**Author Contributions**

JYL and PRB designed the framework, performed the analyses. LL provided the guidance on SEM. KD developed and draft the R shiny code. TW prepared gene signatures, processed gene expression matrix data. JLL, SPW, and FJD conceived the idea, provided overall guidance, and oversaw the project progression. JYL and PRB wrote the manuscript with the input of SPW, LL and JLL. SPW, JYL, LL, TW, PRB and JLL revised the manuscript.