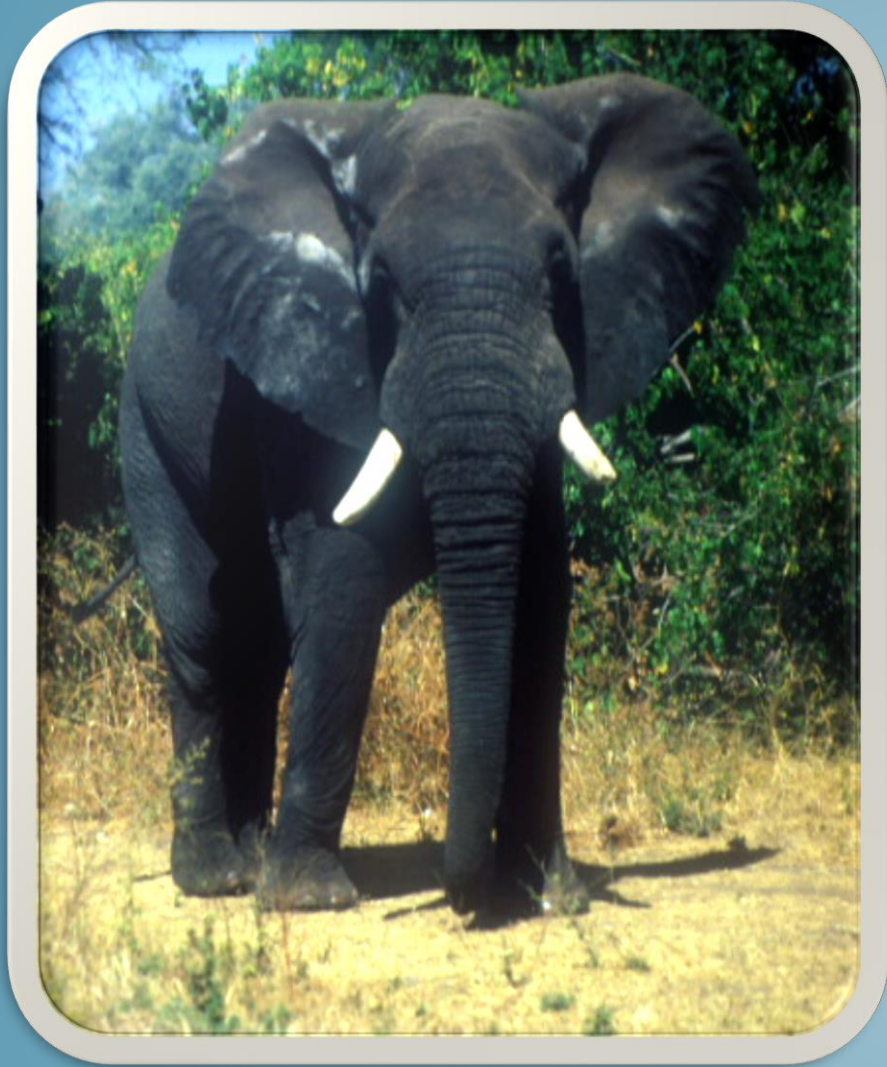




Pilot Study



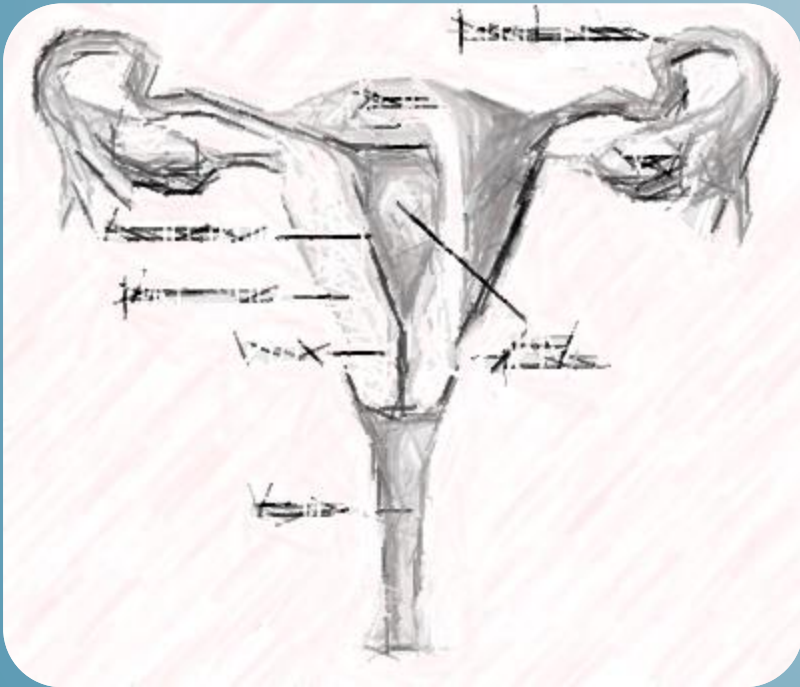
H Miniggio



EJ Raubenheimer

HPV Transformation of tonsillar keratinocytes: structural aspects

Literature extrapolated from cervix



Previous studies on Tonsillar HPV status

- Overwhelming in favour of HPV related neoplasia
- Limited information on the tonsillar microstructural determinants of HPV infection

Kang SYJ et al. Characterization of epithelial progenitors in normal human palatine tonsils and their HPV16 E6/E7-induced per tubation **Stem Cell Reports** 2015

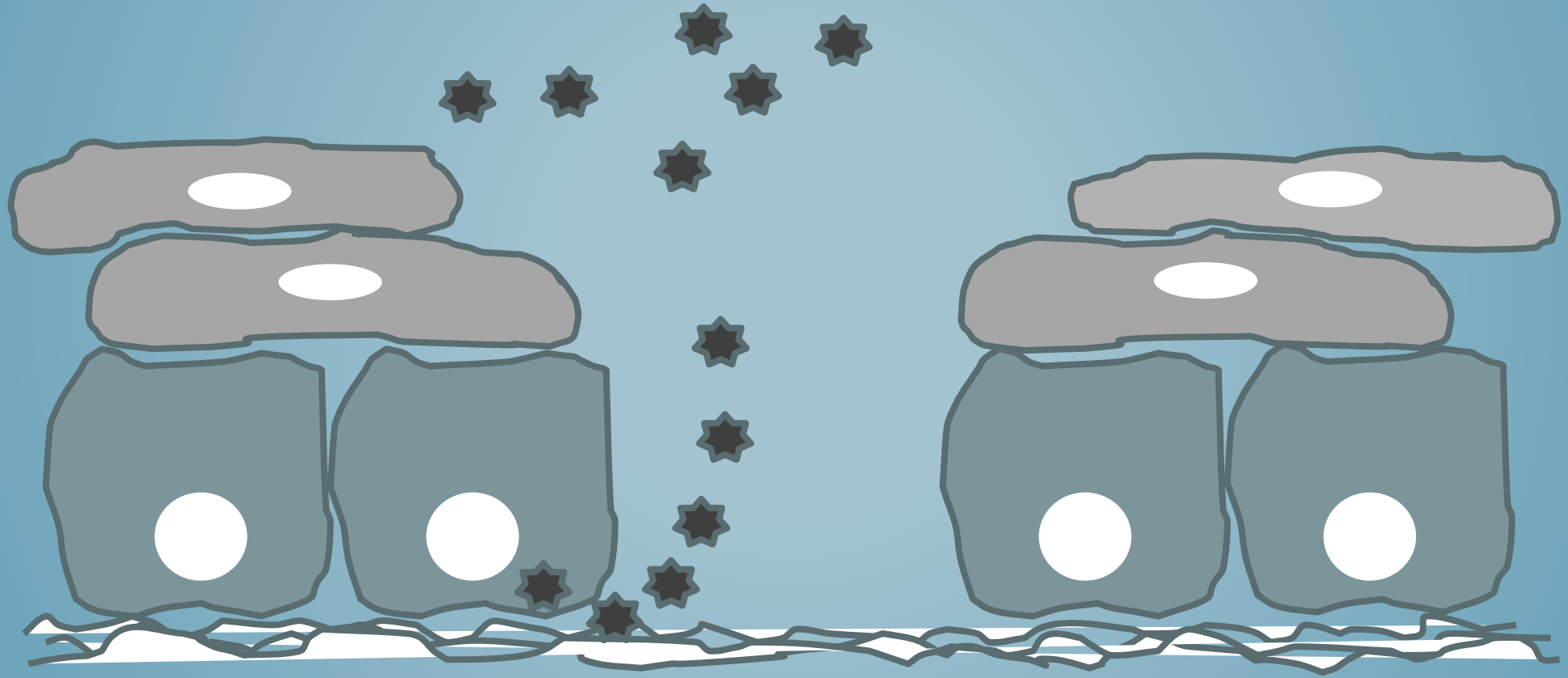
Egawa N et al. Review. Human papillomaviruses; Epithelial tropism, and the development of neoplasia **Virusses** 2015

Klingenberg B et al. p16 INK4A expression is frequently detected in tumor-free tonsil tissue without association with HPV. **Histopathology** 2010

Fakhry et al. Associations between oral HPV 16 infection and cytopathology: evaluation of an oropharyngeal “pap-test equivalent” in high risk populations. **Cancer Prev Res (Phila)** 2011

Hobbs et al. Tonsil T-cell immunity to human papillomavirus in the absence of detectable virus in healthy adults. **Laryngoscope** 2008

HPV gains epithelial entry through the basement membrane



HPV's propagate in specific epithelial niches

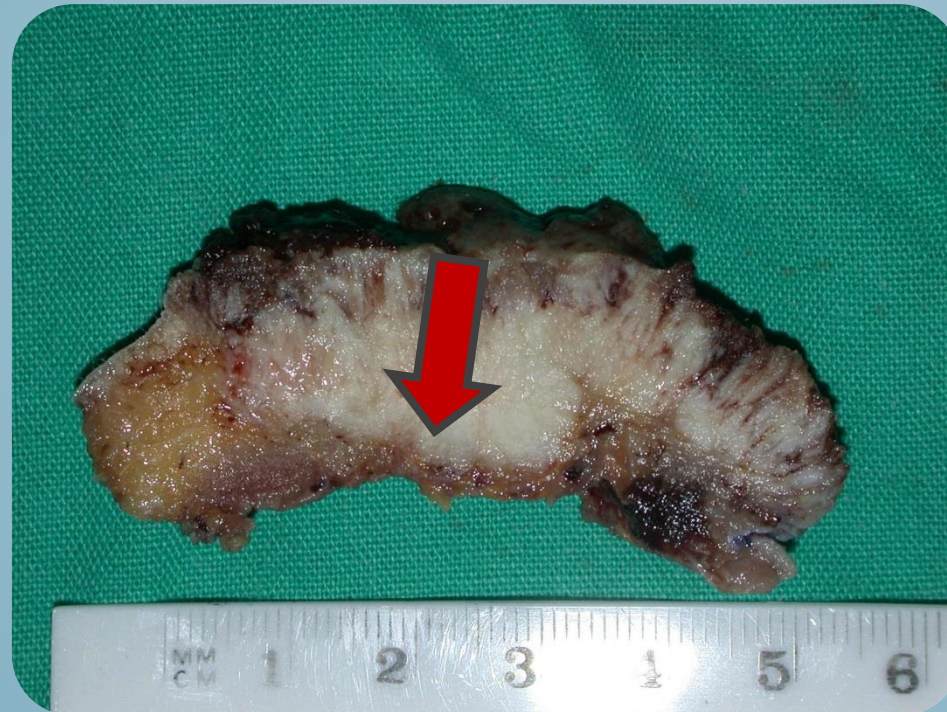
Viral genotype

Oral	-	HPV 11
Skin (butchers warts)	-	HPV 7
Palmoplantar warts	-	HPV 4& 65
Genital sites	-	HPV 6
Cervix & tonsillar epithelium	-	HPV 16

