EVALUATION OF EXPRESSION OF GENES POTENTIALLY REGULATED BY DNA METHYLATION INVOLVED IN WILMS TUMOR PROGRESSION

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ABSTRACT

Wilms tumor (WT) is an embryonic tumor composed by different proportions of blastemal, epithelial and stromal cells. The predominant histological component after pre-operative chemotherapy is used to classify the patients in risk groups (1,2). WTs have a relapse rate of ~25% with a long-term survival of approximately 50% (3). Blastemal predominant WTs present higher risk of relapse and capacity of forming distant metastasis (4). To identify the underlying mechanisms involved with metastasis formation in WT, we performed a gene expression analysis by RNA-Seq of matched normal kidney (NK), WT blastemal component and metastatic tissues (MET) and then these results will be associated with DNA methylation analysis from a previous study.

OBJECTIVES

The aim of this study is to characterize gene expression profiles in matched NK, WT (blastemal component) and MET samples and to correlate with the alterations observed in DNA methylation. Also, to select genes potentially associated with tumor progression and to validate by immunohistochemistry

METHODS AND RESULTS

The steps of sample selection, RNA extraction, quality and integrity assessment, library preparation and sequencing are described in **Figure 1**. The raw data were processed using bioinformatic tools, and DESeq2 package was applied for differential analysis (**Figure 2**). There were 2,590 and 196 differentially expressed genes (DEGs) between WT and NK and between MET and WT, respectively. The **Figure 3** represents the TOP 100 DEGs between both comparisons. In WT Vs NK comparison, DEGs were enriched for pathways associated with tumorigenesis, such as cell cycle (48 genes, FRD=0), Transcriptional misregulation in cancer (56 genes, FDR=3.34e-^{02}) and Wnt signaling pathway (16 genes, FDR=1.46e-02), while among MET Vs WT, DEG were enriched for pathways pathways associated with tumor progression as rRNA processing (35 genes, FDR=0) and Focal Adhesion PI3K-Akt-mTOR signaling pathway (5 genes, FDR=9.37e-^{01}).

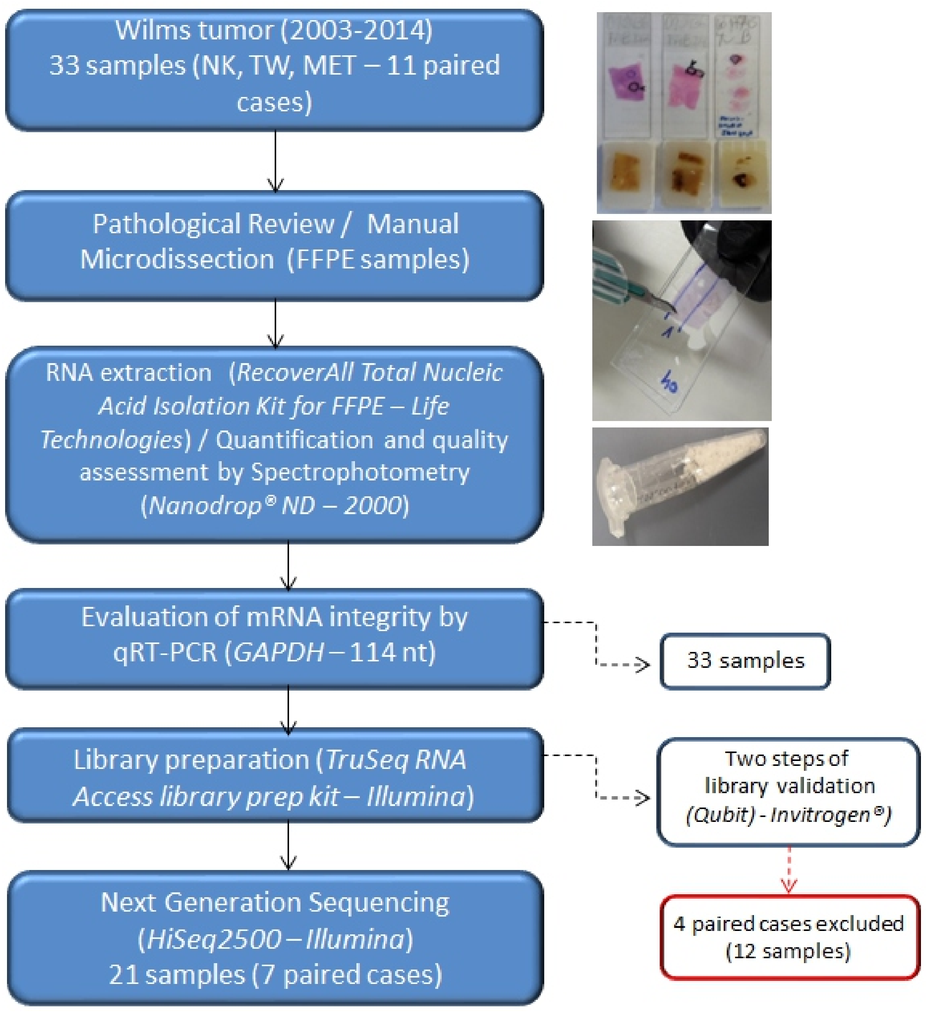
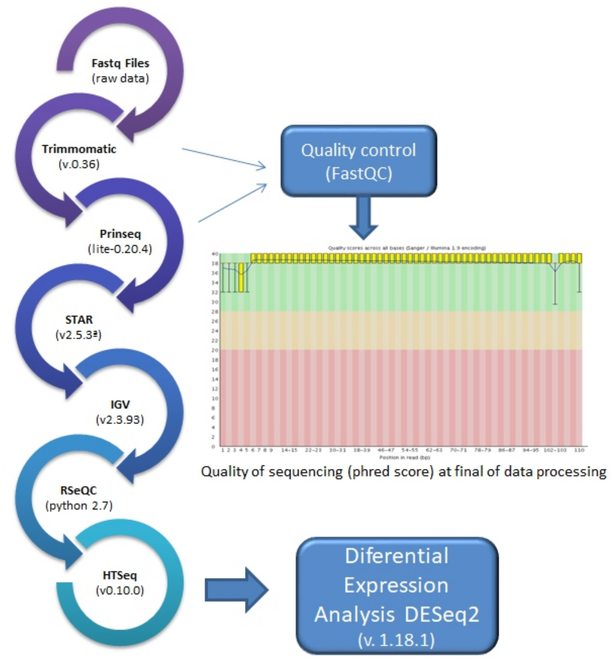


