

Immune responses and mechanisms of protection from mycoplasma vaccination

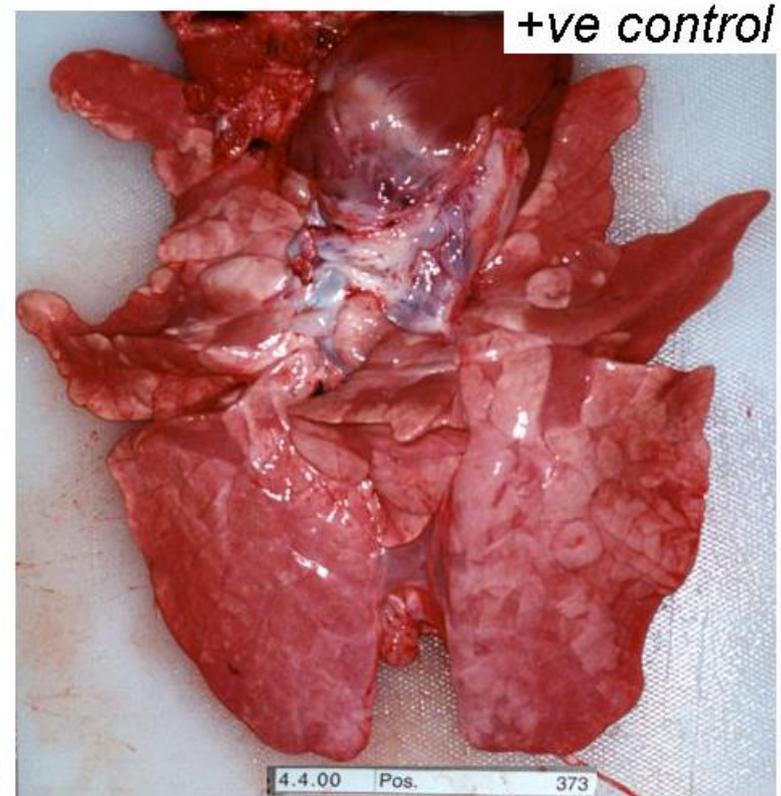
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Mycoplasma hyopneumoniae

