



Supplementary Materials

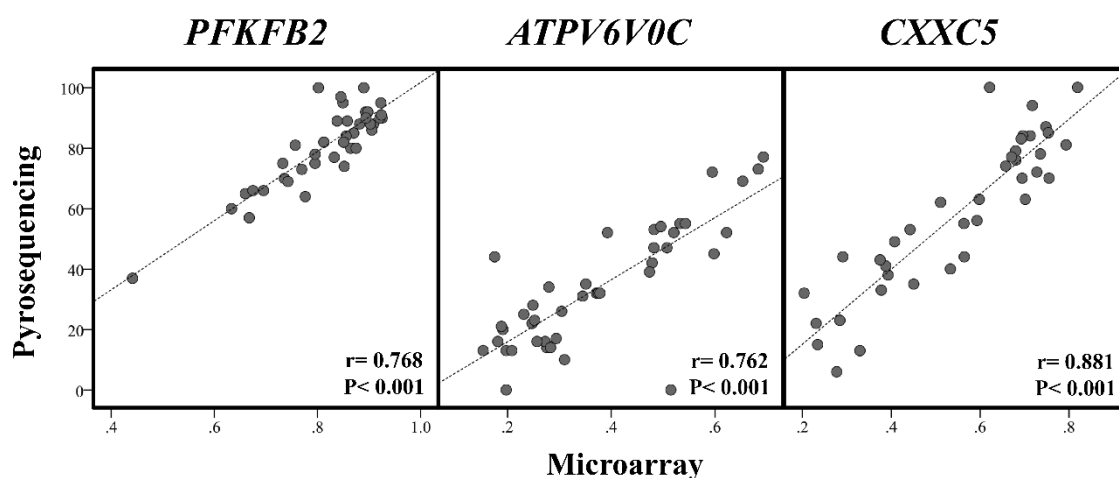


Figure 1. Correlation between values obtained by methylation microarray and bisulfite pyrosequencing assays. Scatterplots showing high values of positive correlation for *PFKFB2*, *ATPV6V0C* and *CXXC5*. r = correlation coefficient, P = p-value from Spearman's correlation test.

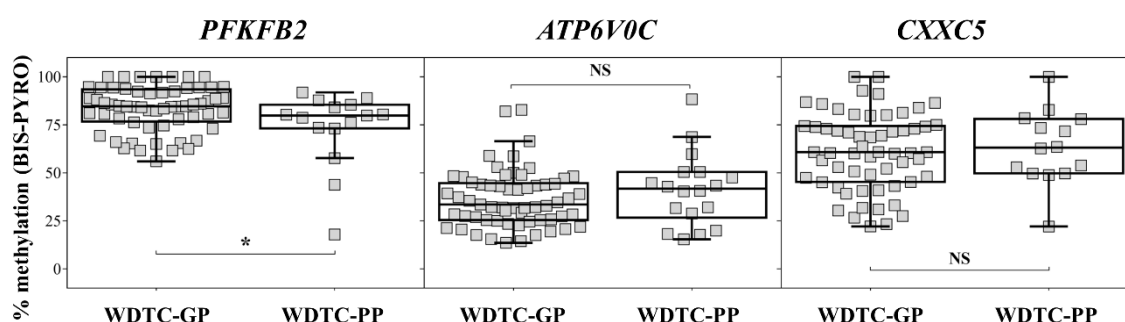


Figure 2. Bisulfite pyrosequencing quantification of CpG allele methylation mapped in *PFKFB2*, *CXXC5* and *ATPV6V0* in well-differentiated thyroid carcinomas (microarray-independent cases). The CpGs methylation levels in WDTC-PP patients were compared with WDTC-GP. BIS-PYRO: bisulfite pyrosequencing; NS> 0.05; * P < 0.05 (Mann-Whitney test); WDTC-GP: well-differentiated thyroid carcinomas of good prognosis; WDTC-PP: well-differentiated thyroid carcinomas of poor prognosis.

