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5-ASA - colorectal cancer - cell death : an intriguing threesome

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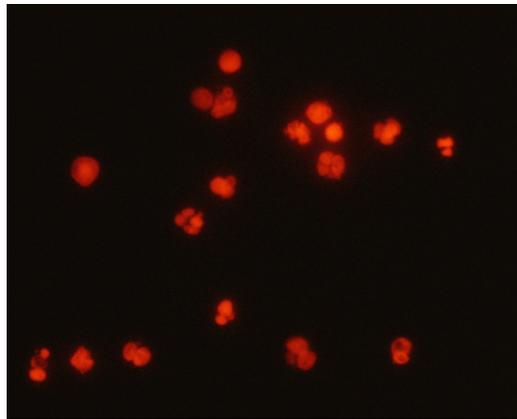
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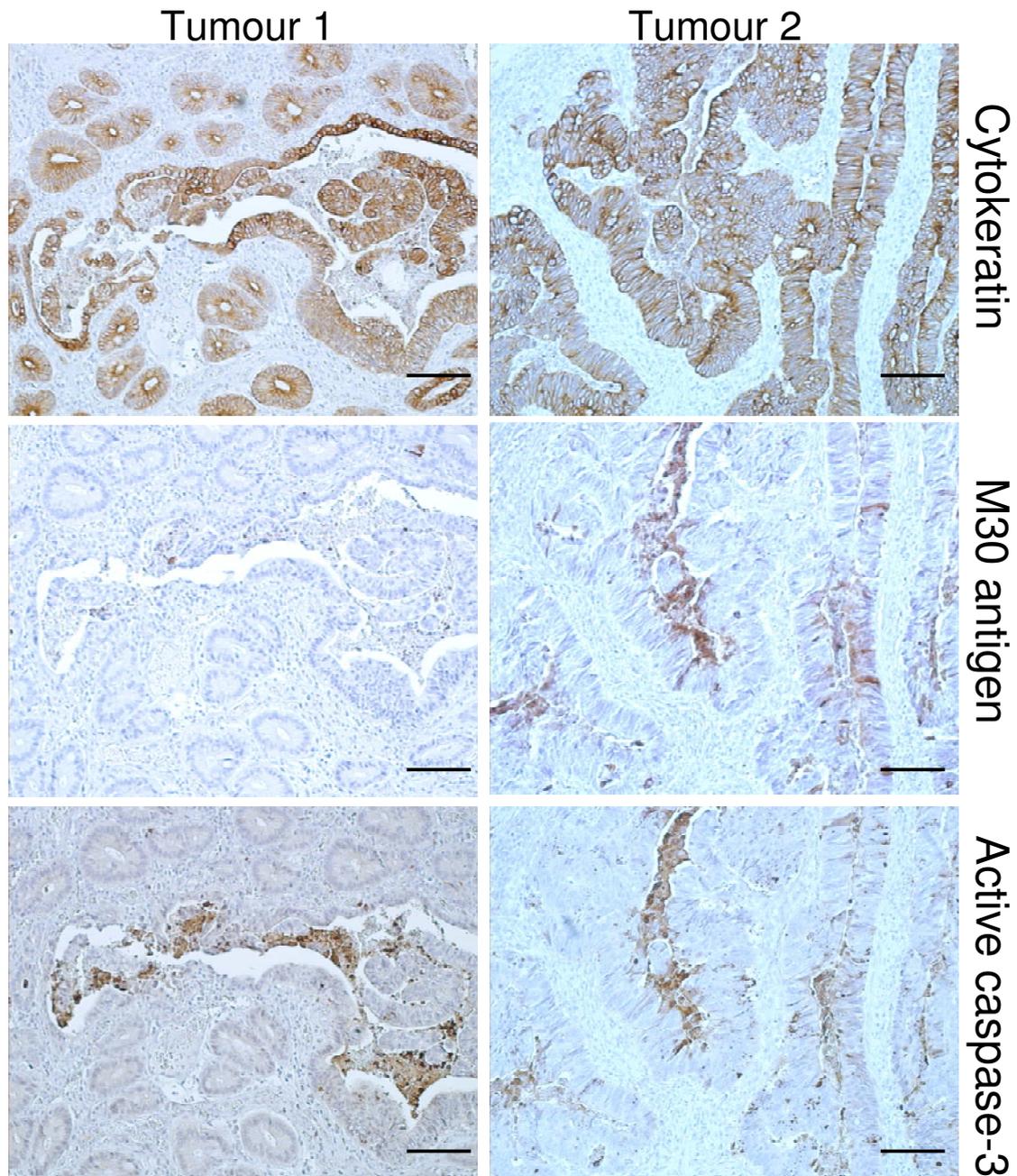
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Full-colour illustrations