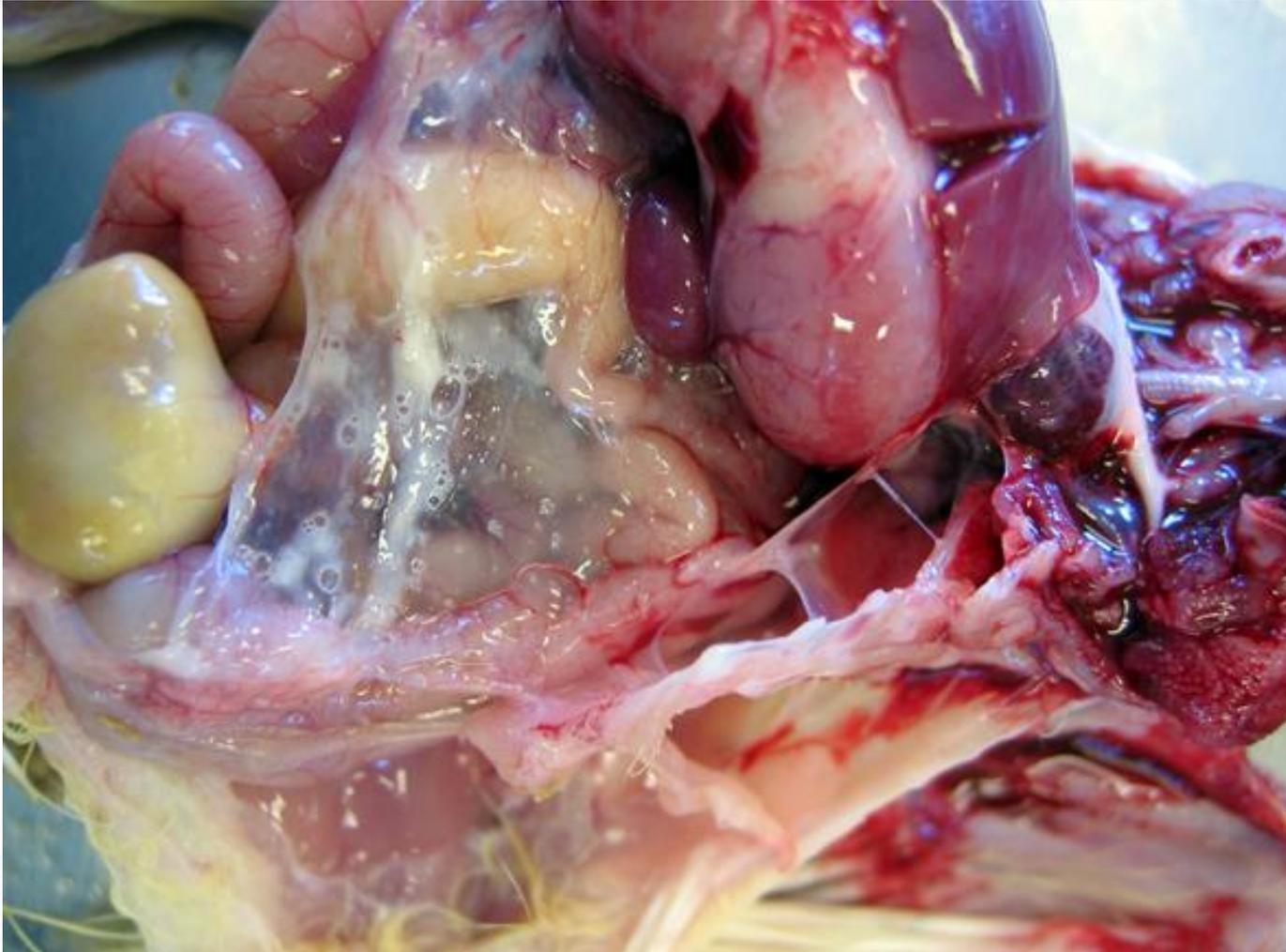
- Enzootic pneumonia
- Synergism with viral pathogens
- Major focus of antimicrobial treatment in pigs
- Primary lesion is damage to cilia



Mycoplasma bovis



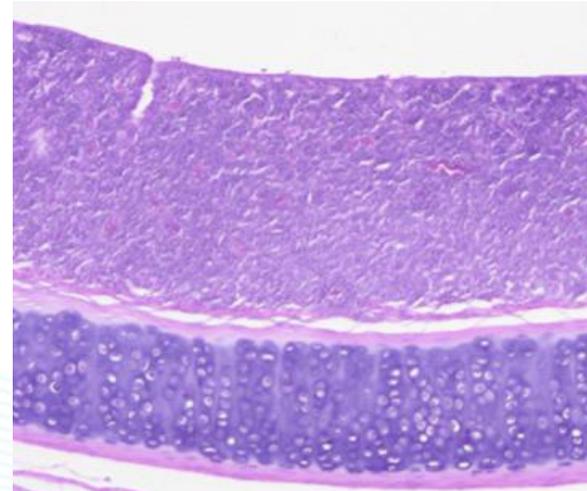
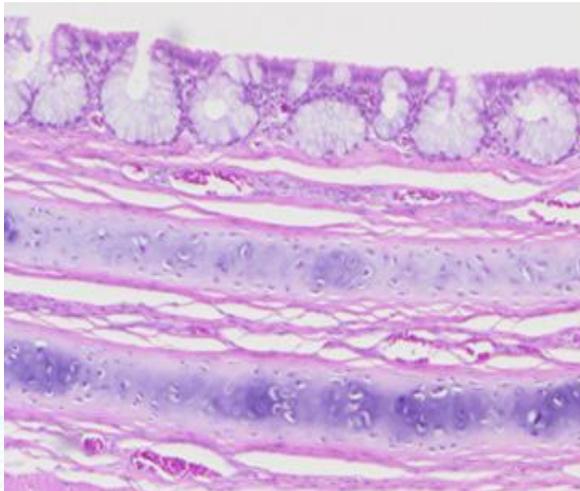
Mycoplasma gallisepticum