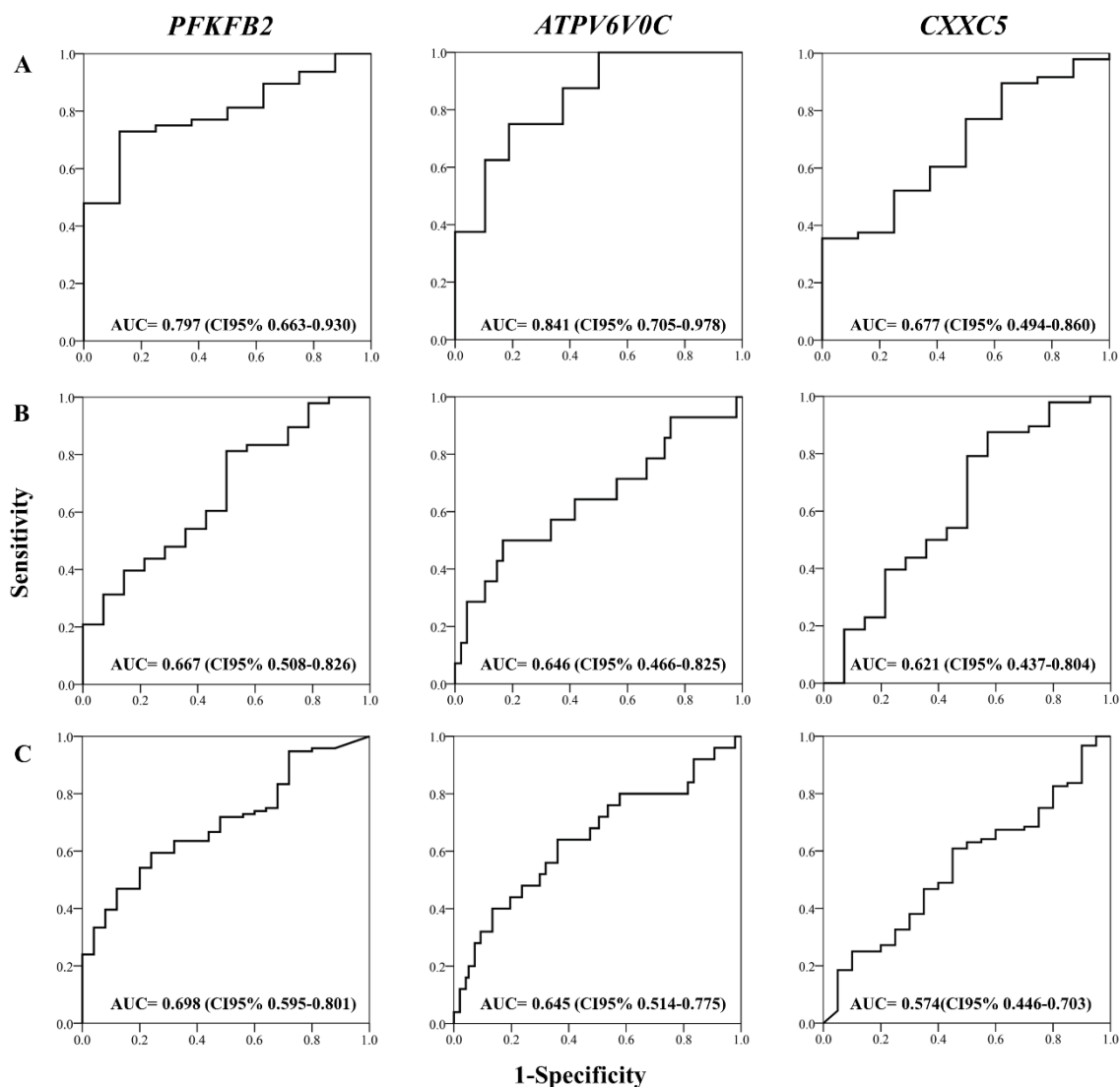


Figure 3. (A). Area under the ROC curve of the epigenetic candidate markers to identify aggressive subtypes of WDTC samples previously evaluated by methylation microarray (BISARRO DOS REIS et al., 2017); (B) TCGA cohort of PTC and (C) cases evaluated by bisulfite pyrosequencing. CI_{95%}: 95% confidence interval; AUC: area under the receiver operating characteristic (ROC) curve.