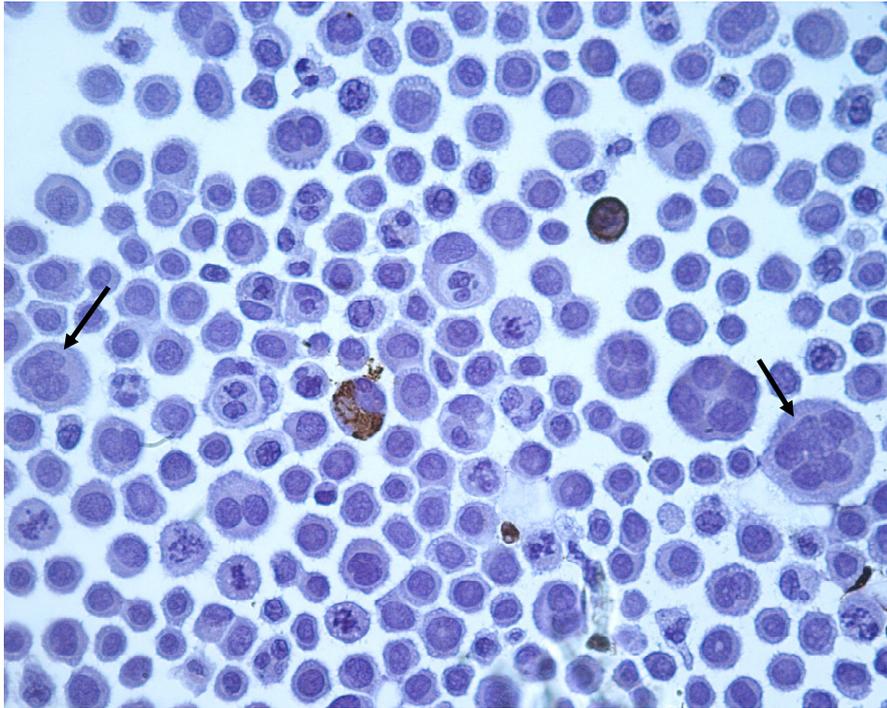


*4N Cytin B1 negative cells with mitotic catastrophe features
(Chapter 4, Figure 5C)*

