Supplementary Figures

Clinical likelihood ratios and balanced accuracy for 44 in silico tools AGAINST multiple large-scale functional assays of cancer susceptibility genes

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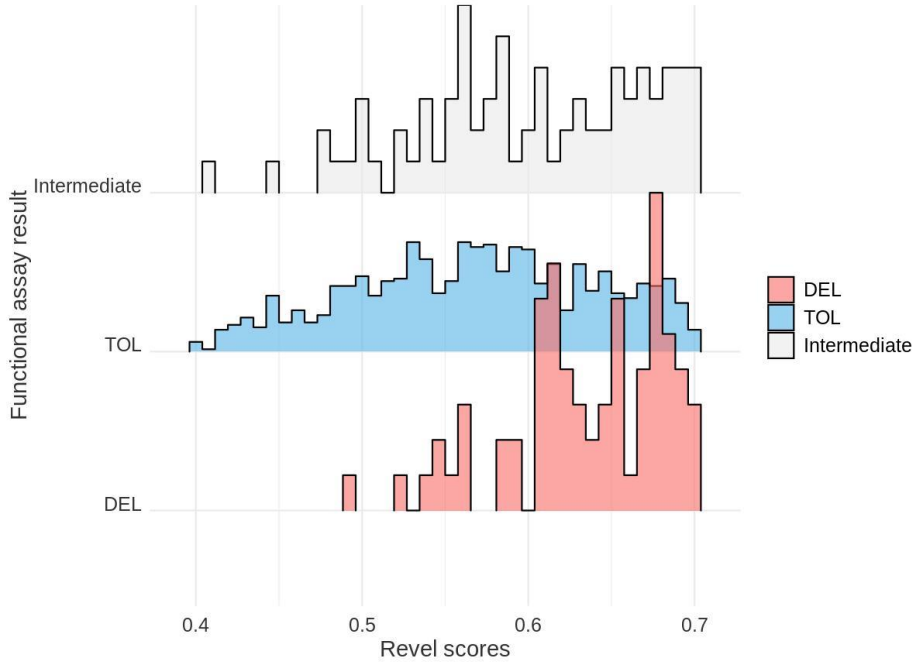
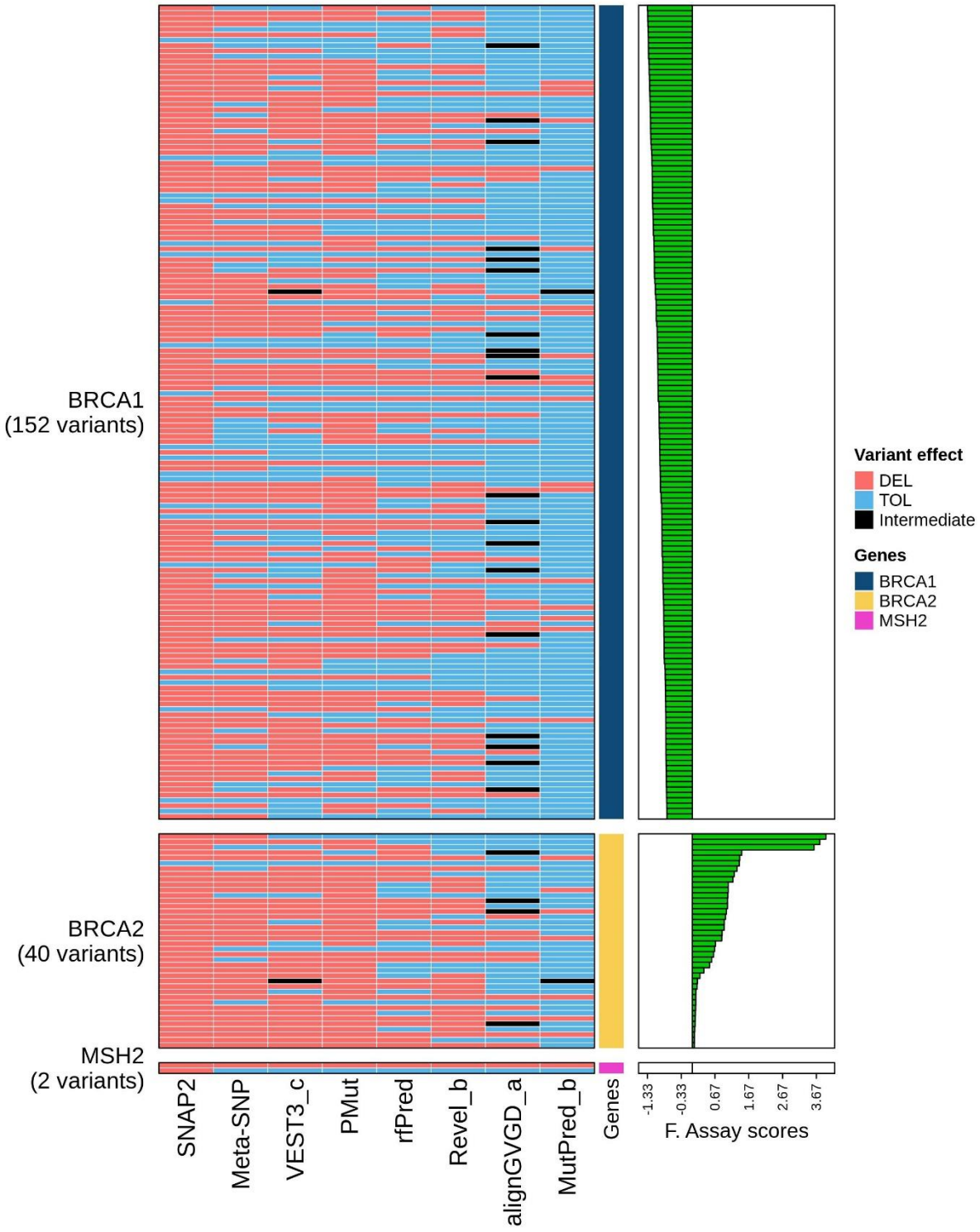
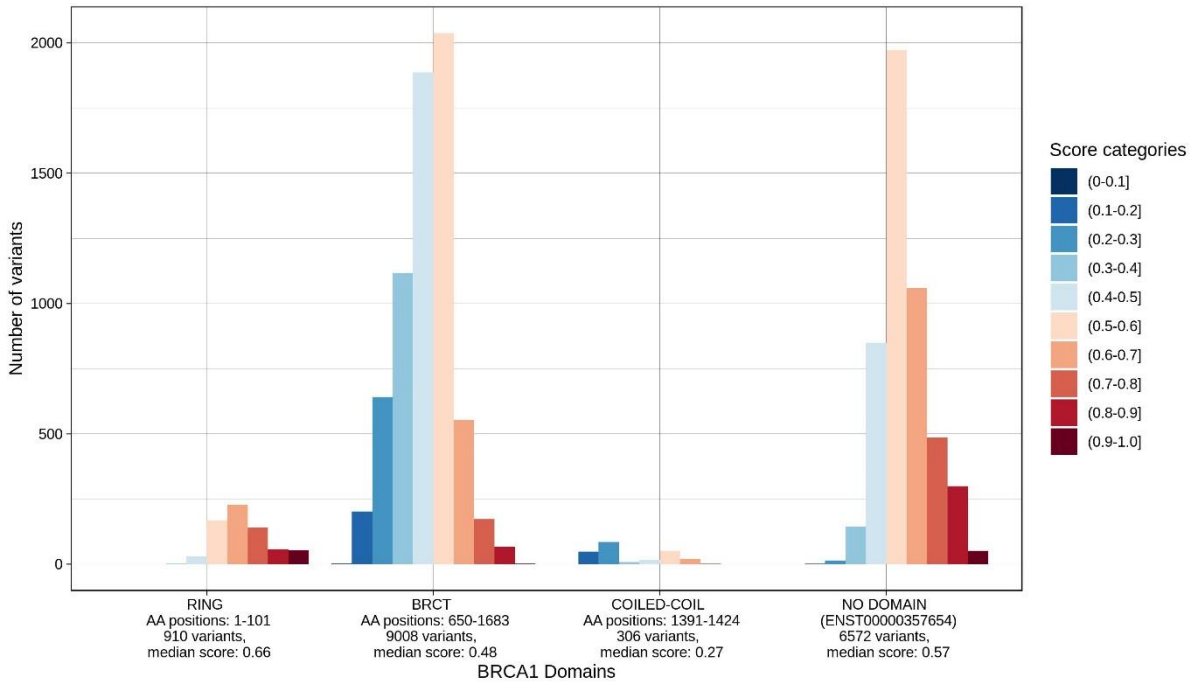


