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Case B

Case C

White

Stroma

Cytoplasm

Nuclei

A

B

C

D

E
Figure S1. (A) The effect of color normalization on the mean nucleus, cytoplasm, stroma, and white space values in rotated hue-saturation-value (HSV) space is shown for two sample Hematoxylin and Eosin (H&E) images at 40x. Dark circles represent values measured from unnormalized images and arrows represent the transformation of these values following color normalization. (B)-(E) Images represented in (B) and (C) are shown in (D) and (E), respectively, after color normalization was applied.
Figure S2. Co-localization between histologic elements in the 40x Hematoxylin and Eosin (H&E) image in (A) was evaluated for every pairing of elements. As a control, the positions of pixels that did not belong to a particular histologic group were randomly shuffled as shown in (B). In this example, nuclei were the only histologic element in the image that were not shuffled. The inset shows a closer view in the region denoted by the box in (B). Co-localization was compared in the shuffled image (B) and the unshuffled image (A), and then subsequently for other histologic elements.
Figure S3. The normalized mutual information (NMI) was computed after randomly shuffling the positions of 3% and 8% of the pixels in two representative 40x Hematoxylin and Eosin (H&E) images. This manipulation resulted in an NMI of 0.66 when the measured histologic content in 40 x 40 pixel blocks was compared between the shuffled and unshuffled images ((B) vs. (A) and (E) vs. (D). The inset in (E) provides a closer view. In contrast, when the positions of 100% of the pixels were shuffled, the measured NMIs reached 0.38 (C) and 0.33 (F).