

Supplementary Table 1. Predicted Effects of the Alterations in *HUWE1* on Protein Function

Alteration		Mutation Taster	SIFT	PolyPhen-2
p.R4063Q	c.12188G>A	Disease-causing	NT*	Probably Damaging (.999)
p.G4310R	c.12928G>C	Disease-causing	NT	Probably Damaging (1.000)
p.R4013W**	c.12037C>T	Disease-causing	NT	Probably Damaging (.999)
p.R4187L**	c.12559C>T	Disease-causing	NT	Probably Damaging (1.000)
p.R2981H**	c.8942G>A	Disease-causing	NT	Probably Damaging (.999)

\*NT- Not Tolerated

\*\*Three missense mutations reported by Froyen et al.[22] and Isrie et al.[23]