Supporting Information

Estimation of Nucleated Cells in the Epithelia of Bladder and Esophagus

A. Bladder

To estimate the number of cells in the urothelium, we divided the surface area of the urothelium by the product of the surface area of the cells in each layer and the number of cells that make up the thickness in each layer. We extrapolated the surface area of the urothelium to be approximately 250 cm^2 from data obtained using a three-dimensional ultrasound on numerous subjects in a previous study.[1] The urothelium is made up of three cell layers - the basal cell layer, the intermediate cell layer, and the apical cell layer – that have different cellular morphologies.[2] Based on the histology of the bladder,[3] we assume these three layers are two cells, three cells, and one cell thick, respectively. We assume basal cells are cuboidal with equal sides and a diagonal of 7.5 µm. We assume the intermediate and apical cells contribute a circular geometry to the surface area with diameters of 20 and 85 µm, respectively, with the acknowledgement that apical cells change in size and morphology depending on the volume in the bladder. With these assumptions, we estimate the urothelium has approximately 2.9 billion nucleated cells.

B. Esophagus

Like the estimation of nucleated cells in the urothelium, we divided the surface area of the esophageal epithelium by surface area of the cells to reach our approximation. We determined the surface area of the epithelium by assuming it has the shape of a hollow cylinder with the diameter[4] of 2.4 cm and a length[5] of 28 cm. The epithelium is made up of the basal, spinous, and functional layers that are three, two, and five cells thick, respectively.[6] Histology images from Martincorena *et al.* enabled us to estimate the surface areas of the cells in each layer.[7] Assuming these cells are symmetrical in two dimensions, we measured surface areas of 7.5 μm^2, 11.9 μm^2, and 18.3 μm^2 for basal, spinous, and functional layers, respectively. We estimate that the esophageal epithelium has approximately 1.9 billion cells.

References

1. Chalana, V., Dudycha, S., Yuk, J.-T. & McMorrow, G. Automatic Measurement of Ultrasound-Estimated Bladder Weight (UEBW) from Three-Dimensional Ultrasound. *Rev. Urol.* **7 Suppl 6**, S22-8 (2005).

2. Lewis, S. A. Everything you wanted to know about the bladder epithelium but were afraid to ask. *Am. J. Physiol. Physiol.* **278**, F867–F874 (2000).

3. Bolla, S. R. & Jetti, R. *Histology, Bladder*. *StatPearls* (StatPearls Publishing, 2019).

4. Lee, J. *et al.* Esophageal Diameter Is Decreased in Some Patients With Eosinophilic Esophagitis and Might Increase With Topical Corticosteroid Therapy. *Clin. Gastroenterol. Hepatol.* **10**, 481–486 (2012).

5. Awad, Z. T. *et al.* Correlations between Esophageal Diseases and Manometric Length: A Study of 617 Patients. *J. Gastrointest. Surg.* **3**, 483–488 (1999).

6. Zhang, X. *et al.* The microscopic anatomy of the esophagus including the individual layers, specialized tissues, and unique components and their responses to injury. *Ann. N. Y. Acad. Sci.* **1434**, 304–318 (2018).

7. Martincorena, I. *et al.* Somatic mutant clones colonize the human esophagus with age. *Science* **362**, 911–917 (2018).