Effective Mycoplasma Vaccines

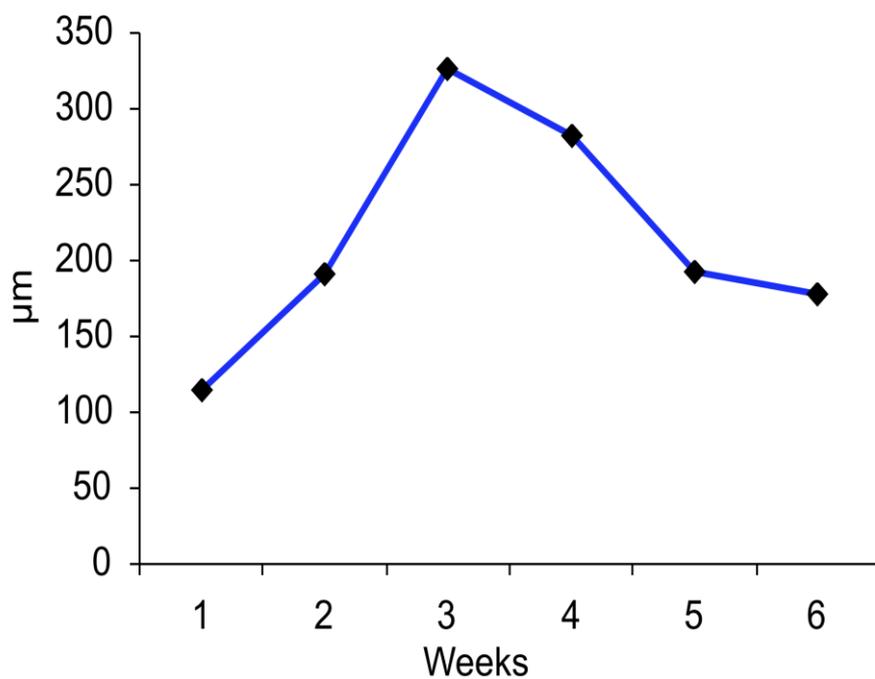
- Inactivated vaccines effective against *M. capri* ss *capripneumoniae* but limited efficacy against *M. hyopneumoniae* and not effective against *M. bovis*
- Attenuated vaccines effective against *M. mycoides* ss *mycoides* SC, *M. gallisepticum*, *M. synoviae* and *M. hyopneumoniae*

- Chronic respiratory disease in chickens
- Characteristic lymphoproliferative response
- Tracheitis and airsacculitis