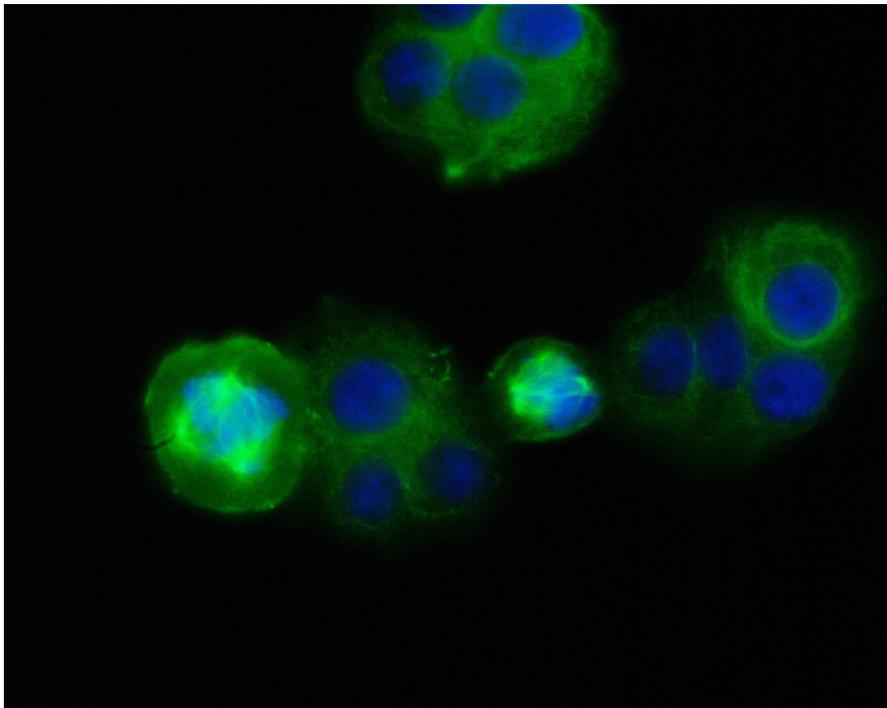


Chapter 2, Figure 2: Caspase-activity in CRC.

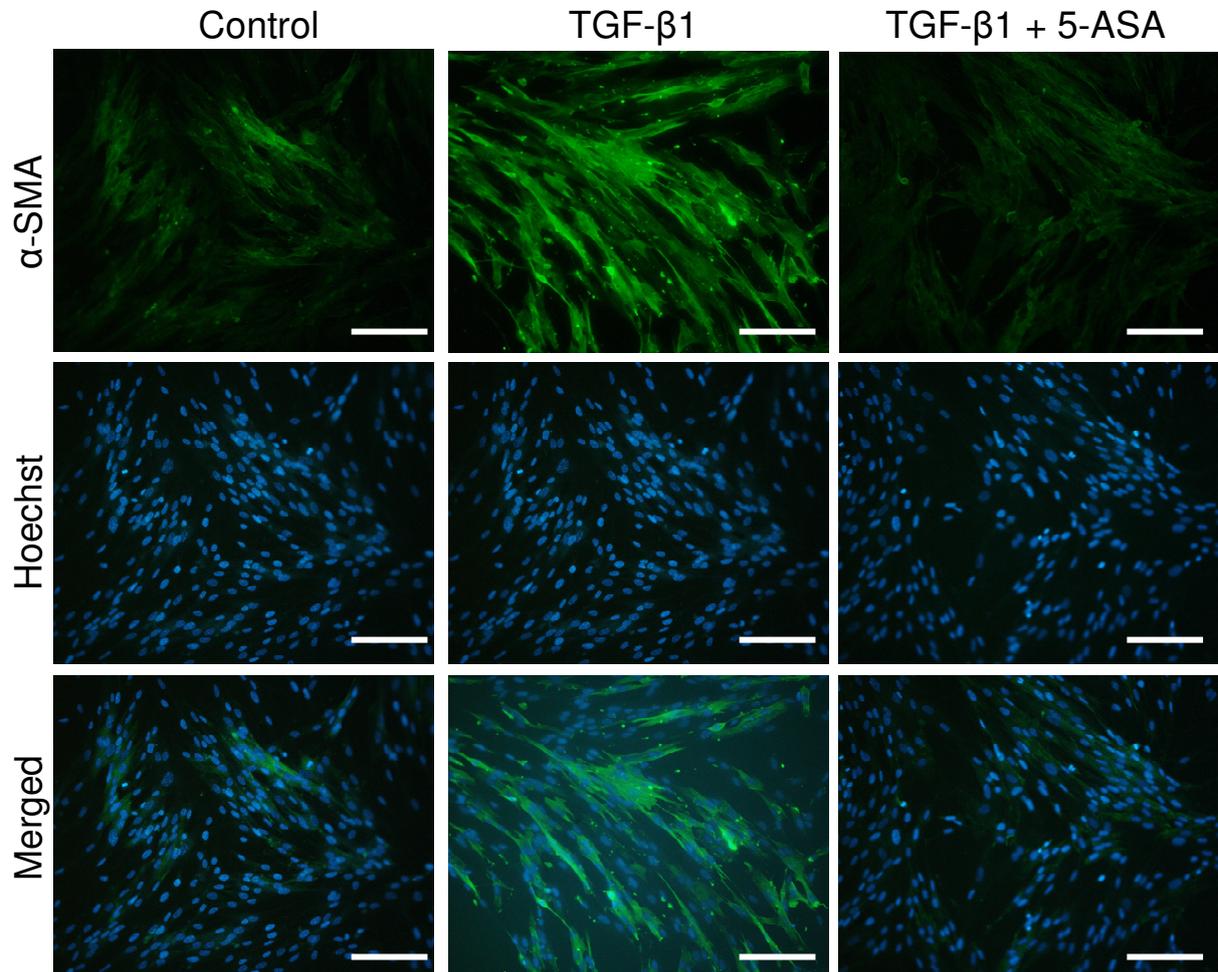
Photomicrographs of immunohistochemical stainings for active caspase-3, M30 and pan-cytokeratin showing tumors with stromal cells expressing active caspase-3 (as represented by Tumour 1, left), and tumors with mainly epithelial cells expressing active caspase-3, correlating with M30 staining (represented by Tumour 2, right). Scale bars: 100 μ m.



