**Supplementary Methods Description**

*Second Harmonic Generation Imaging*

All samples in this study were imaged with a custom built integrated second harmonic generation (SHG)/bright field imaging system.1 A MIRA 900 Ti: Sapphire laser (Coherent, Santa Clara, CA) tuned to 780 nm, with a pulse length of approximately 100 fs, was directed through a Pockels cell (ConOptics, Danbury, CT, USA), half and quarter waveplates (ThorLabs, Newton, NJ, USA), beam expander (ThorLabs), a 3 mm galvanometer driven mirror pair (Cambridge, Bedford, MA), a scan/tube lens pair (ThorLabs), through a dichroic beam splitter (Semrock, Rochester, NY) and focused by a Nikon Plan Fluor 20x/0.75 N.A. objective lens (Nikon, Melville, NY). SHG light was collected in the forward direction with a 0.54 NA condenser (ThorLabs) and filtered with an interference filter centered at 390 nm with a full width at half maximum bandwidth of 22.4 nm (Semrock). The back aperture of the condenser lens was imaged onto the 5 mm aperture of a H7422-40P GaAsP photomultiplier tube (Hamamatsu, Hamamatsu, Japan) the signal from which was amplified with a C7319 integrating amplifier (Hamamatsu) and sampled with an analog to digital converter (Innovative Integration, Simi Valley, CA). Timing between the galvo scanners, signal acquisition, and motorized stage positioning was achieved using custom-designed acquisition software called WiscScan. Bright field images were captured with the same system using a MCWHL2 white LED lamp (ThorLabs) set up for Kohler illumination. White light from this lamp was separated from SHG light traveling through the condenser assembly using a short pass dichroic mirror with a cutoff at 670 nm (Semrock). An QICAM 12 bit color CCD camera (QImaging, Surrey, BC, Canada) was used to capture bright field images through WiscScan to allow for acquisition within a single application. The SHG and brightfield images were registered using custom MATLAB code.2 Both images were then used to perform a segmentation of the epithelium from the rest of the tissue. This segmentation was turned into a binary mask for boundary creation.

References

1. Bredfeldt JS, Liu Y, Conklin MW, Keely PJ, Mackie TR, Eliceiri KW. Automated quantification of aligned collagen for human breast carcinoma prognosis. *J Pathol Inform.* 2014;5(1):28.

2. Keikhosravi A, Li B, Liu Y, Eliceiri KW. Intensity-based registration of bright-field and second-harmonic generation images of histopathology tissue sections. *Biomed Opt Express.* 2020;11(1):160-173.