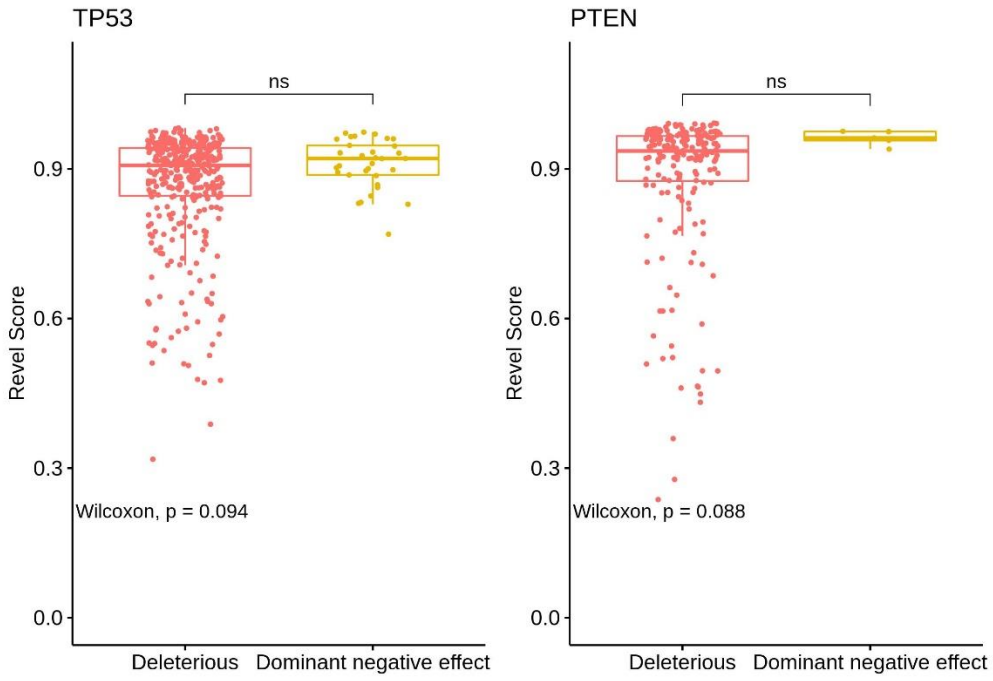
Supplementary Figure 1: Distribution of Revel Scores 0.4-0.7 for BRCA1 variants by functional assay group, deleterious (70 variants), tolerated (1016 variants) or intermediate (79 variants)