Chapter 4, Figure 3E: 5-ASA induces apoptosis and mitotic catastrophe.
*M30 positive (apoptotic, brown) and mitotic catastrophic (indicated by arrows)
5-ASA treated HT29 cells are shown (original magnification 100 x).*

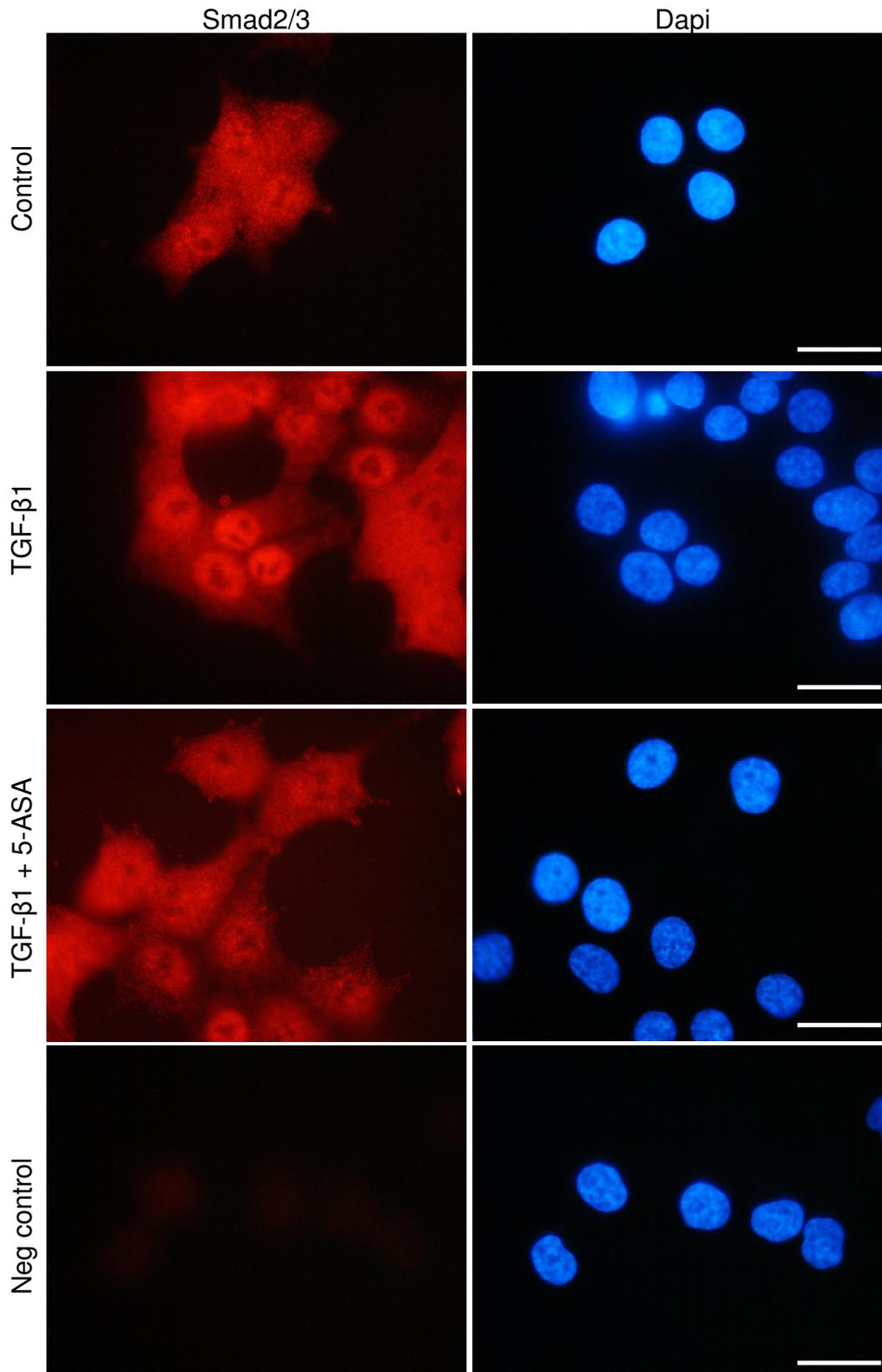


Chapter 4, Figure 5A: 5-ASA induces spindle abnormalities.
*5-ASA induces spindle abnormalities as shown by a merged image of
40 mM 5-ASA treated HT29 cells stained for α -tubulin (green) and DNA (blue).
Original magnification 1000 x.*



Chapter 6, Figure 3D: 5-ASA reduces TGF-β1 induced trans-differentiation of fibroblasts.

TGF-β1 (5 ng/ml) trans-differentiates normal colonic fibroblast into myofibroblasts as shown by increased α-SMA levels by immunofluorescence (original magnification 200 x, scale bars: 50 μm) which is reduced by 5-ASA treatment.