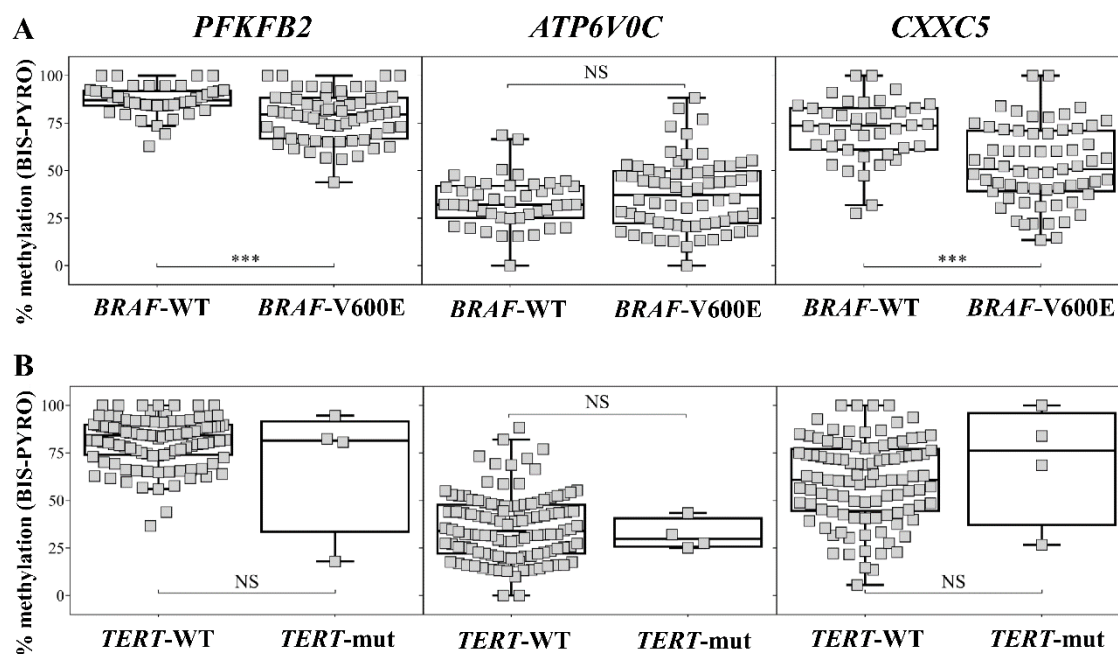


Figure 4. DNA methylation in *PFKFB2*, *ATP6B0C* and *CXXC5* according to *BRAF* (V600E) and *TERT* (C228T and C250T) mutation status. BIS-PYRO: bisulfite pyrosequencing; NS> 0.05; *** $P < 0.001$ (Mann-Whitney test).

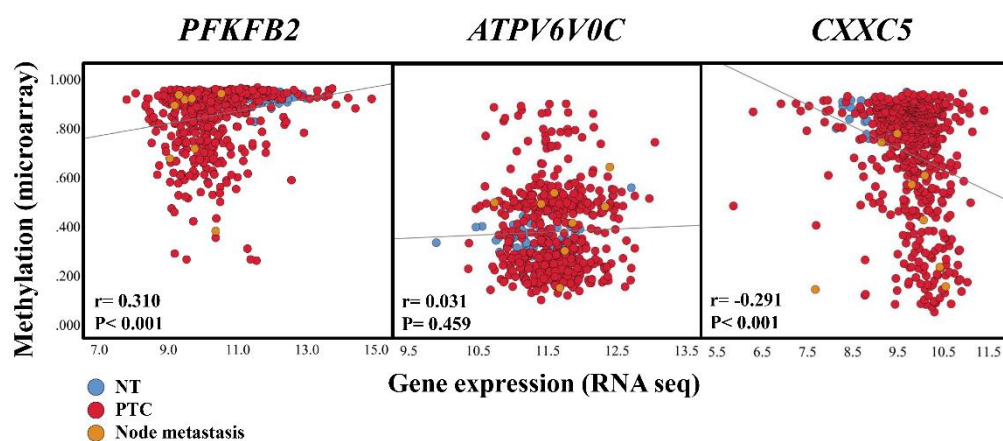


Figure 5. Correlation between CpG methylation and gene expression levels of the studied genes in the thyroid cohort from TCGA database. A positive correlation was observed between DNA methylation (probe cg02710090) and *PFKFB2* expression and negative correlation between DNA methylation (probe cg19628988) and *CXXC5*. No correlation was noted to *ATP6V0C* (methylation probe cg05884711). r = correlation coefficient, P = p-value from Spearman's correlation test. NT: non-neoplastic thyroid; PTC: papillary thyroid carcinoma.