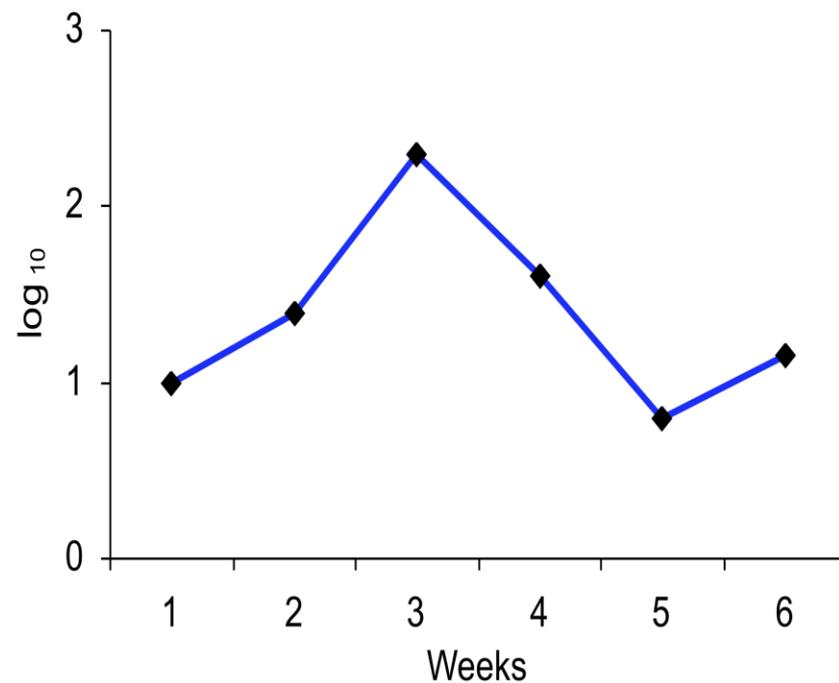


M. gallisepticum - Chicken Relationships

Mucosal Thickness



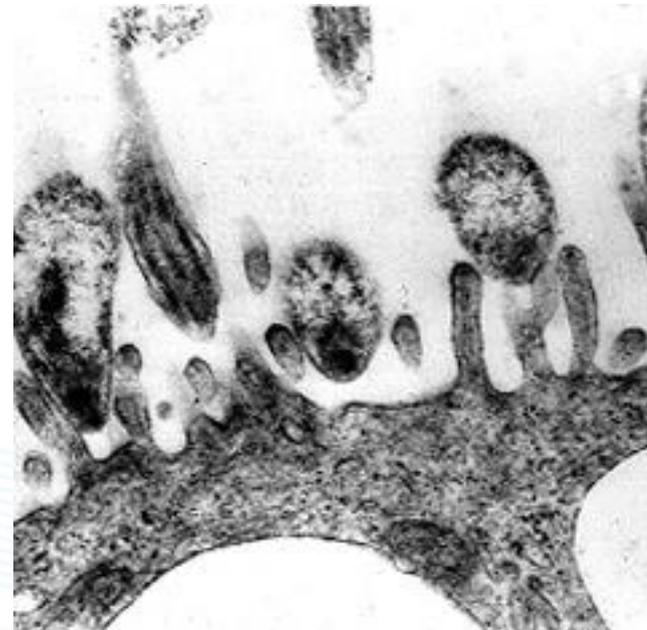
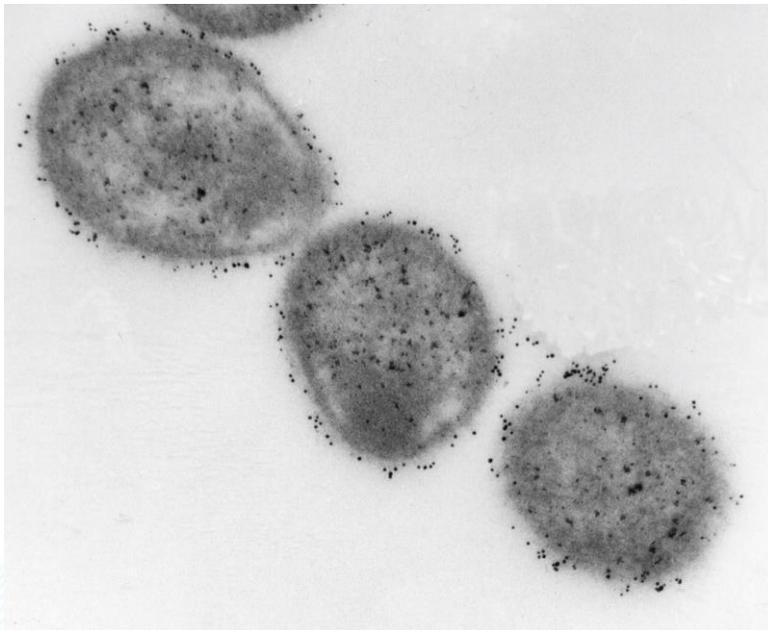
Genome Titre



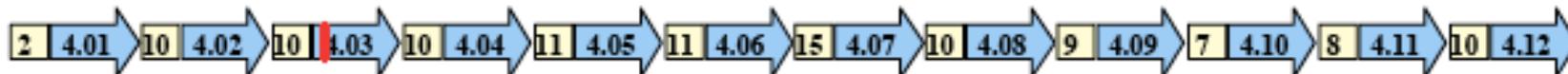
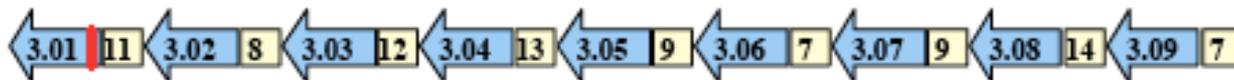
Adhesins of *M. gallisepticum*