Nature of the epithelial cell and the environment

Status of host immunity

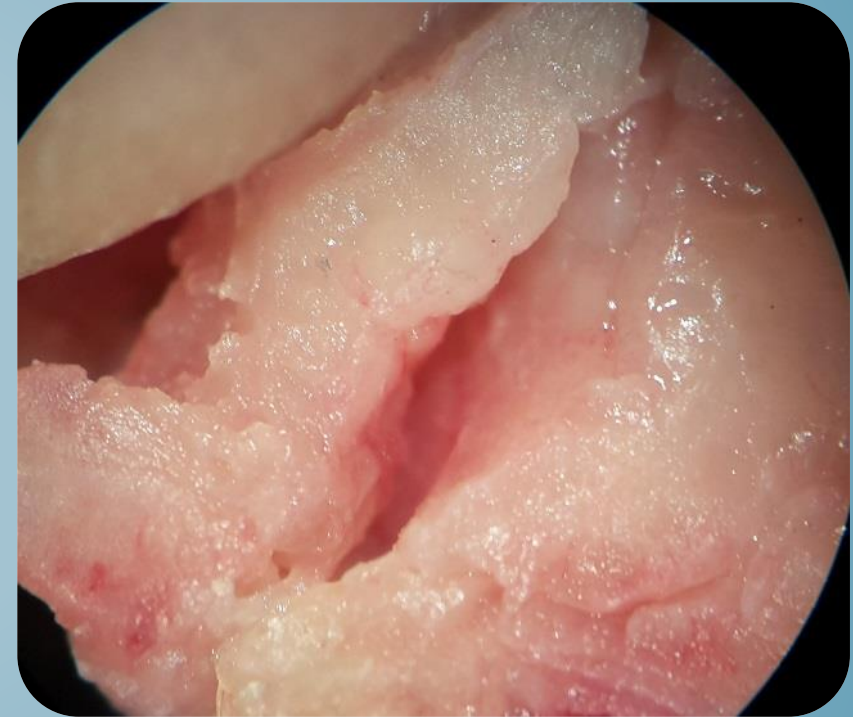
High risk HPV's drive cell cycle entry



Carcinogenic to humans - HPV 16, 31 & 35

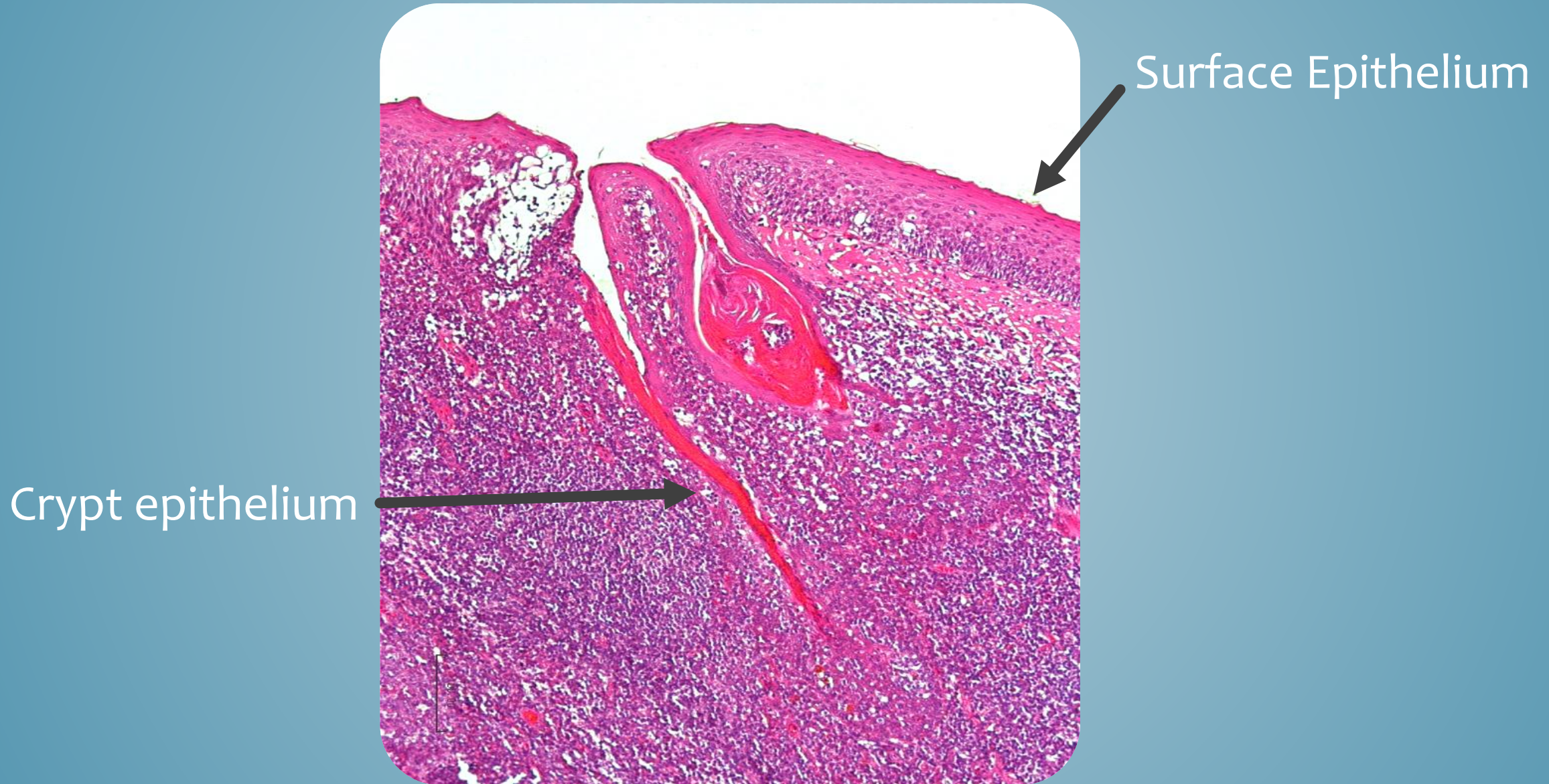
The Pharyngeal Tonsil

Specialized B-lymphoid structure

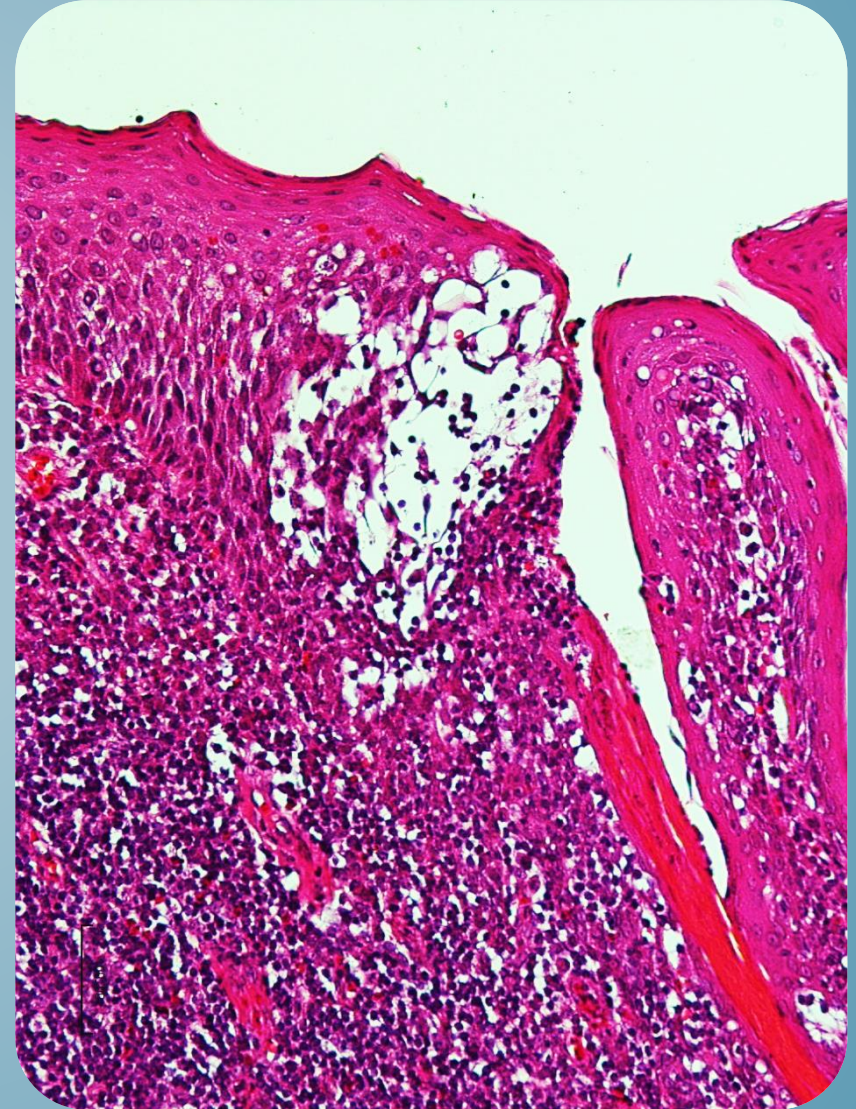
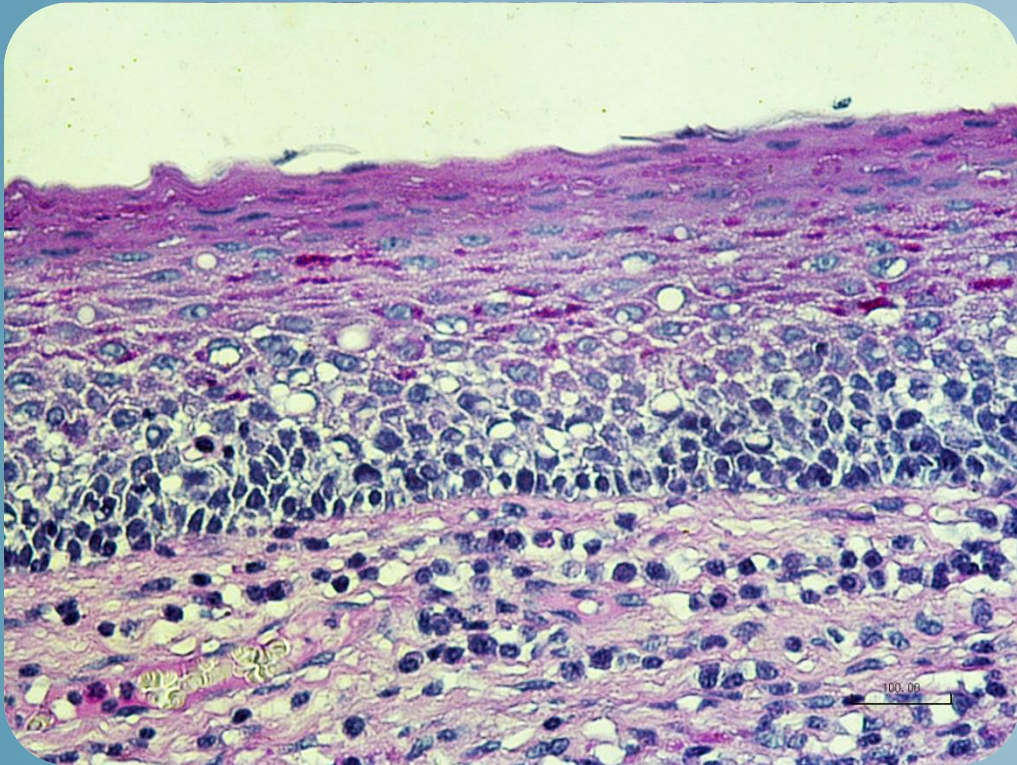


