Supplementary Figure 1

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Supplementary Figure 2

A

**TGFβ1-2-3 ligands**

B

**Fibroblast TGF-beta response signature (F-TBRS)**

C

**CAF-A and CAF-B**

**myCAF and iCAF**

D

**Matrix Index – HIF stage II CC**

**p33 Pathway – HIF stage II CC**

E

**Differential contractility**

**Inflammatory-related**

F

**TGFβ1-2-3 ligands in HIF tumours**

G

**F-TBRS in HIF tumours**

- **Relapse**
- **Non-relapse**

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**doi: 10.1136/gutjnl-2021-326183**

Corry SM, et al.
Supplementary Figure 3

A

Discovery cohort

Validation cohort

B

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Supplementary Figure 4

A

Stage II/III Validation

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C

Stage II/III Validation

D

HiFi – Stage II/III Validation

LoFi – Stage II/III Validation

E

- StromalScore
- ImmuneScore
- Isella CAF
- Isella Endothelial
- Isella Leucocyte
- Epithelial Mesenchymal Transition
- Myogenesis
- UV Response Dn
- Coagulation
- TNFA Signalling via NFKB
- KRAS Signalling Up
- Apical Junction
- Inflammatory Response
- Allograft Rejection
- Angiogenesis
- Complement
- Hypoxia
- IL6 JAK STAT3 Signalling
- Hedgehog Signalling
- Interferon Gamma Signalling
- IL2 STAT5 Signalling
- Apoptosis
- TGFβ Signalling
- Notch Signalling
- Apical Surface
- Androgen Response
- Interferon Alpha Signalling
- p53 Pathway
- Glycolysis
- Unfolded Protein Response
- Spermatogenesis
- DNA Repair
- Oxidative Phosphorylation
- MYC Targets V1
- MYC Targets V2
- G2M Checkpoint
- E2F Targets

F

HiFi – Low (n=26)

HiFi – High (n=26)

G

Stage II Discovery

Stage II/III Validation

Supplementary Figure 6

A

Discovery

Validation

B

C

Co-culture

MSC + MD

Treat

Add DO-Ova

Analyse

Corry SM

D

HPS vs dsRNA UP in Discovery HiFi patients

HPS vs dsRNA UP in Validation HiFi patients

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Supplementary Figure 7

A

Saline Poly(I:C) 0 20 40 60 Tumour Burden (%)✱✱

Saline Poly(I:C) 0 20 40 60 80 Tumour Burden (%)✱✱

B

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Supplementary Figure 8

Colorectal cancer cohort

Histological data
- H&E slide image
  - QuPath
    - Identifying stroma-rich tumours
  - Stromal classifier
  - Highest correlation
    - Fibroblast score
      - Translational fibroblast gene list defined (n=66)
      - Enables identification of stroma-rich tumours when H&E images are not available

Transcriptional data
- RNA-seq data
  - Pre-defined transcriptional markers
    - Identifying stroma-rich tumours
  - MCP Fibroblast Genes
  - ACTA2
  - FAP

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Corry SM et al. Gut 2022; Gutfil:16. doi: 10.1136/gutjnl-2021-326183
## Supplementary Table 1

### Custom fibroblast gene set

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Supplementary Table 2

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<th>LoFi (n = 140) (%)</th>
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HiFi patients were defined as those with ssGSEA fibroblast scores greater than the cutoff for the cohort which was generated using the findcut function.
### Supplementary Table 3

Clinical information for validation data

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HiFi patients were defined as those within the top 20% of the ssGSEA fibroblast scores for the cohort, with the other 80% considered LoFi.
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