

## **An Integrated RNA and DNA Molecular Signature for Colorectal Cancer Classification**

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Colorectal cancer (CRC) is the third most common cancer among women and men in the USA. The KRAS gene is mutated in 40% of the CRC cases and hence the RAS pathway activation has become a major focus of drug targeting efforts. However, nearly 60% of patients with wild-type KRAS fail to respond to RAS-targeted therapies, for example the anti-epithelial growth factor receptor inhibitor (EGFRi) combination therapies. Thus, there is a need to develop more reliable molecular signatures to better predict mutation status. In this study, we develop a hybrid (DNA mutation and RNA expression) signature and assess its predictive properties for the mutation status of CRC patients. Publicly-available microarray and RNA-Seq data from 54 matched formalin-fixed paraffin embedded (FFPE) samples from the Affymetrix GeneChip and RNA-Seq platforms, were used to obtain differentially expressed genes between mutant and wild-type samples. For classification, the support-vector machines, artificial neural networks, random forests, k-nearest neighbors and the naive Bayes algorithms were employed. Compared to the genelist from each of the platforms, the hybrid genelist had the highest accuracy, sensitivity, specificity and AUC for mutation status and could therefore be useful in clinical practice, especially for colorectal cancer diagnosis and therapeutics.

**Keywords:** Colorectal cancer; FFPE; microarray; RAS pathway signature; RNASeq.