

Table S1: Primary Molecular Components included in SEGMEiT

Signal	Primary Function	Ref.
Wnt- β -catenin	Deactivates β -catenin destruction complex; maintain cells in undifferentiated state; direct migratory paths (via EphB receptor - Ephrin B ligand signaling); increase cellular proliferation.	[32-35][77]
Dkk1	Inhibits Wnt signaling by binding to and neutralizing Wnt receptors; balance Wnt self-stimulation to limit the size of the proliferative compartment of the crypt.	[79, 80]
Noggin	Binds to and neutralizes BMP molecules; protects the proliferative compartment from BMP signaling.	[32, 81]
BMP	Inhibits nuclear accumulation of β -catenin; up-regulated differentiation; limits crypt, villus growth.	[32, 38, 81, 82]
Hedgehog	Controls villus height through regulation of apoptosis; controls strength of GEC adhesion to villus; loss of Akt initiates signaling cascade leading to anoikis.	[43, 44, 83]
TGF- β -SMAD3	Increases apoptosis through up-regulation of SMAD3, an Akt inhibitor.	[84-86]
Akt	Controls villus height through regulation of apoptosis; controls strength of GEC adhesion to villus; loss of Akt initiates signaling cascade leading to anoikis.	[32, 79, 87-90]
PTEN/PI3K	Interrupts PI3K activity by converting PIP3 to PIP2; up-regulated by inflammation, down-regulates Hh (putative).	[32, 79, 87, 88]
NF κ B	Anti-inflammatory response which inhibits apoptosis and necrosis. NF κ B displays self-regulation through I κ B.	[58][57, 91, 92]
TNF- α	Induces apoptosis and necrosis (if combined with RIP1); secreted primarily by inflammatory cells; up-regulates NF κ B to prevent excess inflammation; inhibits proliferation through up-regulation of Dkk1.	[58-60, 93]
RIP	Induces cell death, but also up-regulates the expression of NF κ B; modulates TNF functionality from apoptosis to necrosis.	[94-97][51]

JAK/STAT3	Various IL's up-regulate JAK, which activates STAT3. STAT3 leads to apoptosis in all cell types represented in SEGMEnt.	[61, 62]
IFN- γ	Prevents apoptosis through up-regulation of PI3K activity.	[98]
ROS	Induces cell death through necrosis; primarily secreted by neutrophils to assist in phagocytosis of necrotic debris.	[57, 91]