Spatial Statistics in Histology Images

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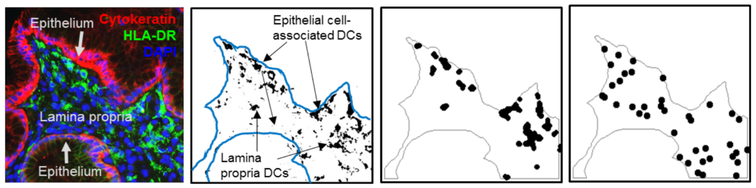
Introduction

Dendritic cells (DCs) are professional antigen-presenting cells that induce adaptive T cell responses, thereby bridging the innate and adaptive immune system. Our research is focused on the gastric immune response to *H. pylori* infection, specifically on how regulation of DCs in the gastric mucosa impacts disease outcomes.



Gastric DCs are distributed throughout the lamina propria (LP), with a subset of cells in contact with the gastric epithelium.

Hypothesis: gastric DCs are recruited to epithelial sites upon *H. pylori* infection for improved immunosurveillance and DCs establish specific interactions with gastric epithelial cells.

This Project: Create an image and simulation based statistical framework to assess randomness or specificity of DC cell distributions and interactions.

Image Processing

Formalin-fixed, paraffin-embedded sections of gastric biopsy tissue from healthy and *H. pylori*-infected adults was immunofluorescently labeled for HLA-DR (dendritic cells) and epithelial cells (cytokeratin):

- **Epithelial Cells**
- **Dendritic Cells**
- **Cell Nuclei**

Additionally, a region of interest (ROI) was provided which splits the epithelium information from the LP.

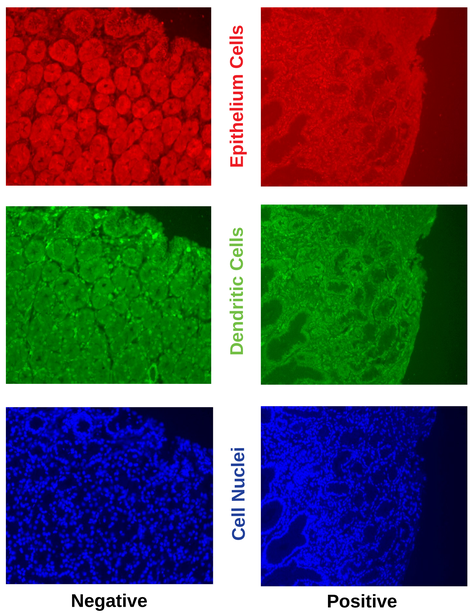
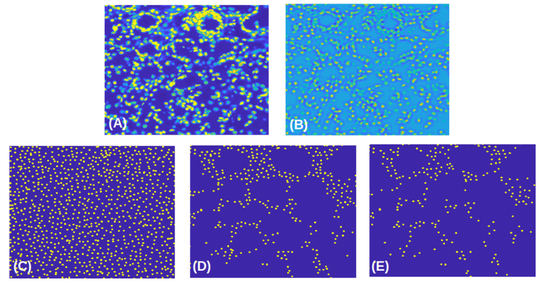


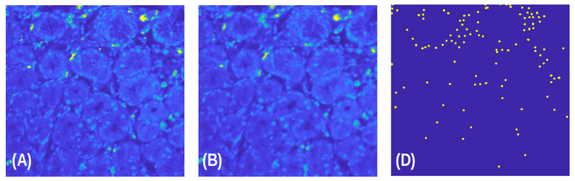
Image Processing Goal: Isolate gastric DCs found in the LP and represent those cells as points. Cell nuclei in the LP can be classified as dendritic nuclei if enough dendritic information is found nearby.

Finding Nuclei Centers



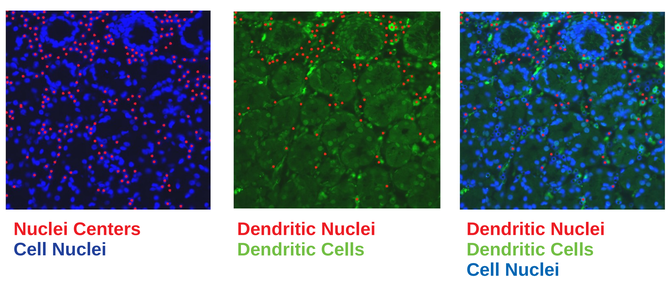
Ⓐ Begin with the cell nuclei channel
Ⓑ Convolve nuclei image with a Difference Of Gaussian filter
Ⓒ Use MATLAB's `imregionalmax` function to locate centers
Ⓓ Remove any information found outside the ROI
Ⓔ Remove any information generated from `imregionalmax` that does not correspond to the original nuclei information

Classifying Dendritic Nuclei



Ⓐ Begin with the DC channel
Ⓑ Convolve the image of dendritic cells with a single Gaussian filter
Ⓒ Calculate a tolerance value based on the median and standard deviation of the convolved dendritic image
Ⓓ Remove any nuclei centers where the dendritic information is less than the tolerance value

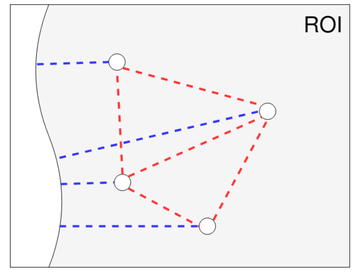
Image Processing Results



Along with the delineation of the epithelium (ROI), the locations of dendritic cell nuclei centers are now fed into a statistical pipeline to assess DCs distribution and impact of *H. pylori*-status.

Spatial Statistics Bootstrap Methodology

In order to determine if the positions of the DC nuclei are random or exhibit evidence of structure, a bootstrap approach is used and outlined below. Two statistics of interest are computed for DC nuclei: the distance to the boundary of the region of interest and the distance to the nearest DC nucleus neighbor.



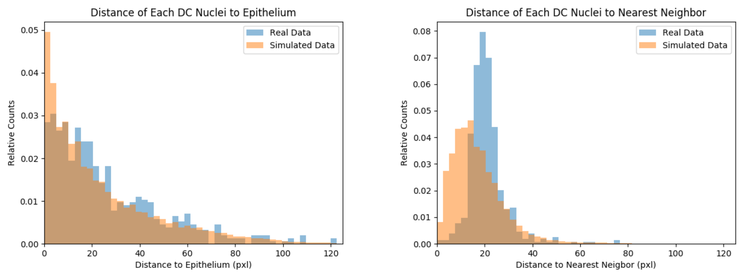
Bootstrap Procedure

1. Generate random DC locations using assumption of randomness
2. Compute statistic of interest to form a "Null distribution"
3. Compare observed statistic from actual image to Null distribution

Current Results

For each spatial statistic described, a resulting χ^2, p-value, and simulation distribution plot is generated (not shown). Statistical evidence was not found against the hypothesis of Complete Spatial Randomness in this image in terms of both the Nuclei-Edge distance and Minimum Inter-Nuclei distances:

DC nuclei may be distributed randomly and exhibit little structure in this sample.



The histograms show the respective distributions for both real and simulated data for each statistic of one sample.

Acknowledgments

This work supported by a **Montana INBRE** undergraduate research grant, the **Simons Foundation** (Collab. Grant for Mathematicians, D.Z.), and a pilot award from the NIH COBRE Center for Zoonotic and Emerging Infectious Diseases, P30-GM110732 (D.B. and D.Z.). The tissue microarray used for this study was kindly provided by Dr. P. Harris, Catholic University of Santiago, Chile.