Surface area 300 sq cm

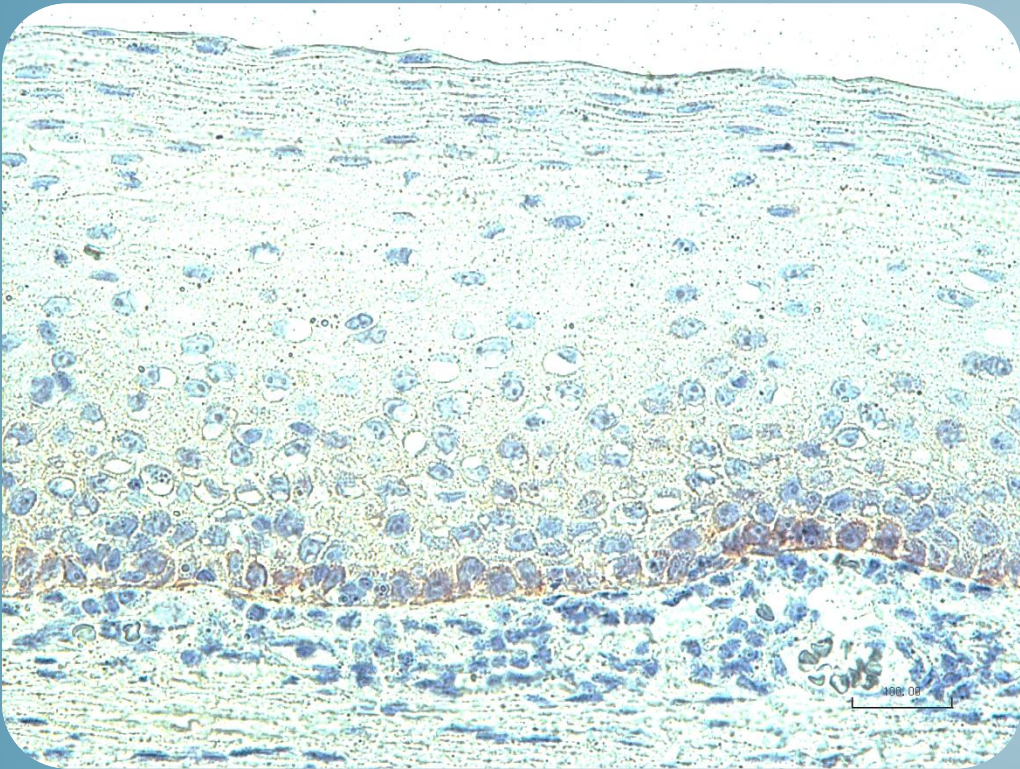
Two epithelial components



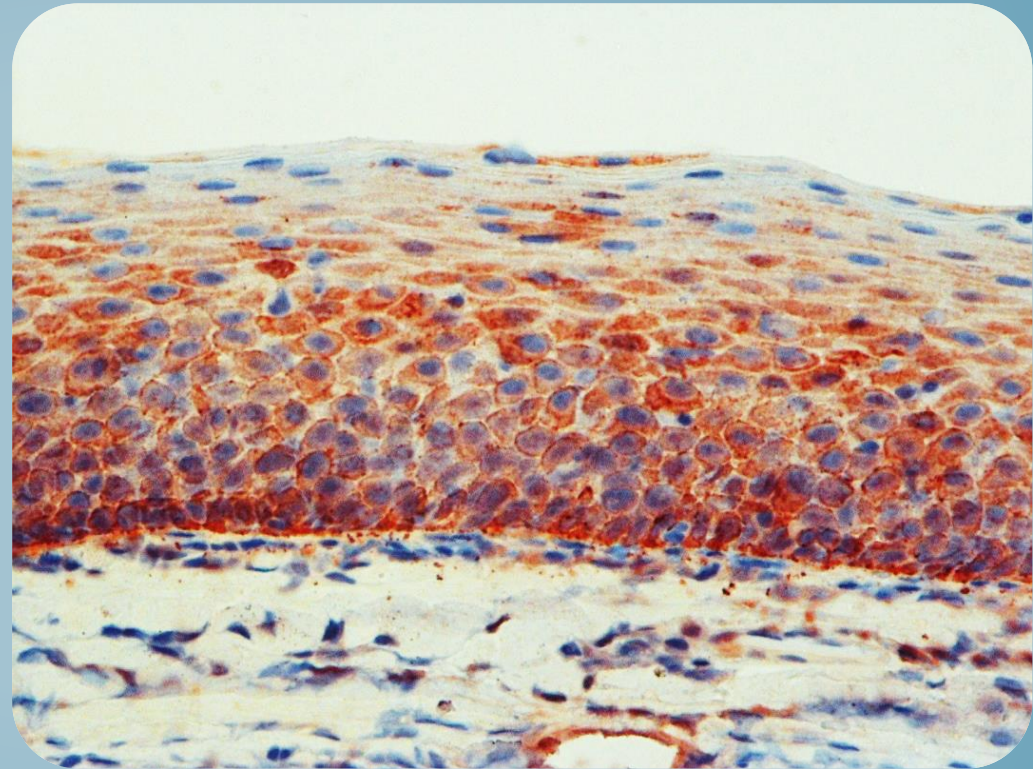
Surface Epithelium



Surface epithelium: Cytokeratins

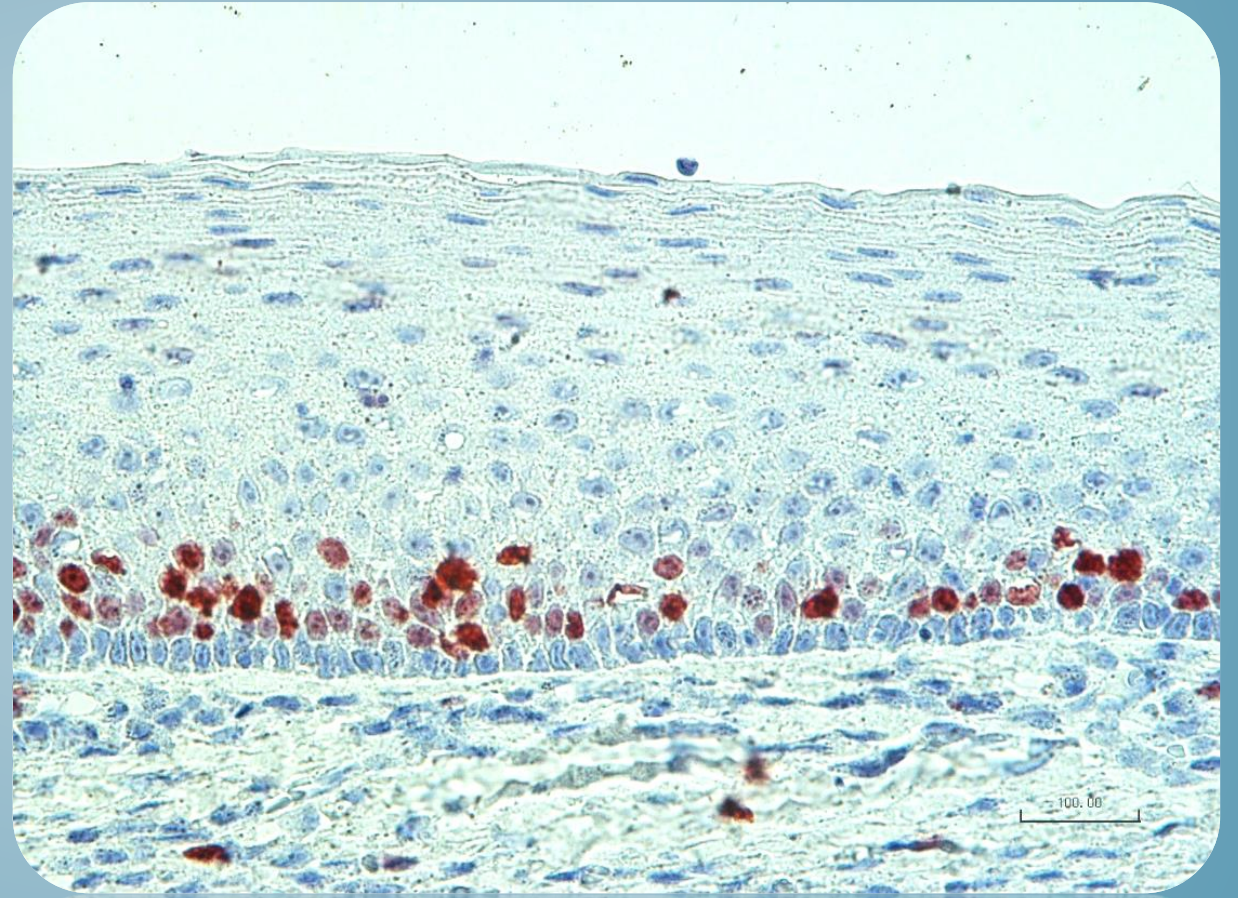
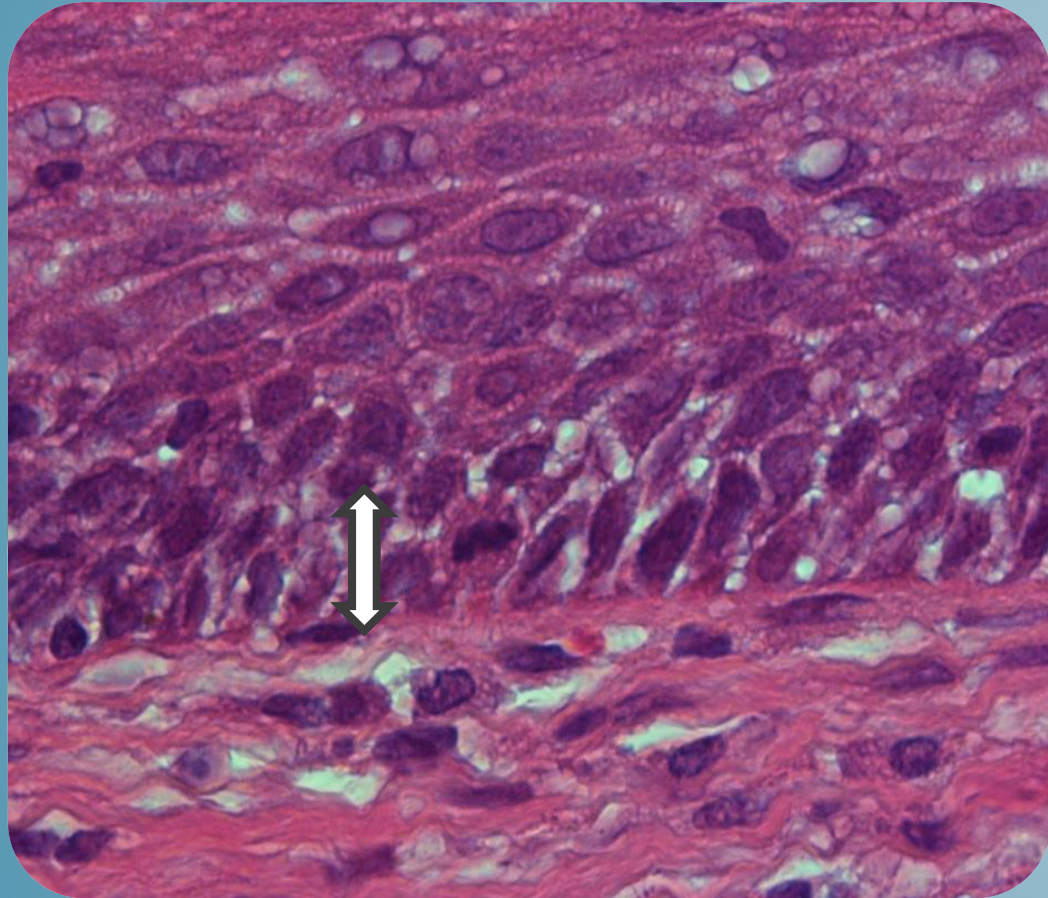


Pan CK



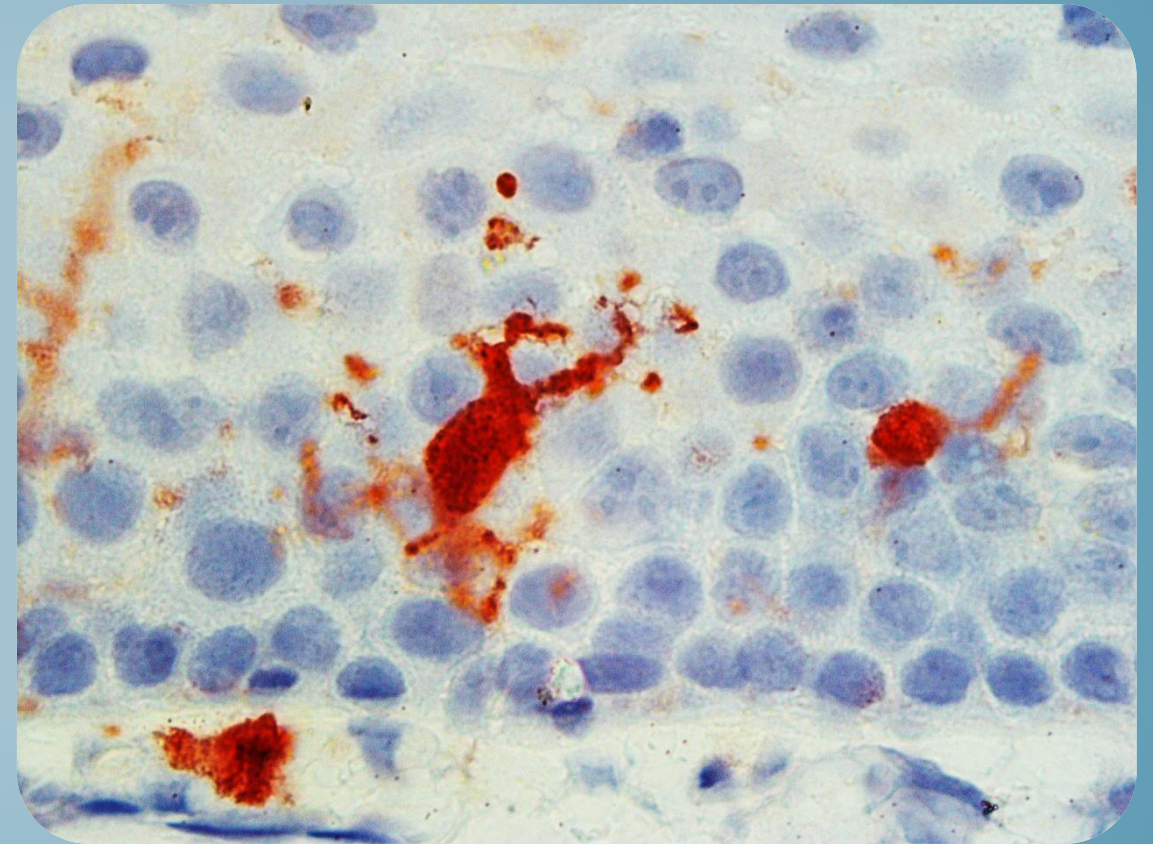
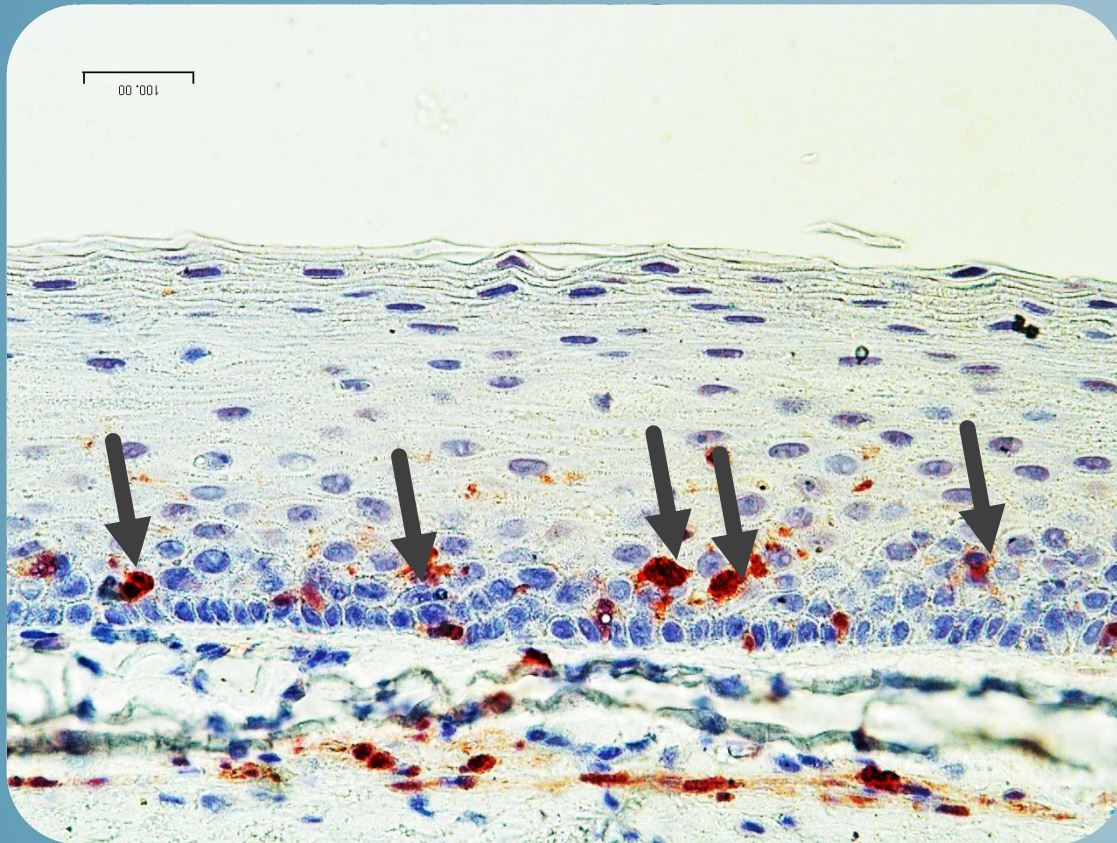
HMW CK