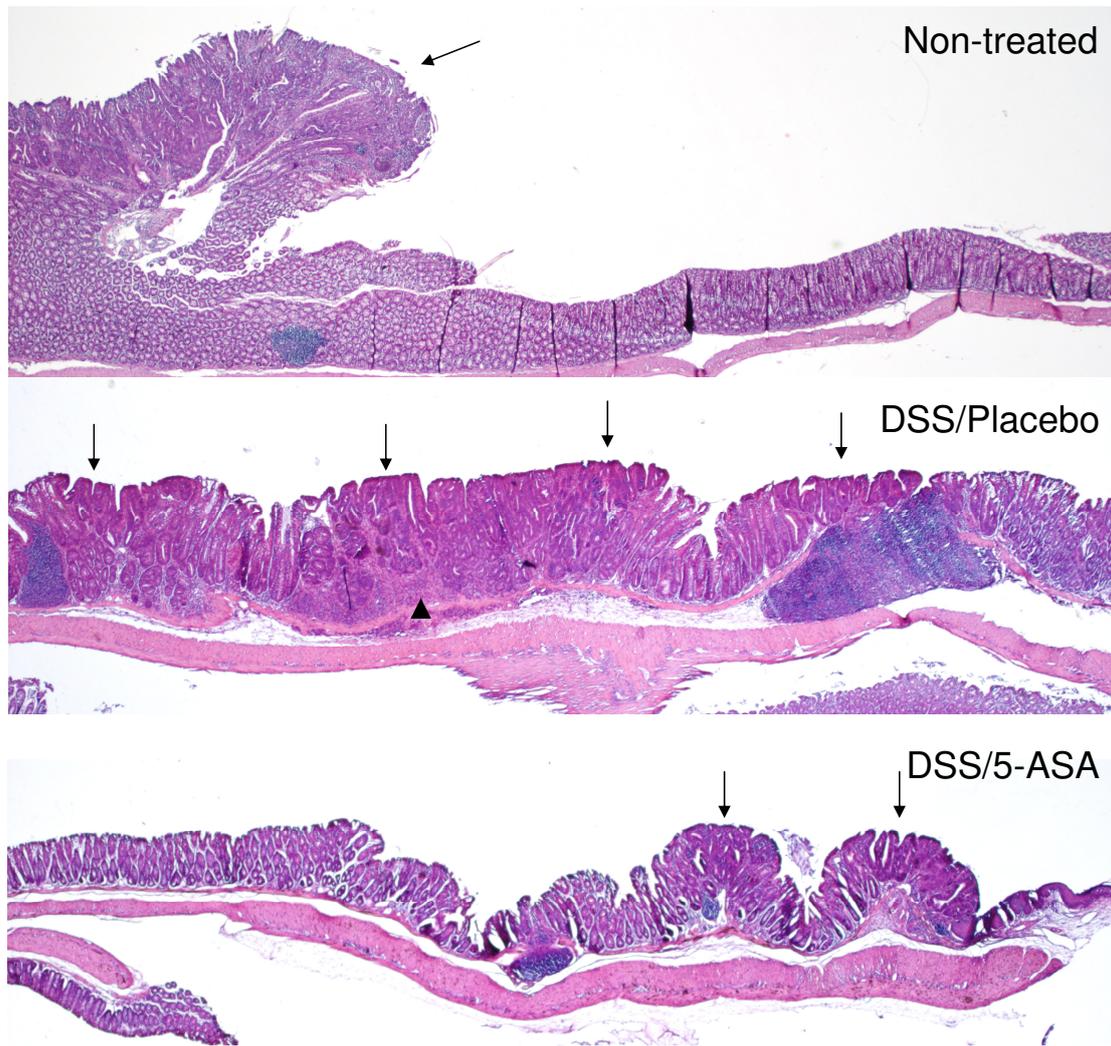
Chapter 6, Figure 5: 5-ASA blocks TGF-β1 induced Smad2/3 nuclear localization. TGF-β1 induces a translocation of Smad2/3 towards the nucleus after 60 minutes, which is blocked by 5-ASA, as judged by immunofluorescent detection of Smad2/3 (original magnification 1000 x, scale bars: 5 μm).



