

**Supplementary Figure S1:** Flowchart for Statistical Analysis. Circulating miRNAs were evaluated in IPMN cases versus healthy controls and malignant versus benign IPMNs using linear models for microarray data (LIMMA), principal component analysis (PCA), and receiver operating characteristic (ROC) curve analyses, followed by pathway enrichment analyses. We also correlated abundance of plasma miRNAs and tissue miRNAs for cases with both sample types.

**Supplementary Figure S2: miR-145-5p expression differentiates between cases and non-diseased controls.** A) Box plot reveals miR-145-5p expression is higher in cases versus controls. B) ROC analysis reveals that miR-145-5p expression can differentiate between groups with an AUC=79.3 (95% CI: 68.3-90.3). Estimates of sensitivity, specificity, positive predictive value, and negative predictive value are 81%, 62.5%, 79%, and 65%, respectively.

**Supplementary Figure S3: A 5-miRNA signature discriminates Malignant (N=21) and Benign (N=21) IPMN Cases.** A) Percentage of variation explained in the 5 principal components using the 5 miRNA signature. B) Association of the 5-miRNA signature with IPMN malignancy status. Box plots were used to display the distribution of the IPMN-risk malignancy score within each group. Two-sample t-tests were used to determine associations between the continuous PC1 score and IPMN malignancy status. C) ROC curve analysis of the 5-miRNA signature yielded an AUC of 73.2 (95% CI: 57.6-88.9) in differentiating between groups.