Surface epithelium: Mitotic activity



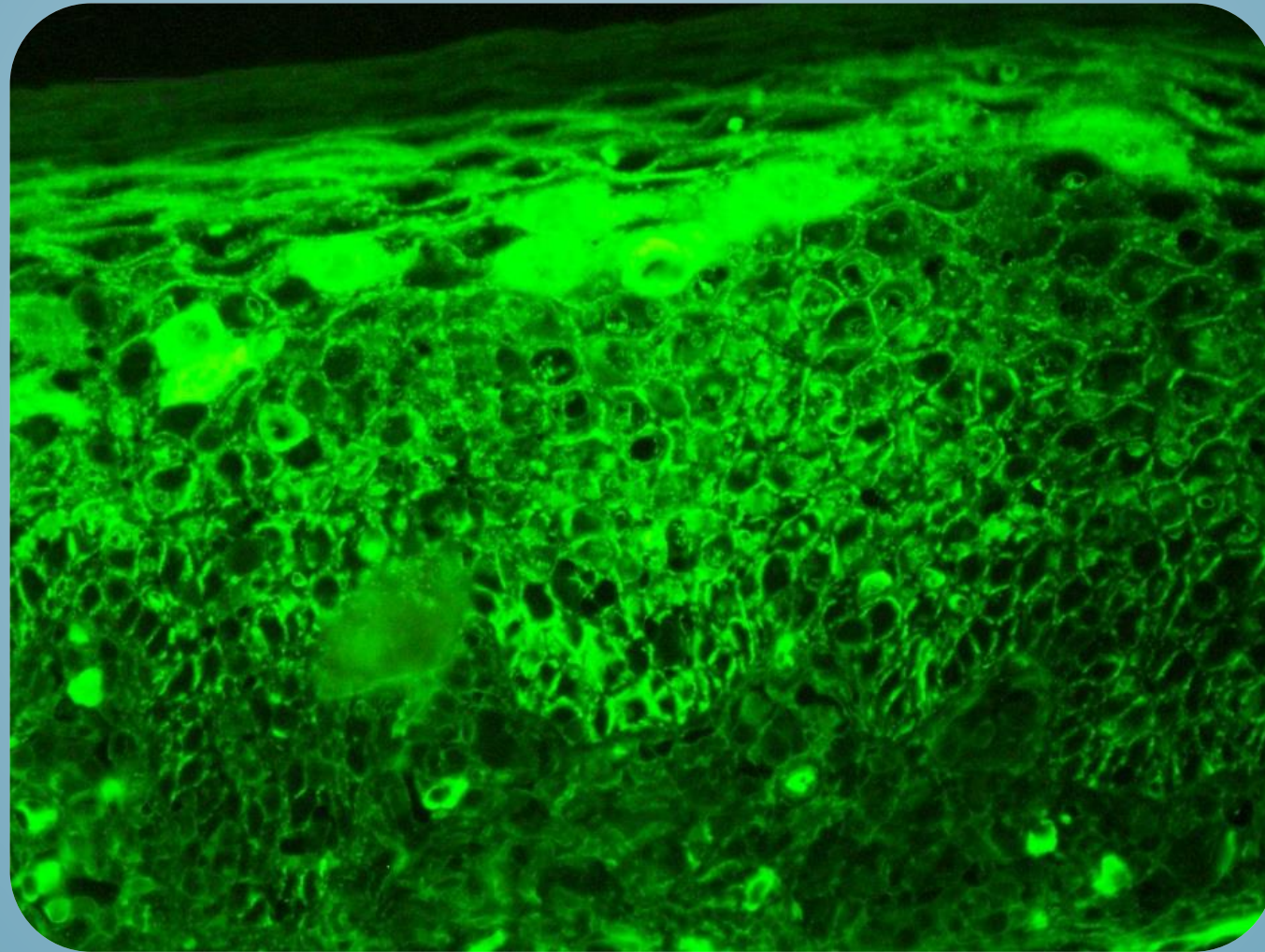
Ki 67

Langerhans cells



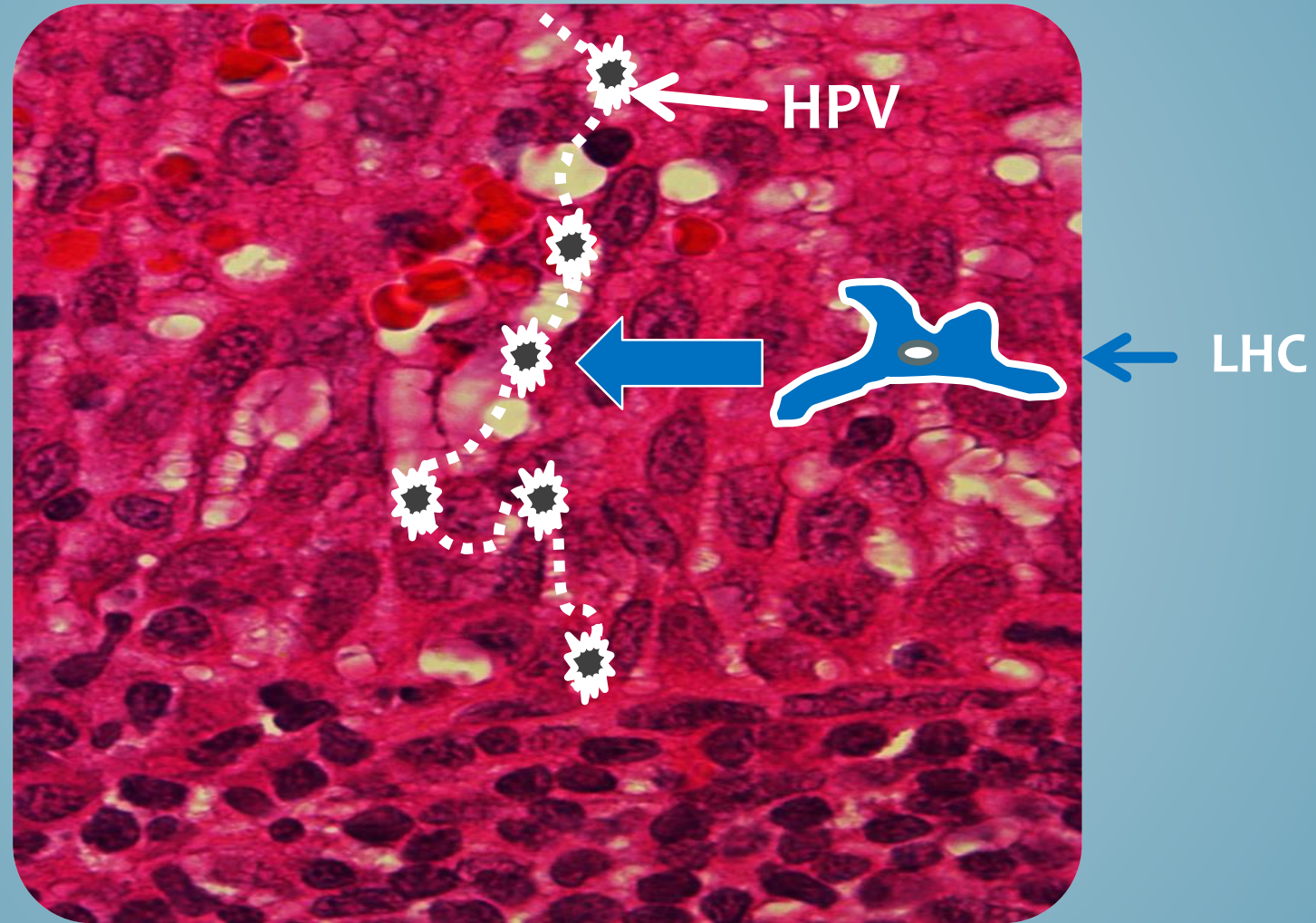
S100

Surface epithelium: Spongiosis

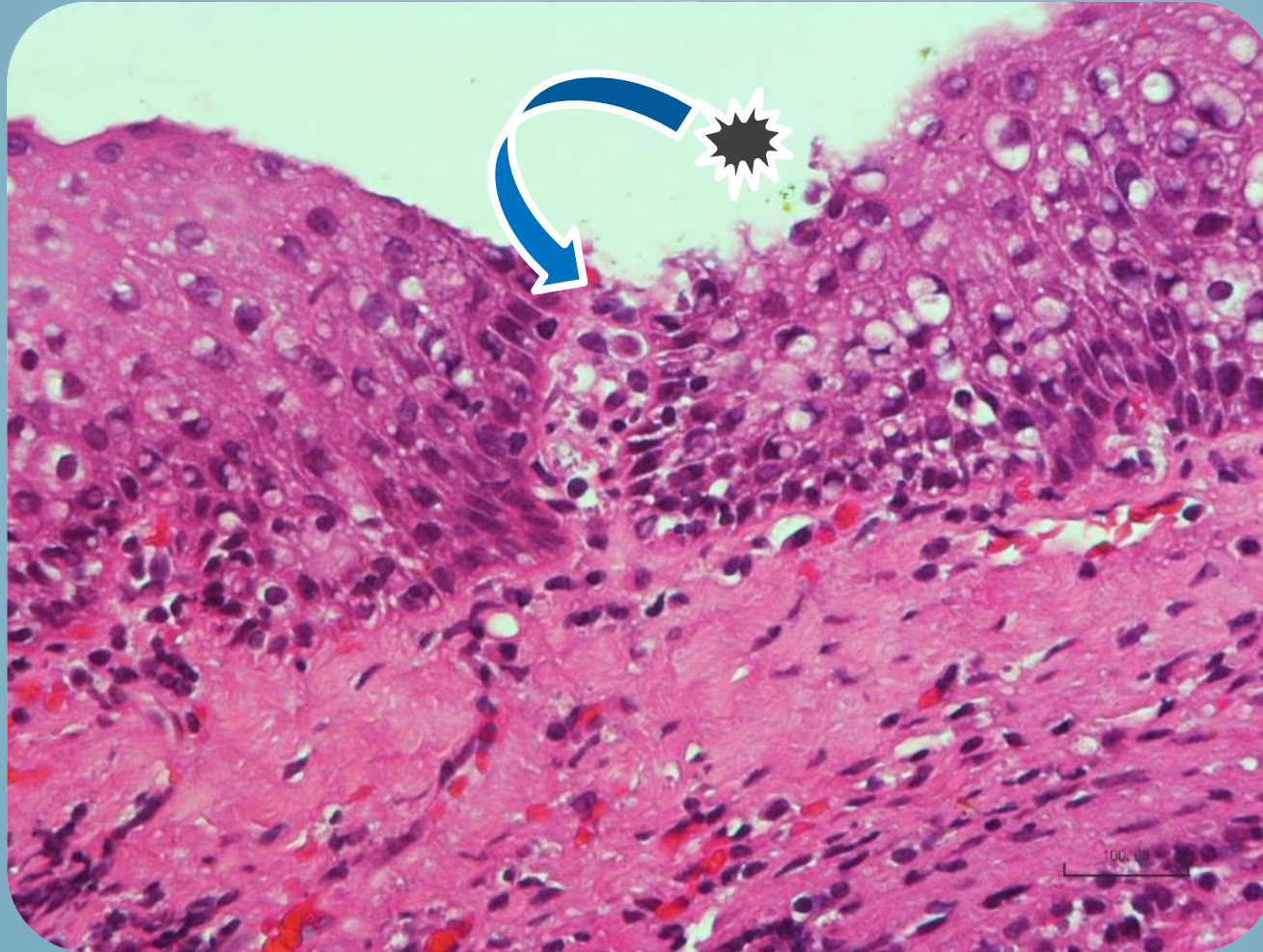


IF IgA

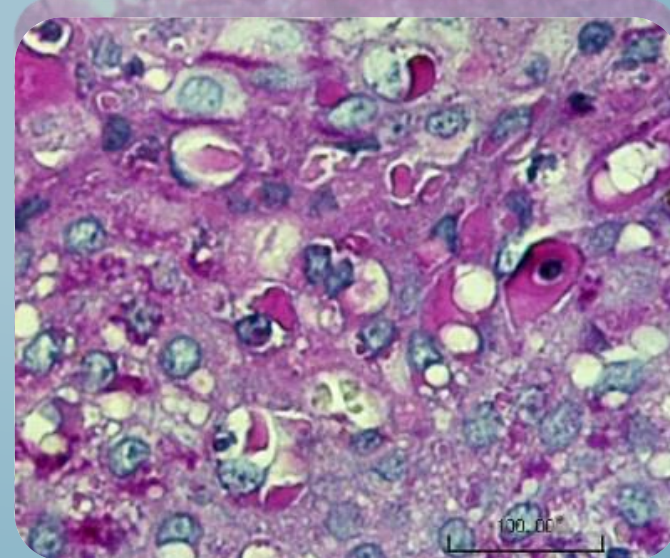
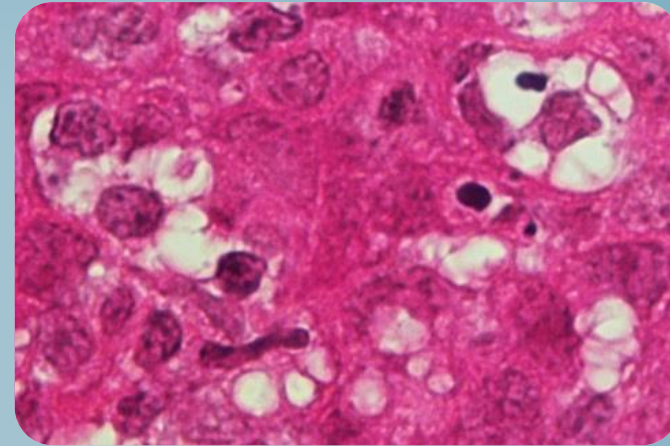
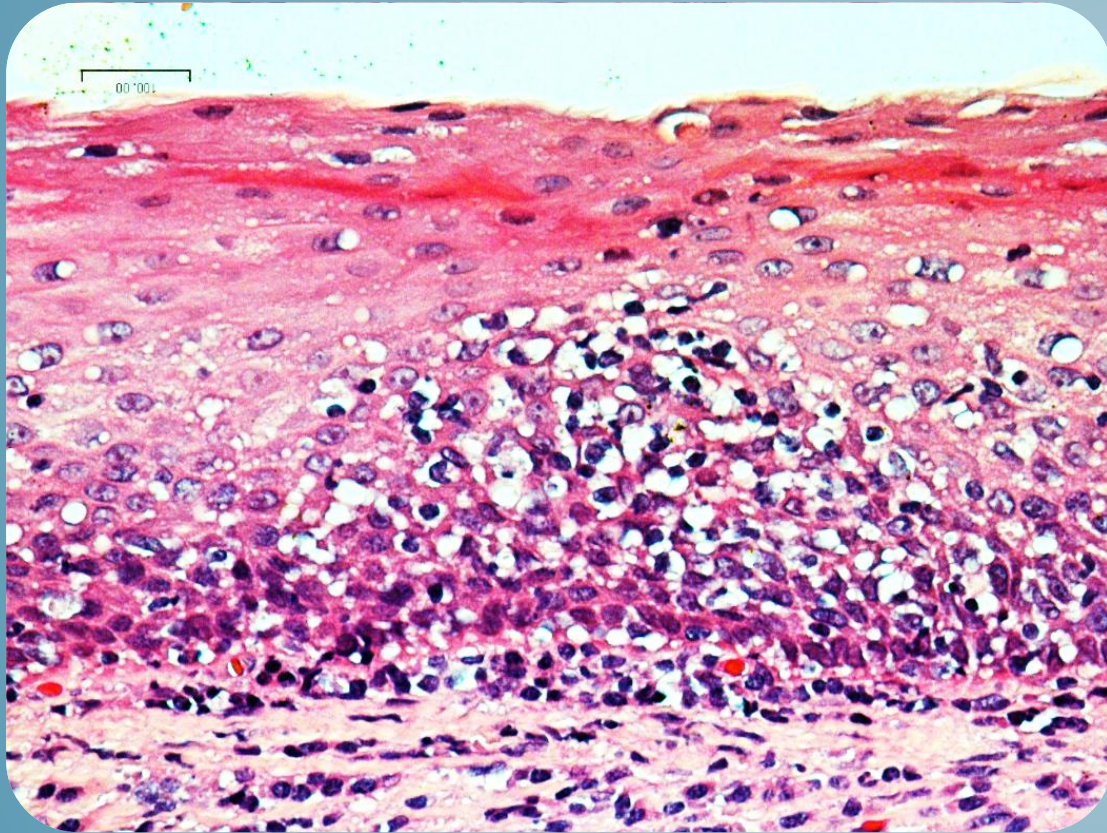
Possible site of entry: Spongiosis



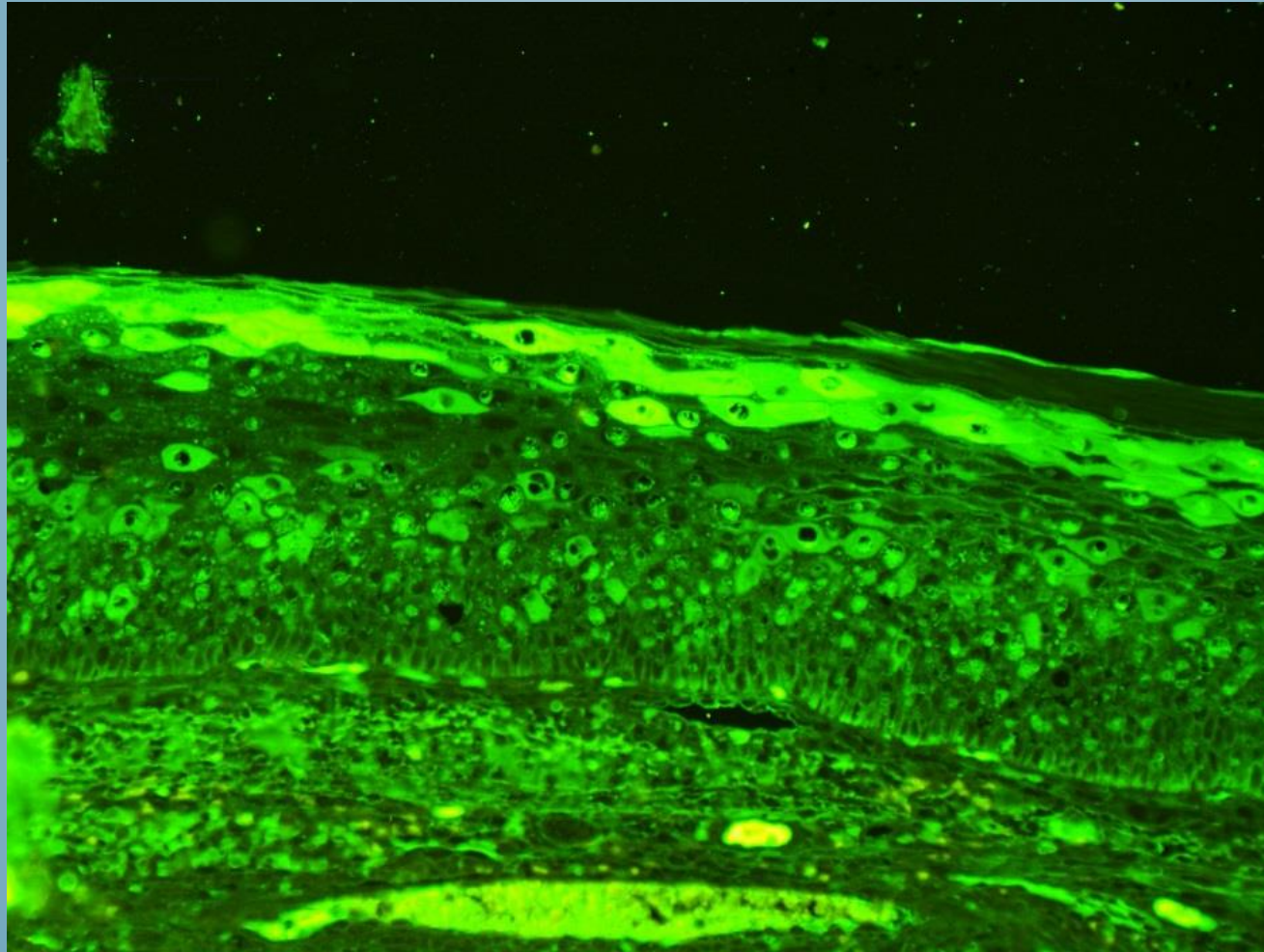
Possible site of entry: micro ulceration



