

**Supplementary Table 1. Small Intestinal Organoid Mass Cytometry Antibody Panel**

Isotope-Metal	Antigen / Target	Antibody Clone	Supplier
89-Y	Phospho-Histone H3 [S28]	HTA28	BioLegend
113-In	CD326 (EpCAM)	G8.8	BioLegend
115-In	Pan-Cytokeratin (Pan-CK)	AE1/AE3	BioLegend
124-Te	TOBis Barcode	-	Prof. Mark Nitz
126-Te	TOBis Barcode	-	Prof. Mark Nitz
127-I	IdU (S-phase)	-	Fluidigm
128-Te	TOBis Barcode	-	Prof. Mark Nitz
130-Te	TOBis Barcode	-	Prof. Mark Nitz
141-Pr	Phospho-PDPK1 [S241]	J66-653.44.22	BD Biosciences
142-Nd	Cleaved-Caspase 3 [D175]	D3E9	CST
143-Nd	C-MYC	D84C12	CST
144-Nd	Lysozyme	BGN/06/961	Abcam
145-Nd	FABP1	328605	R&D Systems
146-Nd	Phospho-MKK4/SEK1 [S257]	C36C11	CST
147-Sm	Phospho-BTK [Y551]	24a/BTK	BD Biosciences
148-Nd	Phospho-SRC [Y418]	SC1T2M3	Thermo
149-Sm	Phospho-4E-BP1 [T37/46]	236B4	CST
150-Nd	Phospho-RB [S807/811]	J112-906	BD Biosciences
151-Eu	Phospho-PKCα [T497]	K14-984	BD Biosciences
152-Sm	Phospho-AKT [T308]	J1-223.371	BD Biosciences
153-Eu	Phospho-CREB [S133]	87G3	CST
154-Sm	Phospho-SMAD1 [S463/465] Phospho-SMAD5 [S463/465] Phospho-SMAD9 [S465/467]	D5B10	CST
155-Gd	Phospho-AKT [S473]	D9E	CST
156-Gd	Phospho-NF-κB p65 [S529]	K10-895.12.50	BD Biosciences
157-Gd	Phospho-MKK3 [S189] / MKK6 [S207]	D8E9	CST
158-Gd	Phospho-p38 MAPK [T180/Y182]	D3F9	CST
159-Tb	Phospho-MAPKAPK2 [T334]	27B7	CST
160-Gd	Phospho-AMPKα [T172]	40H9	CST
161-Dy	Phospho-BAD [S112]	40A9	CST
162-Dy	LRIG1	Polyclonal	R&D Systems
163-Dy	Phospho-p90RSK [T359]	D1E9	CST
164-Dy	Phospho-p120-Catenin [T310]	22/p120 (pT310)	BD Biosciences
165-Ho	β-Catenin [Active]	D13A1	CST
166-Er	Phospho-GSK-3β [S9]	D85E12	CST
167-Er	Phospho-ERK1/2 [T202/Y204]	20A	BD Biosciences
168-Er	Phospho-SMAD2 [S465/467] Phospho-SMAD3 [S423/425]	D27F4	CST
169-Tm	GFP	5F12.4	Fluidigm
170-Er	Phospho-MEK1/2 [S221]	166F8	CST
171-Yb	CLCA1	EPR12254-88	Abcam
172-Yb	Phospho-S6 [S235/236]	D57.2.2E	CST
173-Yb	DCAMKL1	6F9	Sigma
174-Yb	Chr-A	C-12	Santa Cruz
175-Lu	CD44	IM7	BioLegend
176-Yb	Cyclin B1	GNS-11	BD Biosciences
191-Ir	DNA	-	Fluidigm
193-Ir	DNA	-	Fluidigm
194-Pt	Cisplatin (Dead Cells)	-	Fluidigm
196-Pt	TOBis Barcode	-	Fluidigm
198-Pt	TOBis Barcode	-	Fluidigm
209-Bi	Di-Methyl-Histone H3 [K4]	C64G9	CST