Figure 1



Quality of sequencing (phred score) at final of data processing

Figure 2

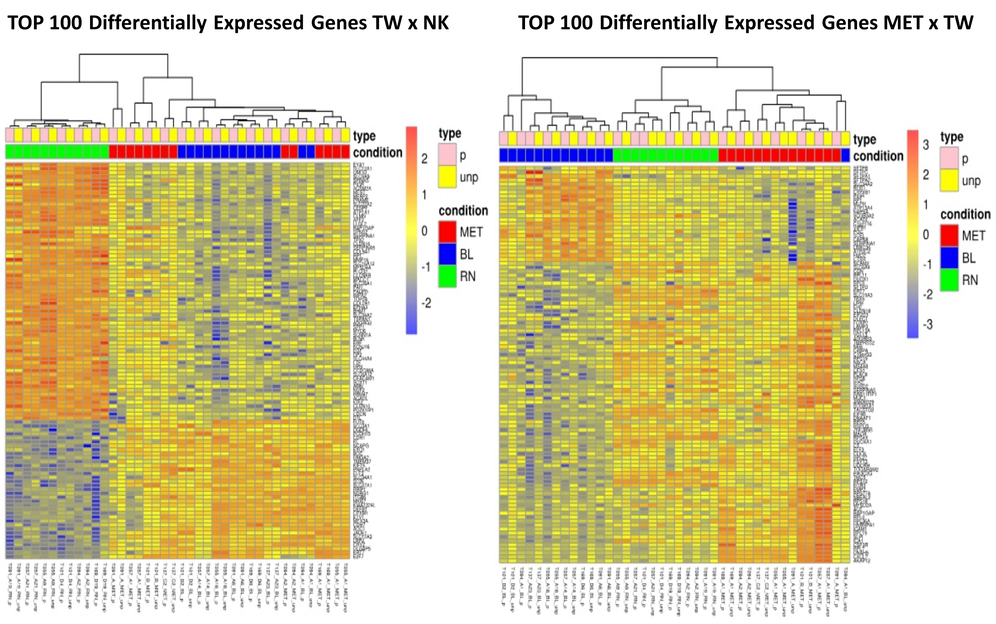


Figure 3

PERSPECTIVES AND CONCLUSION

The differentially expressed genes will be compared to the methylation status of their promoters to evaluate if their regulation could be related to DNA methylation. Further, selected genes will be evaluated by immunohistochemistry in an independent group of cases.

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