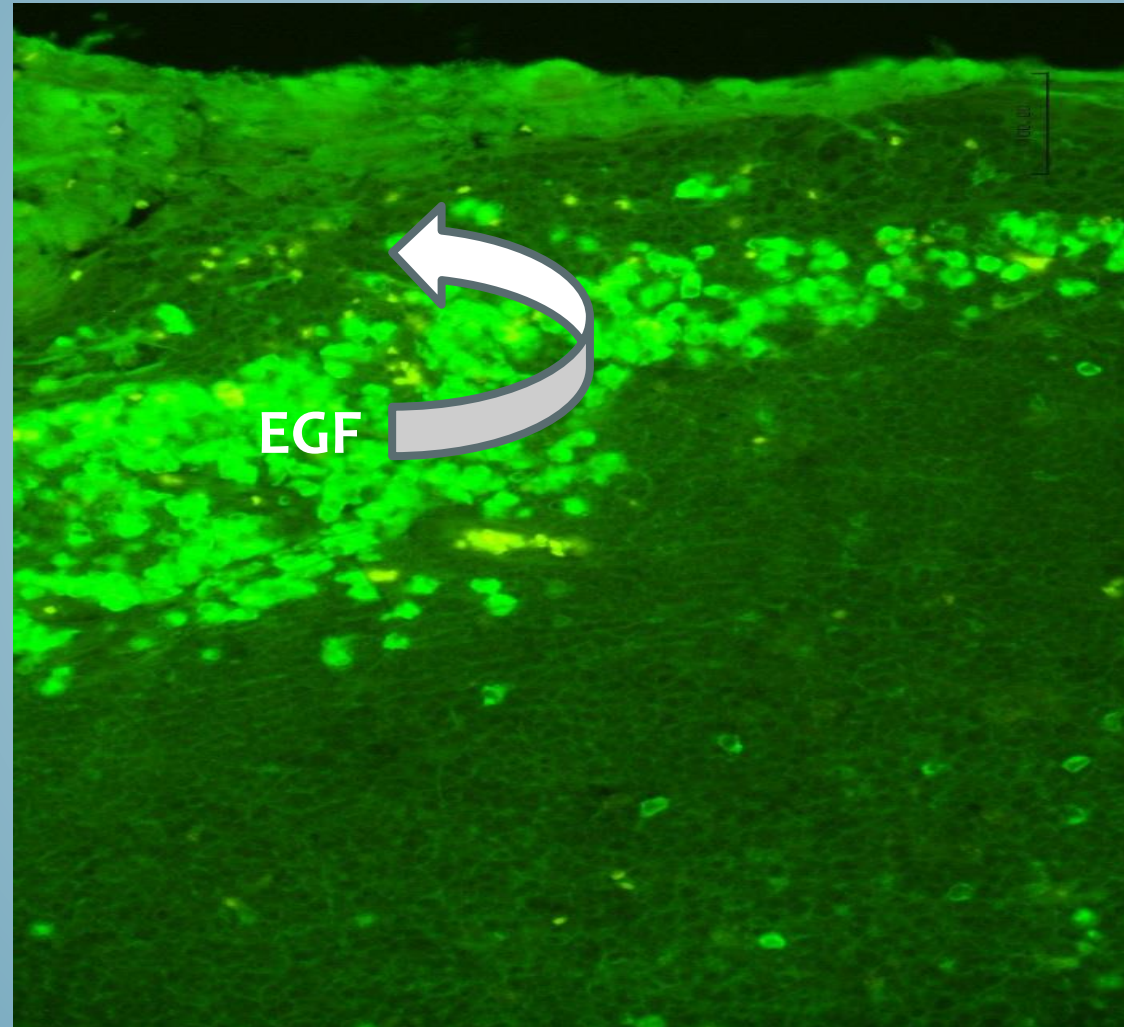
Surface epithelium: Koilocytes



IgG fluorescence of Koilocytes

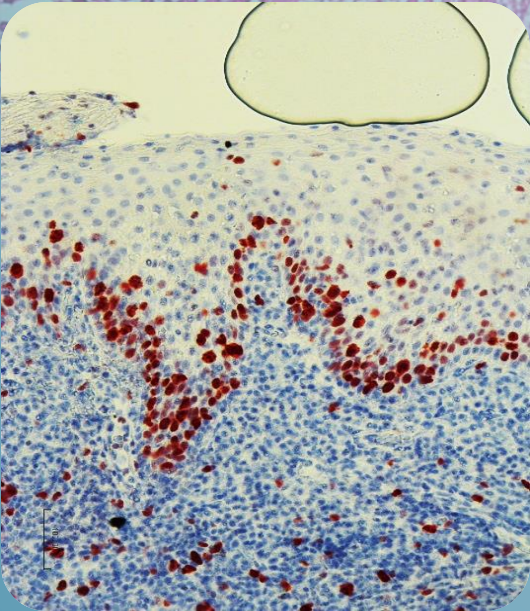
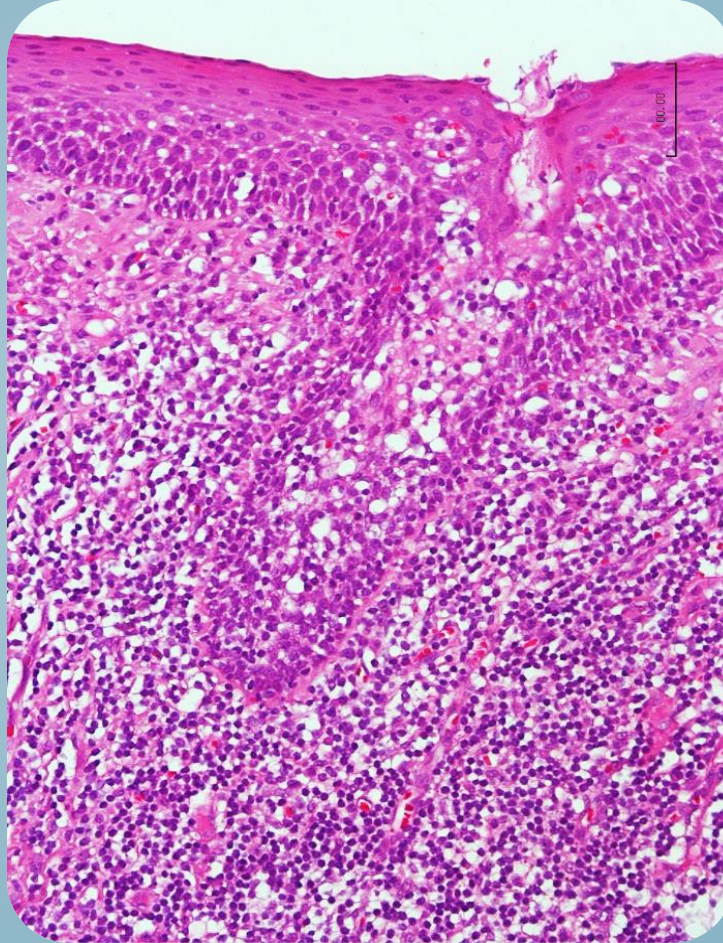
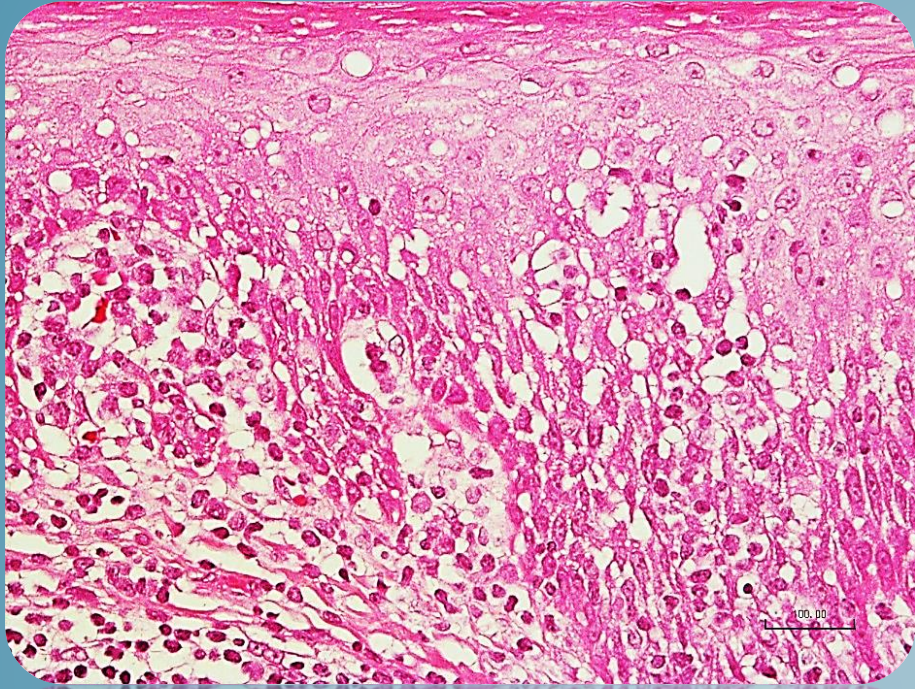


Sub epithelial inflammation and elaboration of EGF

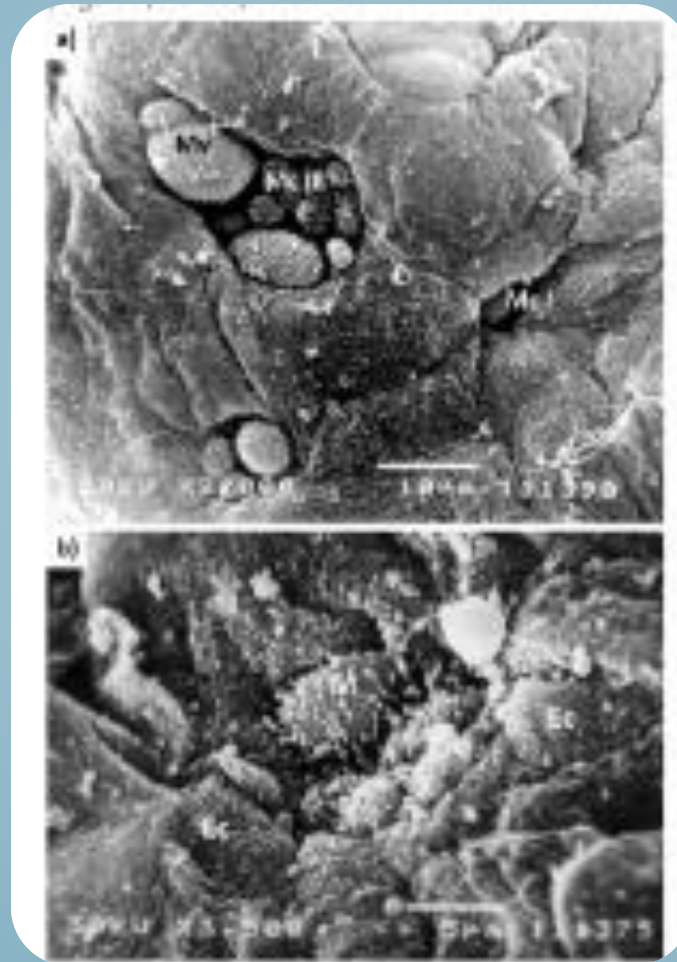


IF for IgA

Epithelial crypts

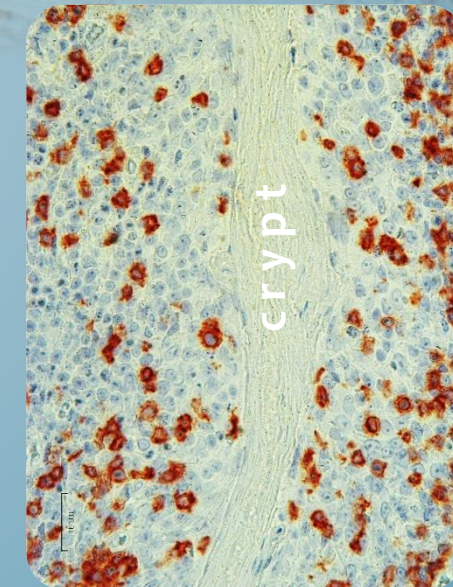
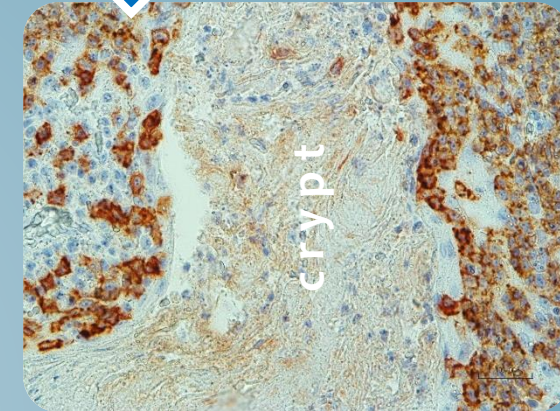
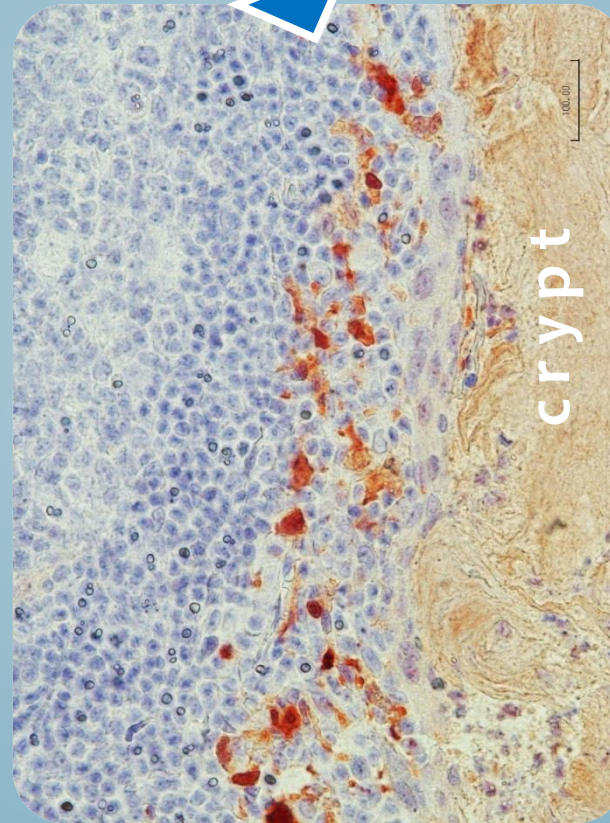
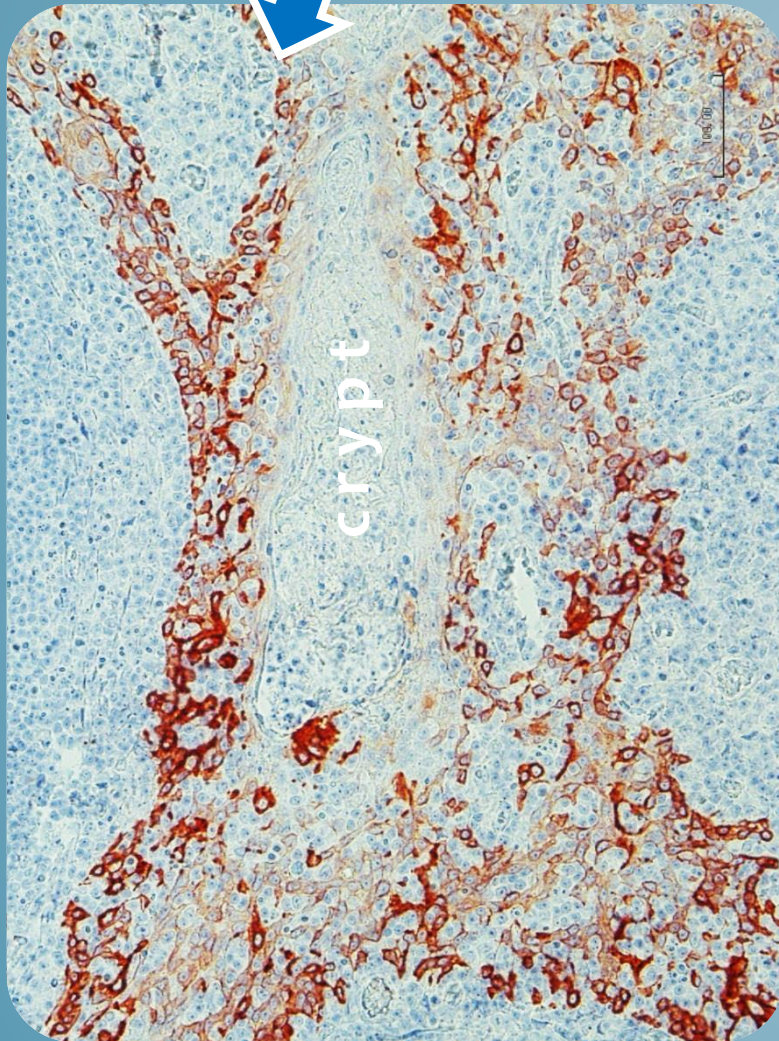