Extracellular  
Intracellular  
Non-Antibody Parameter

## Supplementary Table 2. Colorectal Cancer Tumour Microenvironment Mass Cytometry Antibody Panel

Isotope-Metal	Antigen / Target	Antibody Clone	Supplier
89-Y	Phospho-Histone H3 [S28]	HTA28	BioLegend
113-In	CD66a (CEACAM1)	CC1	Thermo
115-In	Pan-Cytokeratin (Pan-CK)	AE1/AE3	BioLegend
124-Te	TOBis Barcode	-	Prof. Mark Nitz
126-Te	TOBis Barcode	-	Prof. Mark Nitz
127-I	IdU (S-phase)	-	Fluidigm
128-Te	TOBis Barcode	-	Prof. Mark Nitz
130-Te	TOBis Barcode	-	Prof. Mark Nitz
141-Pr	Phospho-PDPK1 [S241]	J66-653.44.22	BD Biosciences
142-Nd	Cleaved-Caspase 3 [D175]	D3E9	CST
143-Nd	C-MYC	D84C12	CST
144-Nd	Phospho-MEK1/2 [S221]	166F8	CST
145-Nd	Na/K-ATPase	EP1845Y	Abcam
146-Nd	Phospho-MKK4/SEK1 [S257]	C36C11	CST
147-Sm	Phospho-BTK [Y551]	24a/BTK	BD Biosciences
148-Nd	Phospho-SRC [Y418]	SC1T2M3	BD Biosciences
149-Sm	Phospho-4E-BP1 [T37/46]	236B4	CST
150-Nd	Phospho-RB [S807/811]	J112-906	BD Biosciences
151-Eu	Phospho-PKCα [T497]	K14-984	BD Biosciences
152-Sm	Phospho-AKT [T308]	J1-223.371	BD Biosciences
153-Eu	Phospho-CREB [S133]	87G3	CST
154-Sm	Phospho-SMAD1 [S463/465] Phospho-SMAD5 [S463/465] Phospho-SMAD9 [S465/467]	D5B10	CST
155-Gd	Phospho-AKT [S473]	D9E	CST
156-Gd	Phospho-NF-κB p65 [S529]	K10-895.12.50	BD Biosciences
157-Gd	Phospho-MKK3 [S189] / MKK6 [S207]	D8E9	CST
158-Gd	Phospho-p38 MAPK [T180/Y182]	D3F9	CST
159-Tb	Phospho-MAPKAPK2 [T334]	27B7	CST
160-Gd	Phospho-AMPKα [T172]	40H9	CST
161-Dy	Phospho-BAD [S112]	40A9	CST
162-Dy	LRIG1	Polyclonal	R&D Systems
163-Dy	Phospho-p90RSK [T359]	D1E9	CST
164-Dy	Phospho- p120-Catenin [T310]	22/p120 (pT310)	BD Biosciences
165-Ho	β-Catenin [Active]	D13A1	CST
166-Er	Phospho-GSK-3β [S9]	D85E12	CST
167-Er	Phospho-ERK1/2 [T202/Y204]	20A	BD Biosciences
168-Er	Phospho-SMAD2 [S465/467] Phospho-SMAD3 [S423/425]	D27F4	CST
169-Tm	Phospho-STAT3 [Y705]	4/P-STAT3	BD Biosciences
170-Er	Arginase-1	D4E3MTM	CST
171-Yb	F4/80	BM8	BioLegend
172-Yb	Phospho-S6 [S235/236]	D57.2.2E	CST
173-Yb	Podoplanin (PDPN)	8.1.1	BioLegend
174-Yb	RFP	8E5.G7	Rockland
175-Lu	CD44	IM7	BioLegend
176-Yb	Cyclin B1	GNS-11	BD Biosciences
191-Ir	DNA	-	Fluidigm
193-Ir	DNA	-	Fluidigm
194-Pt	Cisplatin (Dead Cells)	-	Fluidigm
196-Pt	TOBis Barcode	-	Fluidigm
198-Pt	TOBis Barcode	-	Fluidigm
209-Bi	CD68	FA-11	BioLegend

Extracellular  
Intracellular  
Non-Antibody Parameter

**Supplementary Table 3. TOBis Matrix for Organoid Time-Course**

	TeMal				Cisplatin	
	<sup>124</sup> Te	<sup>126</sup> Te	<sup>128</sup> Te	<sup>130</sup> Te	<sup>196</sup> Pt	<sup>198</sup> Pt
Day 1	+	-	+	-	-	+
Day 2	+	-	-	+	-	+
Day 3	+	-	-	-	+	+
Day 4	-	+	+	+	-	-
Day 5	-	+	-	-	+	+
Day 6	-	-	+	-	+	+
Day 7	-	-	-	+	+	+

**Supplementary Table 4. TOBis Matrix for CRC TME Model**

Genotype	Microenvironment	TeMal				Cisplatin	
		<sup>124</sup> Te	<sup>126</sup> Te	<sup>128</sup> Te	<sup>130</sup> Te	<sup>196</sup> Pt	<sup>198</sup> Pt
WT	Organoid	+	-	-	-	+	+
	Organoid / Macrophage	+	+	-	-	-	+
	Organoid / Fibroblast	-	-	+	+	+	-
	Organoid / Fibroblast / Macrophage	+	-	+	+	-	-
A	Organoid	+	-	+	-	+	-
	Organoid / Macrophage	+	-	-	+	+	-
	Organoid / Fibroblast	+	-	+	-	-	+
	Organoid / Fibroblast / Macrophage	+	-	-	+	-	+
AK	Organoid	+	+	+	-	-	-
	Organoid / Macrophage	-	+	+	-	+	-
	Organoid / Fibroblast	-	+	+	+	-	-
	Organoid / Fibroblast / Macrophage	-	+	+	-	-	+
AKP	Organoid	-	+	-	+	+	-
	Organoid / Macrophage	-	+	-	-	+	+
	Organoid / Fibroblast	-	+	-	+	-	+
	Organoid / Fibroblast / Macrophage	+	+	-	-	+	-
	Macrophage	-	-	+	-	+	+
	Fibroblast	-	-	+	+	-	+
	Fibroblast / Macrophage	-	-	-	+	+	+