**Supplementary Figures:**

**Supplementary Figure 1A**:

Heat Map demonstrating the modification of the Moffitt classifier previously published

Orange and purple **row** bands are basal-like and classical genes, respectively.

Orange and purple **column** bands are basal-like and classical in original and modified Moffitt subtypes.

Original Moffitt subtype identifies basal-like subtype if the basal gene set expression is higher than classical gene set however modified Moffitt signature identifies basal-like subtype only if the basal gene set expression is high and classical gene set is not expressed greatly reducing the number of specimens classified as basal-like.

**Supplementary Figure 1B**:

The modified Moffitt classifier performs better than the Moffitt original classifier in determining outcomes as shown here. Those patients where the tumour shows no expression of classical genes (modified Moffitt basal-like, orange line) have significantly worse prognosis. However, if the patient was classified as basal-like by Moffitt but showed some expression of classical genes (hybrid, blue line), these patients do as well as the classical group (purple line) by the original Moffitt classifier.

**Supplementary Figure 2: Scoring of GATA6 by ISH and IHC**

**A) GATA6 RNA ISH semiquantitative scores**. Score 1, few discernable dots at 20x; score 2, dots (4–9/cell) resolved at 10x, with clusters; score 3, individual dots (10-15/cell) with frequent clusters resolved at 5x; score 4, dots (>15/cell) with numerous clusters throughout tumor cells.

**B) GATA6 IHC semiquantitative scores**. Score 1, weak nuclear stain in (at least 5%) tumor cells; score 2, moderate nuclear staining in the tumor; score 3, strong nuclear immunopositivity; score 4, very strong and diffuse staining.

**Supplementary Figure 3A and 3B:**

Multivariable analysis of clinico-pathological factors impacting overall survival, Figure 3A) includes the modified Moffitt subtypes and Figure 3B) includes GATA6 expression, given the high degree of co-linearity between GATA6 and the modified Moffitt classifier together with our numbers the two have not been included in the same model

**Supplementary Figure 4:**

Correlation of GATA6 detection by IHC with GATA6 ISH by A) semiquantitative scoring and B) image analysis

**Supplementary Figure 5:**

GATA 6 staining by IHC (left) and GATA6 ISH (right) showing variability in expression where some areas demonstrate high levels of staining (H) and others low levels of staining (L)

**Supplementary Figure 6:**

Qupath image analysis showing regional differences reflected in variability of GATA6 expression at the cell level in basal-like vs. classical PDAC. Basal-like cases comprised higher percentages of cells that were negative/weakly positive for GATA6 and classical cases more cells with moderate/strong GATA6 immunoreactivity while a subset of basal and classical cases comprised similar percentages of both; this variability was again comparable between resected A) resected cases and B) advanced biopsies on COMPASS.

**Supplementary Figure 7A:**

Correlation analysis using RNA seq of cytokeratins associated with GATA6 expression showing high anticorrelation of keratin 15, keratin 6, keratin 5 and14.

**7B)** Association of keratin 17, 14, and keratin 5 with the modified Moffitt classifier.

**Supplementary Figure 8**

Heat Map to depicting relationship between GATA6 and KRT5 expression.

**Supplementary Figure 9:**

Association of hypoxia\*, IFN-gamma gene signature¶ PD-L1 and PD-1 expression (RNAseq) with the modified Moffitt classifier.

**Supplementary Table 1:**

Staining patterns of GATA6 and CK5 by immunohistochemistry in resected specimens (whole sections) and COMPASS biopsies. Weak and negative immunoreactivity for GATA6 (>90% of tumour cells with score 0 or 1) was seen in 9/14 (64%) basal-like vs. only 3/16 (19%) classical tumors.