Micro- crypts

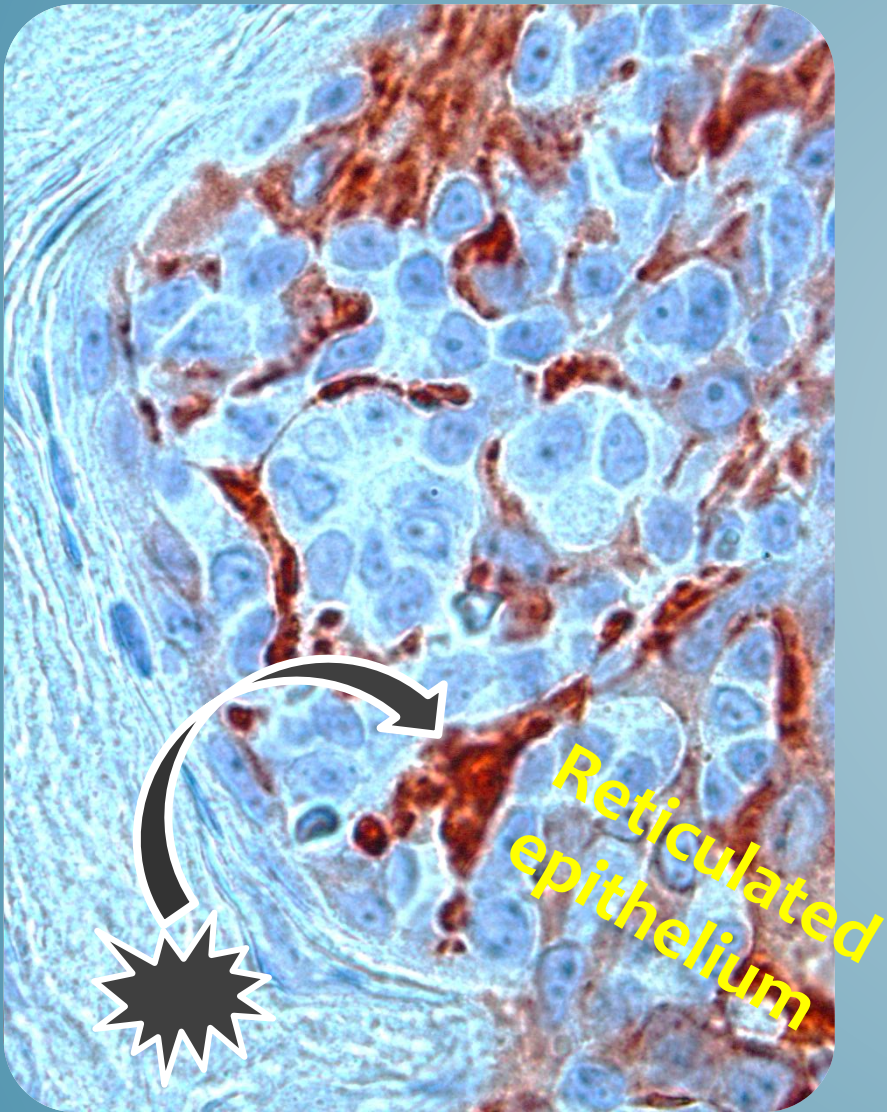


Jovic et al 2015

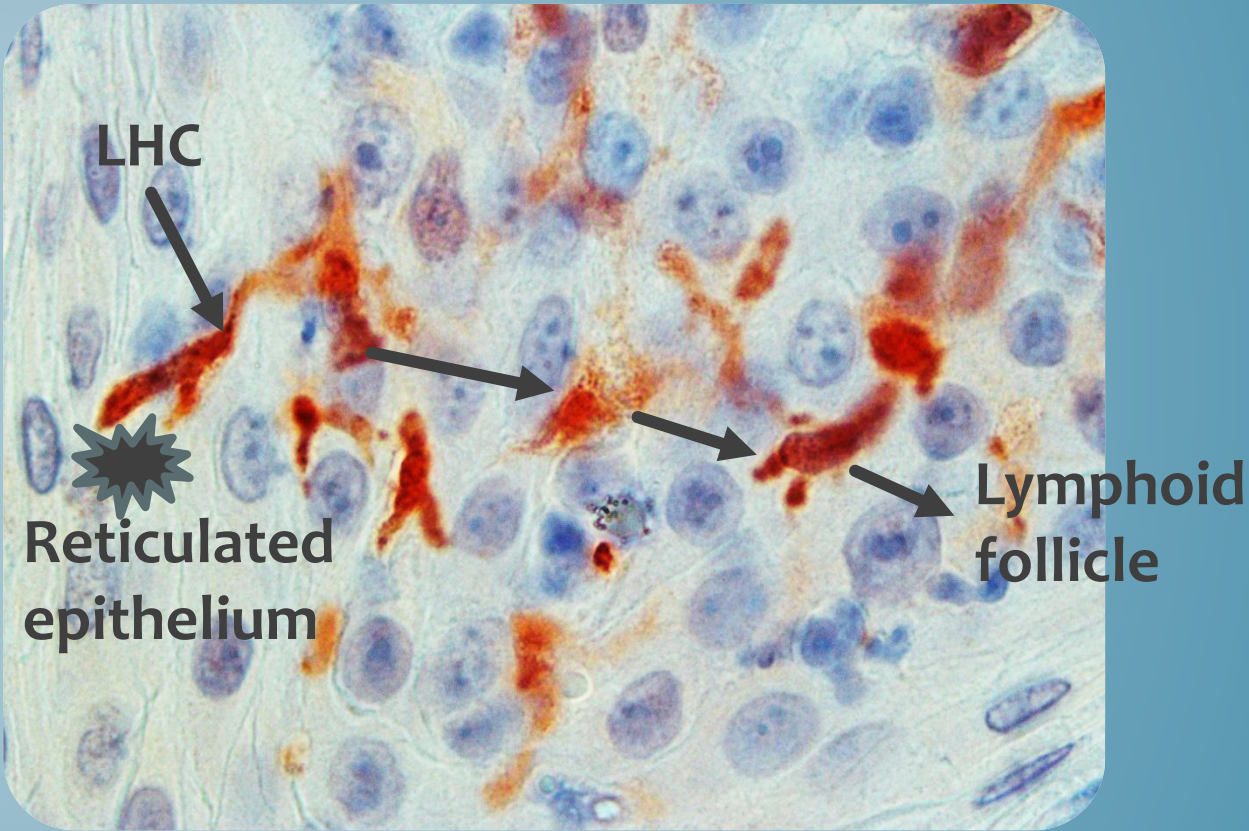
Reticulated crypt epithelium, dendritic cells and lymphocytes



