Protein folding results for VKGL missense variants in the HK1 gene Based on VKGL public consensus release April 2023, FoldX 5.0, and AlphaFold2 human proteome v4 At a $\Delta\Delta G$ threshold of 3.17 the PPV is 100%, the sensitivity is 75%, the NPV is 80% and the specificity is 100% 25 GA414R (DVV) reference and variant protein energy change **VKGL** classification LB/B Difference in Gibbs free between GRCh37 refere LP/P VUS SA445L RA398H DA632N AA889T SA285F SA449L RA518H RA829Q RA425H IA617T RA853G NA190S RA794Q VA248L 0

700

500

Amino acid position within the protein alpha chain of HK1

300