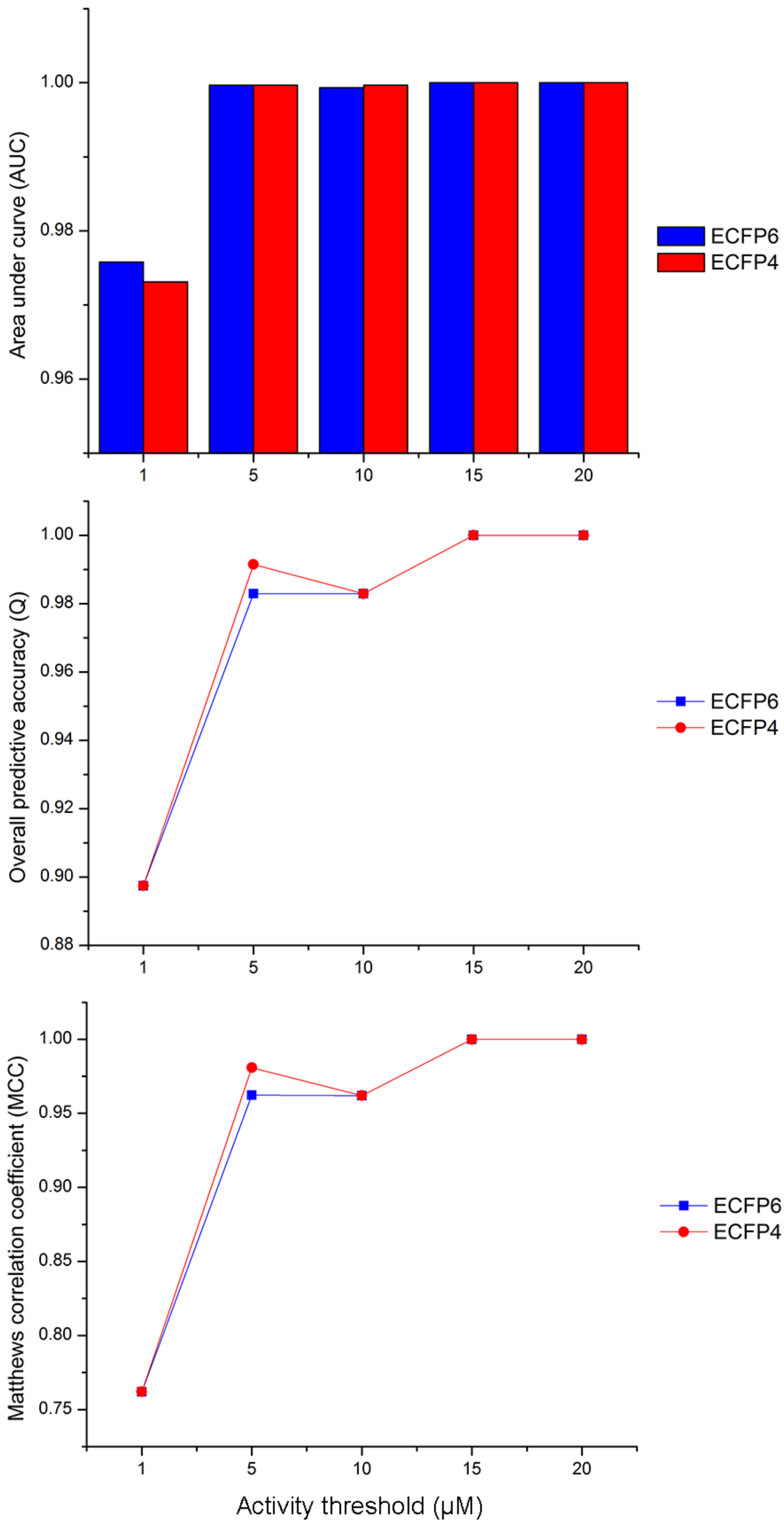

Fig S1. The performance of the na ïve Bayesian models at different activity thresholds. ECFP6 and ECFP4 represent the fingerprints using for building models. According to these results, all the values suddenly increase and stabilize after 5 μM. Therefore, 5 μM is the reasonable activity threshold.

Table S1. The details of performance parameters for the best RP models with the combination of different fingerprints and MPs.

