Tissue Models of Infection

Project #1
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Biologically integrated and increasingly complex 3-D tissue systems with which to study HPV STIs

Aim 1
Organotypic Tissue Infection wounding, cell strata infected, response to wounding

Aim 2
Rodent Genital Tract Infection wounding, cell types infected (i.e., columnar, squamous, vaginal)

FUTURE
Rhesus Genital Tract Infections cell types infected, short-term persistence, immune response
Project #1 - Aims

CENTRAL HYPOTHESIS: monolayer cell cultures fail to display essential aspects of HPV infections in epithelial tissue and important features of HPV infection establishment can be determined from 3-D tissue-based models

Aim 1: Define requirements for HPV infection of cells in differentiated epithelium in vitro

1A. Evaluate the contribution of wounding to infection, identify the cells in the stratified epithelium capable of binding and internalizing virions and those cells able to express viral early genes

1B. Determine how the cellular response to wounding affects tissue infection

Aim 2: Identify the cell types that are susceptible to HPV infection in a rodent genital infection model (interfaces with Project #2).
This work provides knowledge relevant to genital PV infection in our newly established rhesus primate model (Aim 3 - Cut):

• We had proposed establishing a robust PV infection model by defining the time course of genital RhPV infection using different doses of Rhesus papillomavirus (RhPV)
  • Quantitation of viral RNA/DNA, infection peak and longitudinal spectrum of viral early RNA species
  • Clinical disease measures (abnormal cytology, histology)
  • Longitudinal persistence of viral DNA
• Assess the humoral and cellular immune responses to early infection
  – Delineate if Ig isotype, neutralizing antibodies, and/or cytokine and chemokine expression from PBMC can be correlated with initial infection, peak viral replication, persistence/clearance, and/or disease