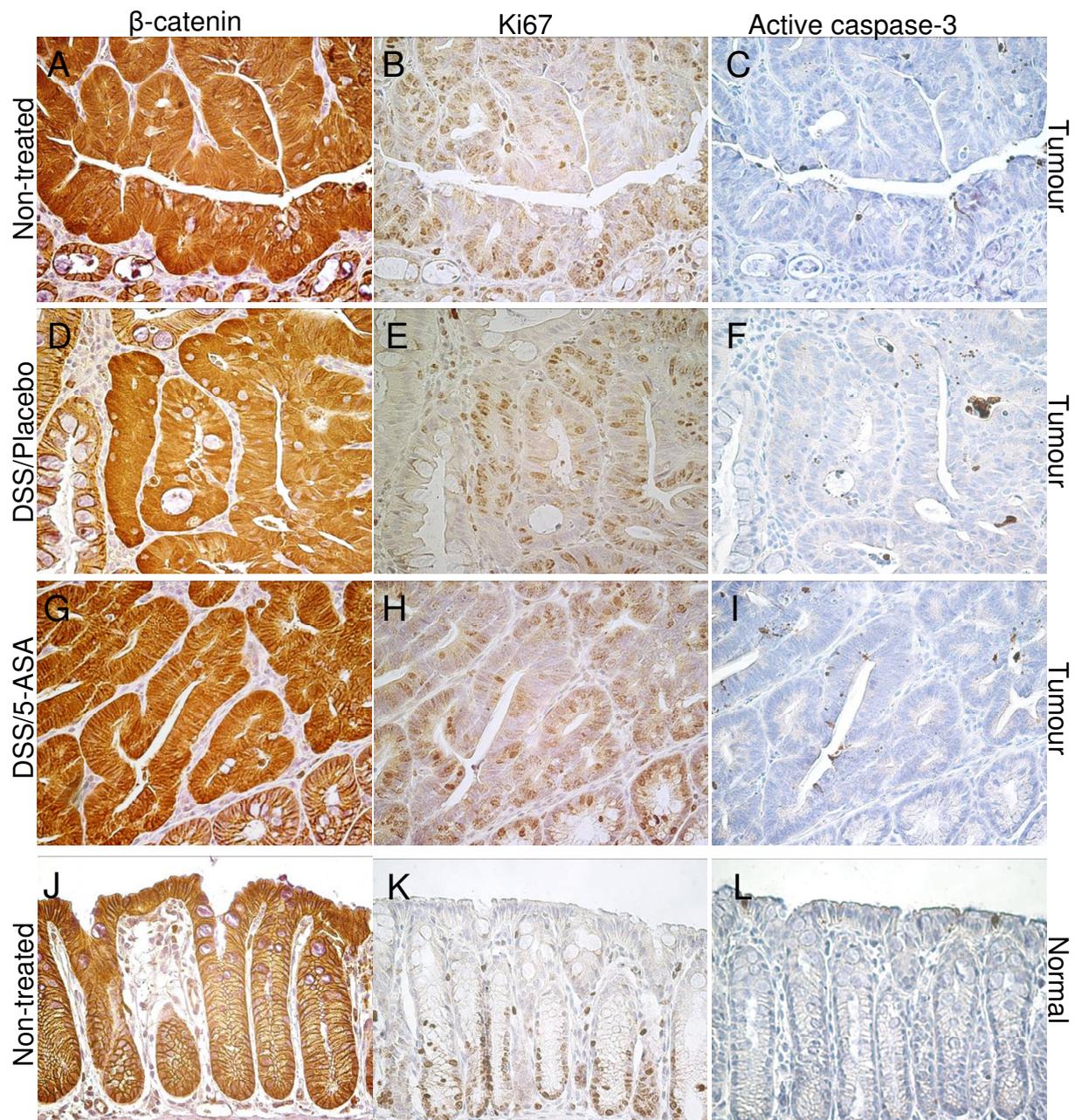
Non-treated DSS/Placebo DSS/5-ASA

Chapter 7, Figure 3A:

Photograph of longitudinally opened large intestines representative for non-treated, DSS/Placebo and DSS/5-ASA panels of Fabp1Cre;Apc^{15lox/+} mice.



Chapter 7, Figure 5: Histopathology of sporadic and IBD-associated tumours, treated with 5-ASA or otherwise. H&E stained sections of the distal large intestine of a non-treated, DSS/Placebo-treated, and DSS/5-ASA-treated *Fabp1Cre;Apc^{15lox/+}* mouse (original magnification 20 x). Neoplastic lesions (arrows) and infiltration of inflammatory cells (arrowhead) are indicated. The distal parts of the intestines are oriented at the right side of the picture.



Chapter 7, Figure 7: Effect of 5-ASA on β -catenin expression, proliferation and apoptosis.

*Immunohistochemical analysis of neoplastic lesions in the distal large intestine from non-treated (A-C), DSS/Placebo-treated (D-F), and DSS/5-ASA-treated (G-I) *Fabp1Cre;Apc^{15lox/+}* mice and normal crypts from non-treated mice (J,K,L) for β -catenin (A,D,G,J), for Ki67 to determine the extent of proliferation (B,E,H,K), and for active caspase-3 to determine the extent of apoptosis (C,F,G,L). Original magnification 400x.*