Crypt immune cascade

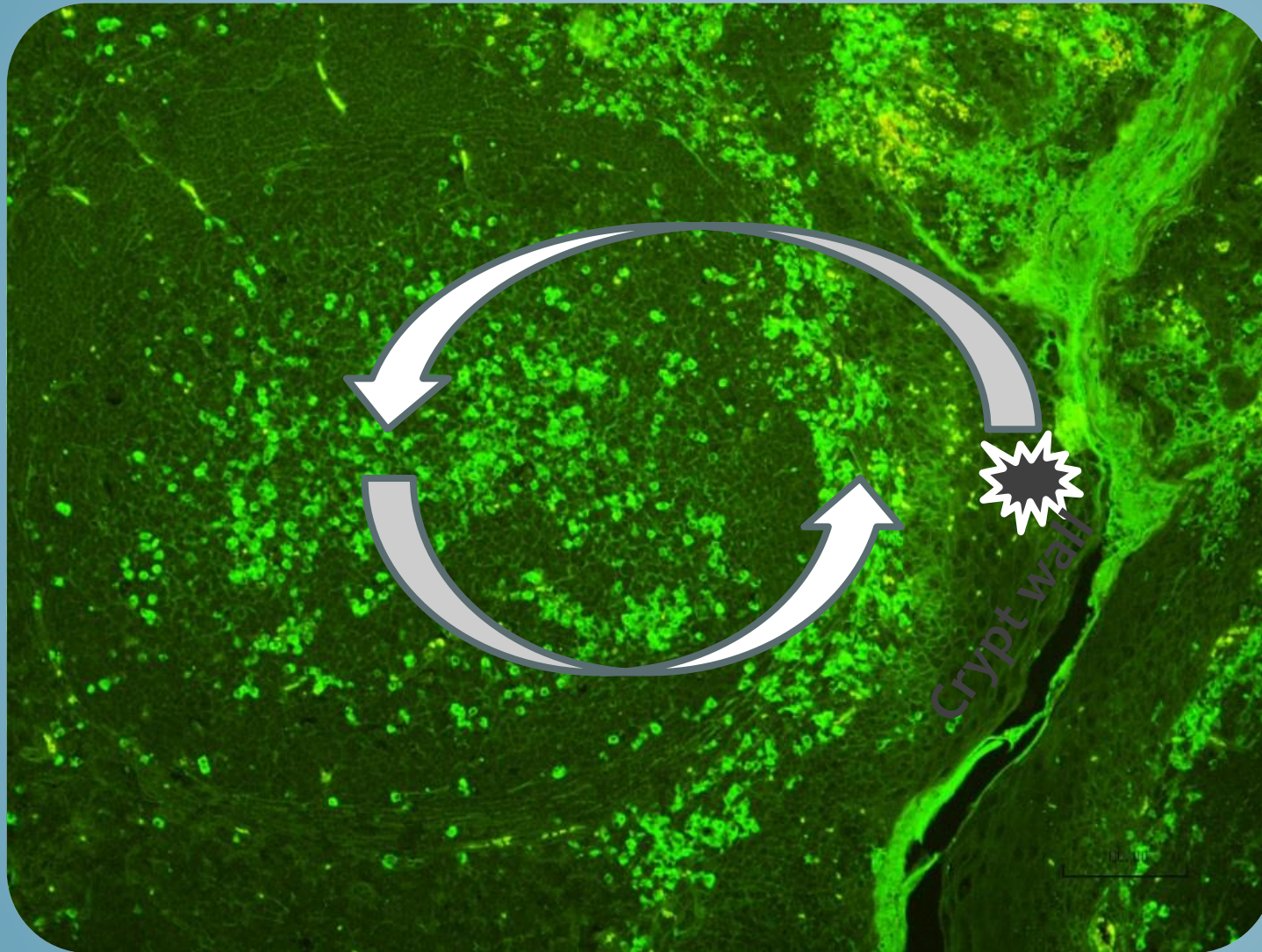


HMW CK



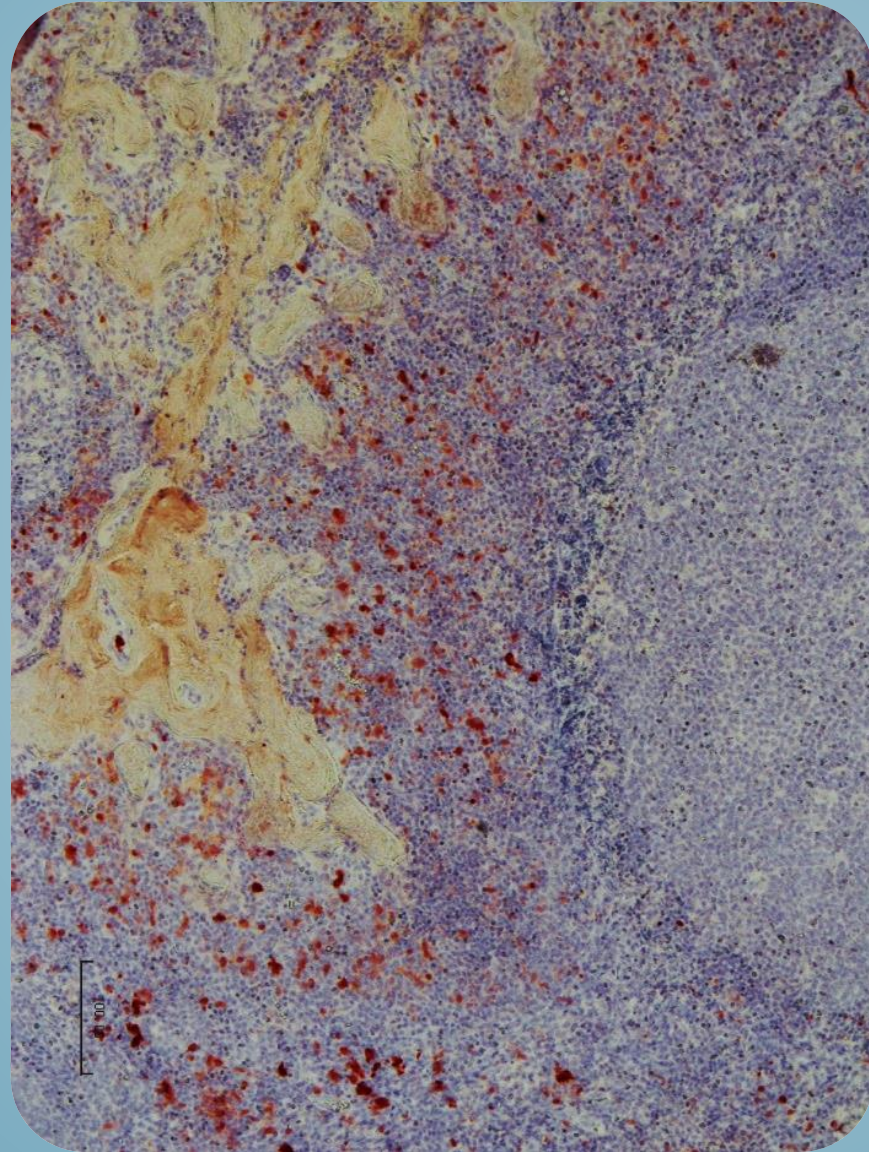
S100

Crypt: priming of the immune system



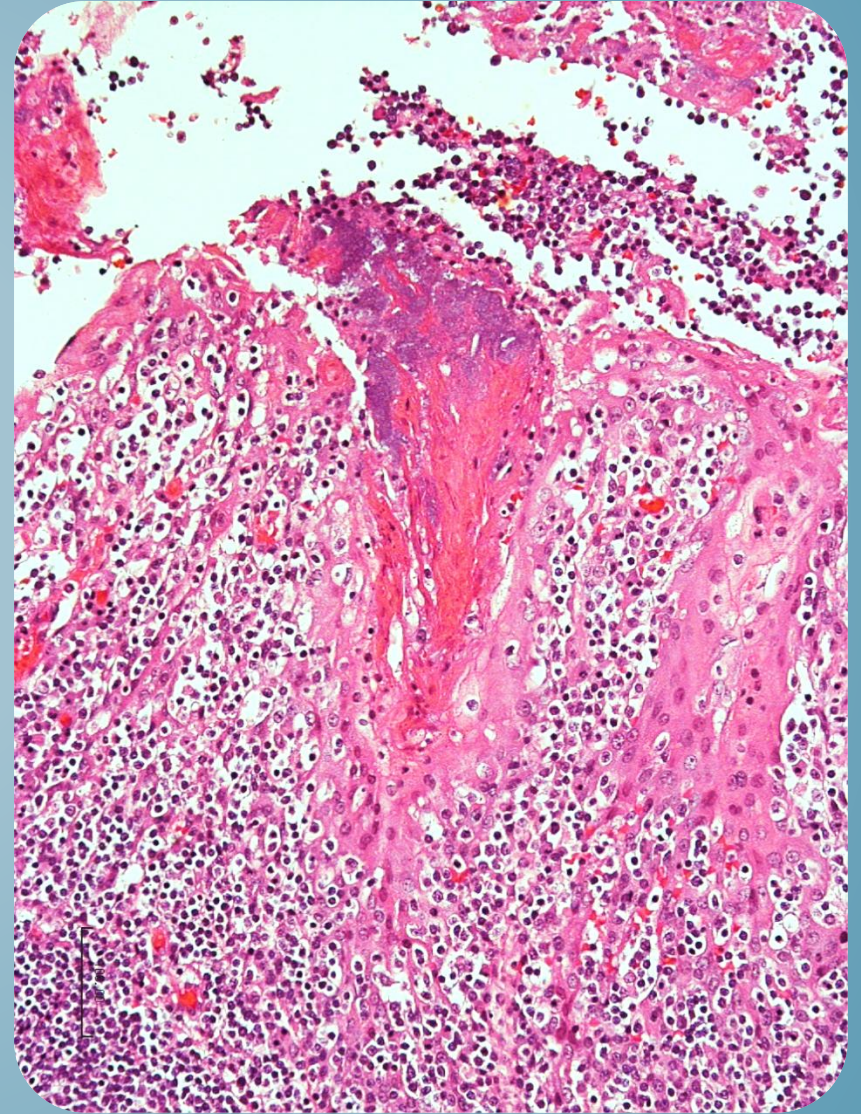
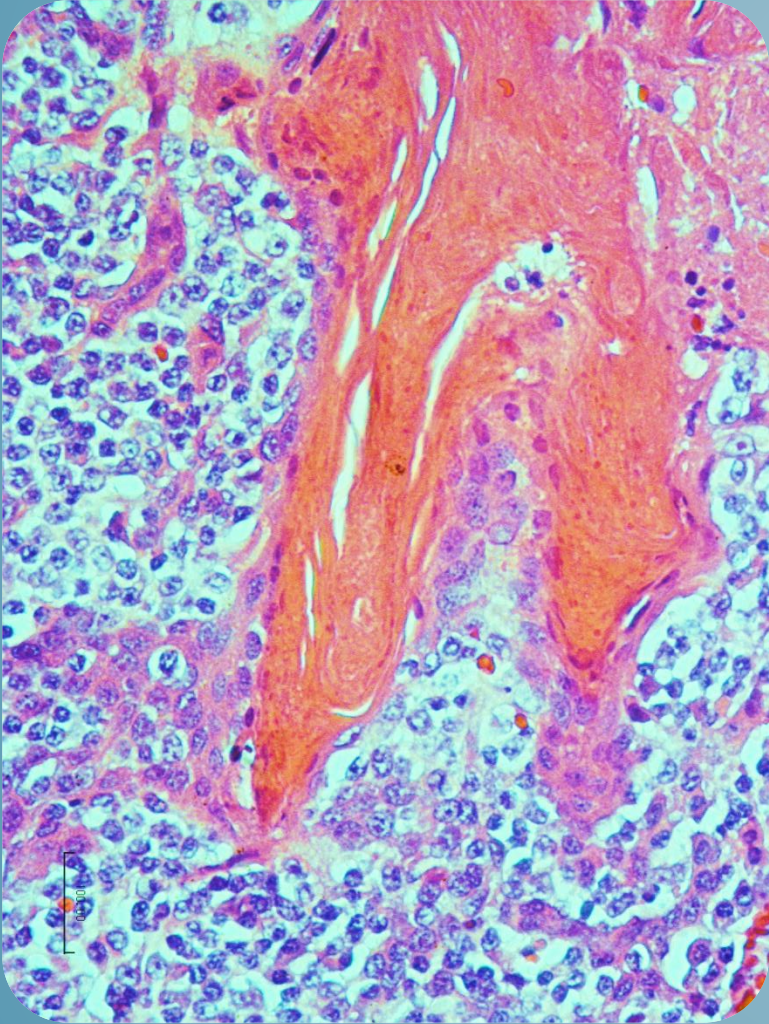
IF IgG

HIV/AIDS: Lack of follicle dendritic cells

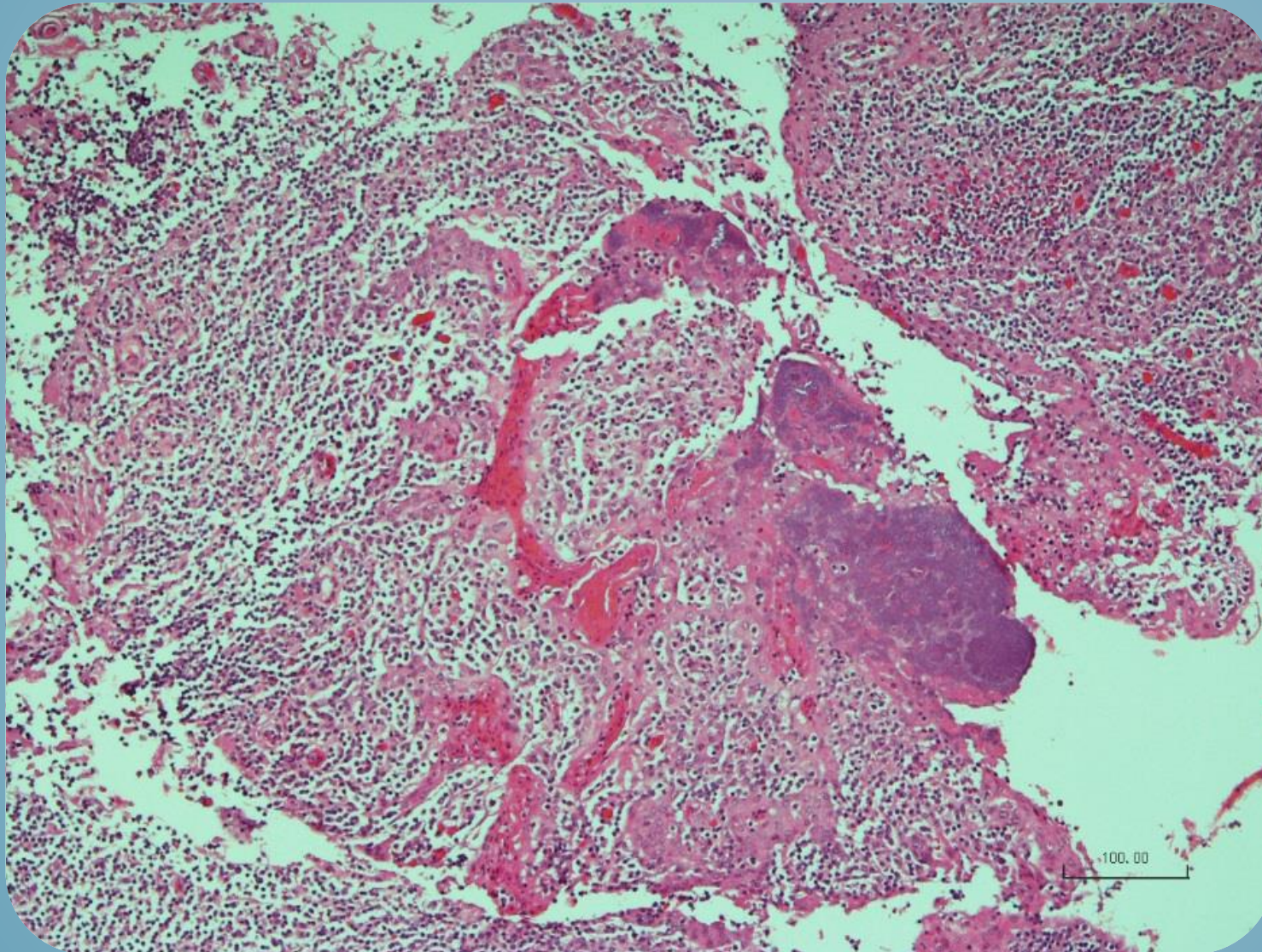


CD35: Zhang et al 1999

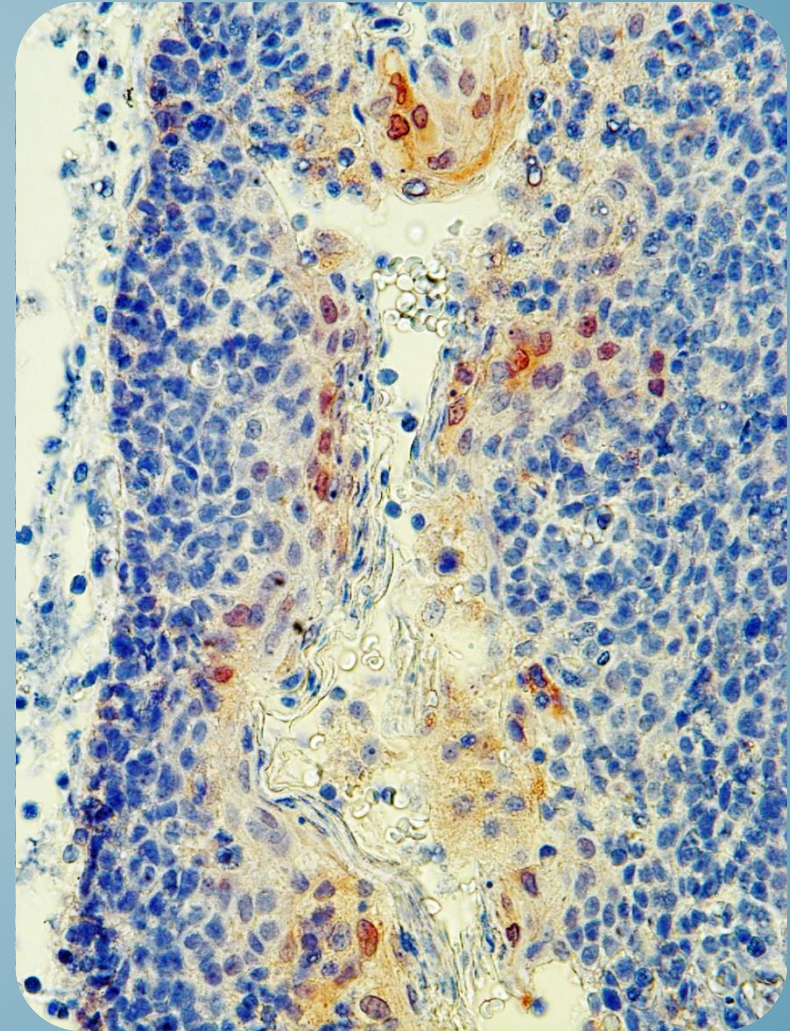
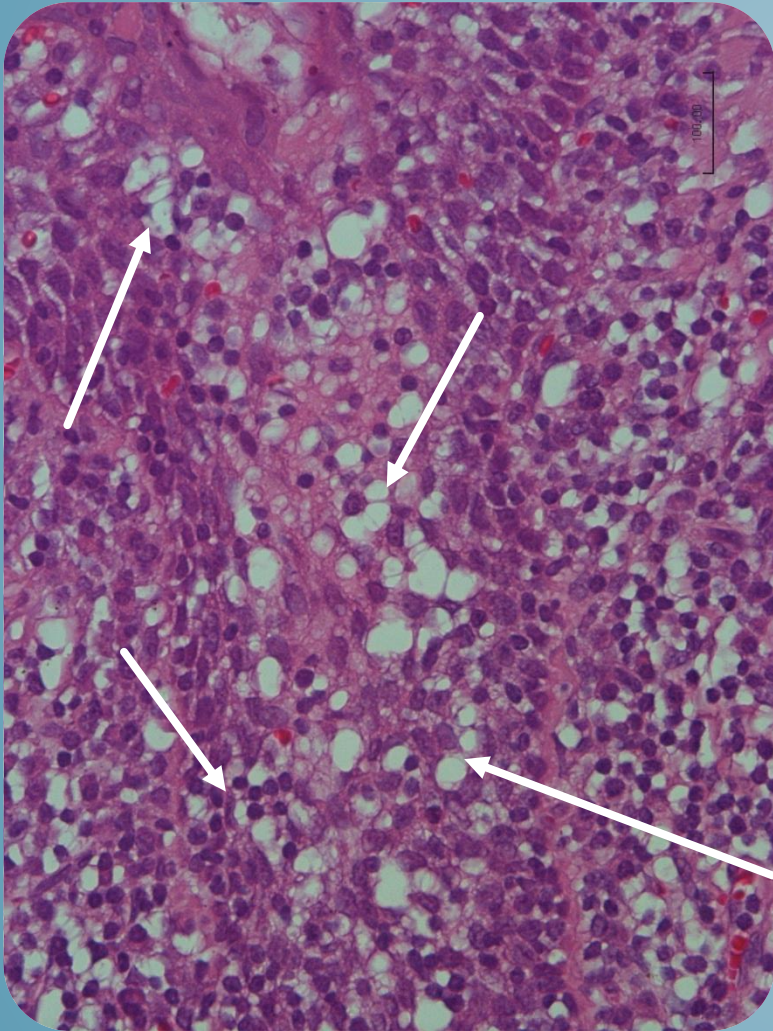
Crypt maturation



Crypt abscess



Crypt: Koilocytes vs. p 16



Conclusion

- Tonsillar epithelium is structurally complex and arranged in 2 distinct micro architectural configurations
- Tonsillar epithelium is dynamic and exhibit complex interactions with the immune system
- Presence of koilocytes and p16+ in reticular epithelium suggests a high probability for HPV viral protein in tonsillar epithelium
- Immuno histochemistry for p35 provides insight into the HIV status of a subject