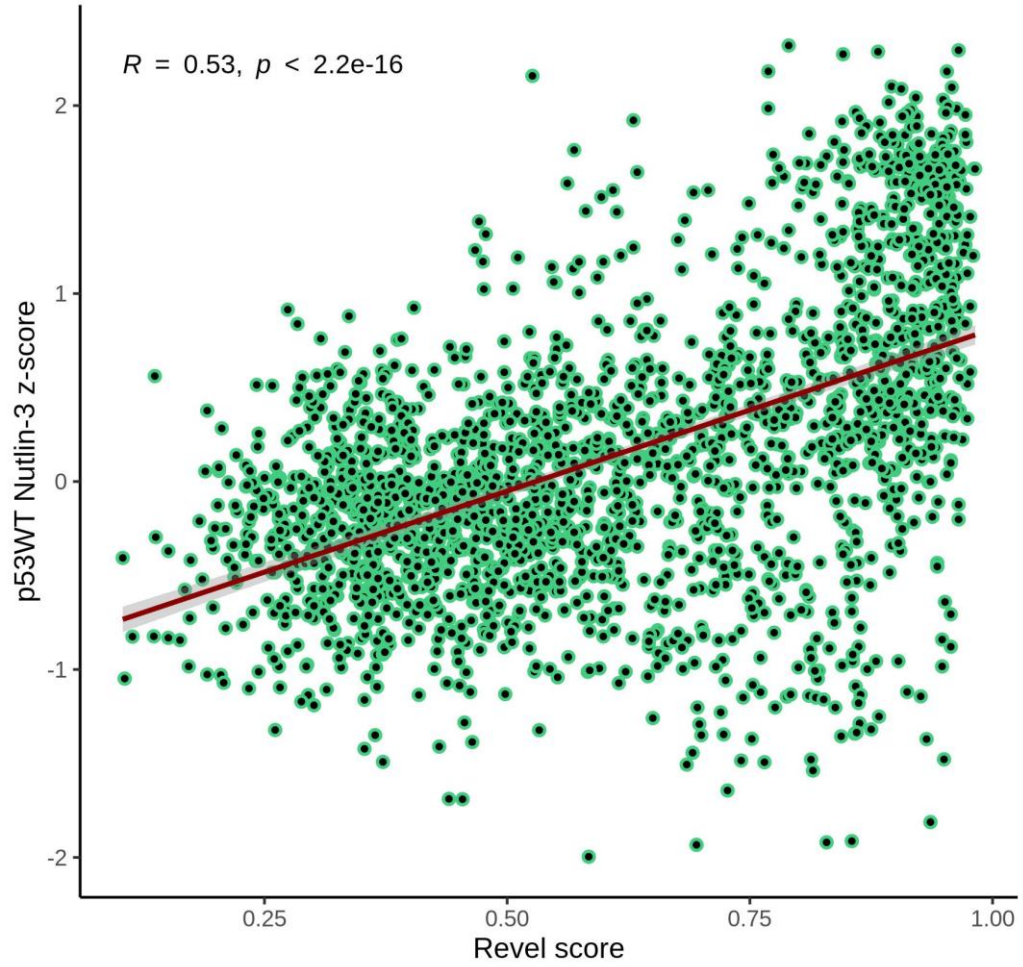
Supplementary Figure 2: Examination of in silico predictions variants scoring in the intermediate range of functional assays for BRCA1, BRCA2 and MSH2 for 8 high-performing tools. Variants are ordered top-to-bottom for their score on the functional assay, with those at the top end being variants scoring nearest to the threshold for being called as deleterious



Supplementary Figure 3: Distribution by gene domain of Revel Scores for all missense BRCA1 variants (including variants with and without assay data)



Supplementary Figure 4: Comparison of Revel scores against all other variants classified by assay as deleterious for variants of established dominant negative effect in TP53 (missense at codons 175, 245, 248, 249, 273 and 282) and PTEN (p.Pro38Ser, p.Cys124Ser, p.Arg130Gly, p.Arg130Gln, p.Gly129Glu)



Supplementary Figure 5: Correlation of p53WT Nutlin-3 z-score (an assay of dominant negative action) against Revel Score for the 1867 TP53 variants included in the analysis