Models	Training set			Test set		
	Q_a	***Q_{na}***	***Q***	***Q_a***	***Q_{na}***	**Q**
MP[a]_depth6[b]	0.461	0.890	0.671	0.406	0.774	0.573
ECFP_4_depth4+MP	0.870	0.967	0.938	0.971	0.940	0.949
ECFP_6_depth4+MP	0.848	0.971	0.932	0.944	0.951	0.949
EPFP_4_depth3+MP	0.789	0.978	0.912	0.756	0.944	0.872
EPFP_6_depth4+MP	0.841	0.971	0.929	0.875	0.961	0.932
FCFP_4_depth3+MP	0.880	0.971	0.943	0.925	0.987	0.966
FCFP_6_depth3+MP	0.880	0.971	0.943	0.925	0.987	0.966
FPFP_4_depth5+MP	0.835	0.975	0.929	0.814	0.959	0.906
FPFP_6_depth3+MP	0.769	0.961	0.895	0.857	0.973	0.932
LCFP_4_depth3+MP	0.842	0.975	0.932	0.872	0.949	0.923
LCFP_6_depth3+MP	0.836	0.979	0.932	0.875	0.961	0.932
LPFP_4_depth3+MP	0.839	0.967	0.926	0.923	0.974	0.957
LPFP_6_depth3+MP	0.855	0.967	0.932	0.923	0.974	0.957

[a]MP: the 13 descriptors calculated with DS 2.5.5. [b]Depth*: the best tree depth for the corresponding model.

Table S2. The details of performance parameters for the best RP and NB models

Models	Training set			Test set		
	Q_a	***Q_{na}***	***Q***	***Q_a***	***Q_{na}***	**Q**
RP_FCFP_4_depth3[b]+MP[a]	0.880	0.971	0.943	0.925	0.987	0.966
RP_FCFP_6_depth3+MP	0.880	0.971	0.943	0.925	0.987	0.966
NB_FPFP_6+MP	0.893	0.992	0.960	0.974	1.000	0.991
NB_FPFP_10+MP	0.870	0.992	0.952	0.974	1.000	0.991

[a]MP: the 13 descriptors calculated with DS 2.5.5. [b]Depth*: the best tree depth for the corresponding model.

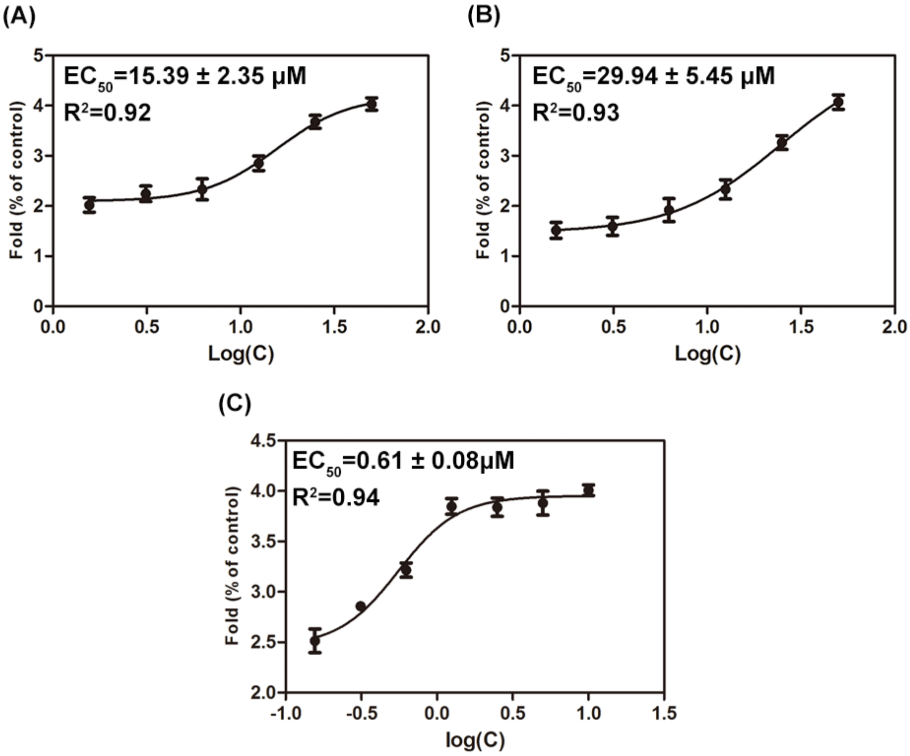

Fig S2. The activation curves of compound 10 (A), compound 13 (B) and GW4064 (C). The EC_{50} values are presented as the mean ±SE.