

**Table S7.** Performance of prediction tools with MMP testing dataset.

	MAPP	nsSNPAnalyzer	PANTHER	PhD-SNP	PPH-1	PPH-2	SIFT	SNAP	PredictSNP
<b>True positives</b>	3,337	2,510	829	3,399	3,330	3,769	3,675	3,163	3,773
<b>False negatives</b>	1,113	1,518	1,428	1,058	944	505	416	1,293	683
<b>True negatives</b>	4,990	4,264	4,336	3,739	4,390	3,518	2,887	5,338	4,291
<b>False positives</b>	2,530	2,687	834	3,798	3,053	3,925	4,463	2,200	3,247
<b>Total</b>	<b>11,970</b>	<b>10,979</b>	<b>7,427</b>	<b>11,994</b>	<b>11,717</b>	<b>11,717</b>	<b>11,441</b>	<b>11,994</b>	<b>11,994</b>
<b>Sensitivity</b> <sup>a</sup>	0.750	0.623	0.367	0.763	0.779	0.882	0.898	0.710	0.847
<b>Specificity</b> <sup>a</sup>	0.664	0.613	0.839	0.496	0.590	0.473	0.393	0.708	0.569
<b>Precision</b> <sup>a</sup>	0.690	0.617	0.695	0.602	0.655	0.626	0.597	0.709	0.663
<b>NPV</b> <sup>a</sup>	0.726	0.619	0.570	0.676	0.728	0.800	0.794	0.709	0.788
<b>Accuracy</b> <sup>a</sup>	<b>0.707</b>	<b>0.618</b>	<b>0.603</b>	<b>0.629</b>	<b>0.684</b>	<b>0.677</b>	<b>0.646</b>	<b>0.709</b>	<b>0.708</b>
<b>MCC</b> <sup>a</sup>	<b>0.415</b>	<b>0.237</b>	<b>0.234</b>	<b>0.268</b>	<b>0.376</b>	<b>0.389</b>	<b>0.337</b>	<b>0.418</b>	<b>0.433</b>
<b>AUC</b> <sup>a</sup>	<b>0.759</b>	<b>0.620</b>	<b>0.676</b>	<b>0.685</b>	<b>0.720</b>	<b>0.774</b>	<b>0.710</b>	<b>0.769</b>	<b>0.787</b>

PPH-1 – PolyPhen-1; PPH-2 – PolyPhen-2; NPV – negative predictive value; MCC – Matthews correlation coefficient; AUC – area under receiver operating characteristics curve; <sup>a</sup> – these metrics were calculated with normalized numbers