- Possesses a P1 operon (GapA or Mgc1)
 - P1 homologues are single copy
- Possess VlhA haemagglutinin
 - 30 + copies in genome
 - Probably acquired from another avian mycoplasma
- Suggests two stage adhesion process

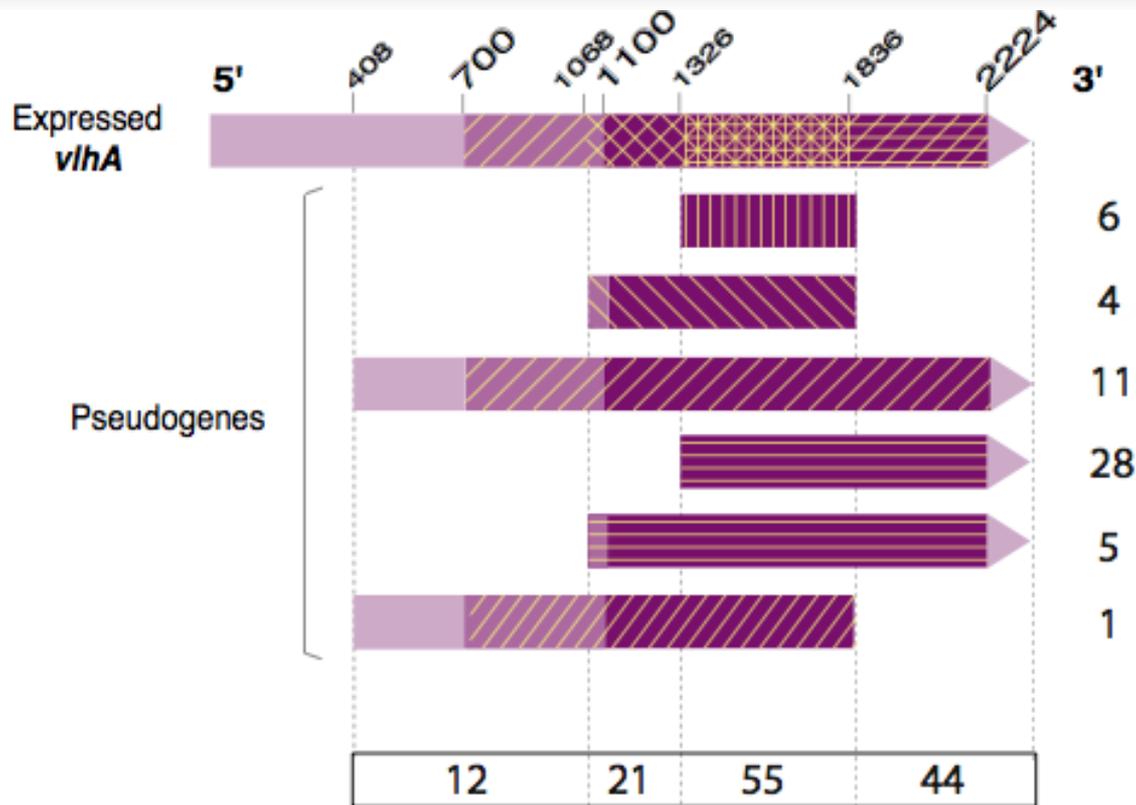
- Initial attachment using VlhA
- Subsequent intimate attachment using GapA



vlhA Family in *M. gallisepticum*



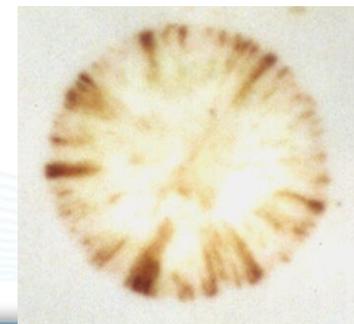
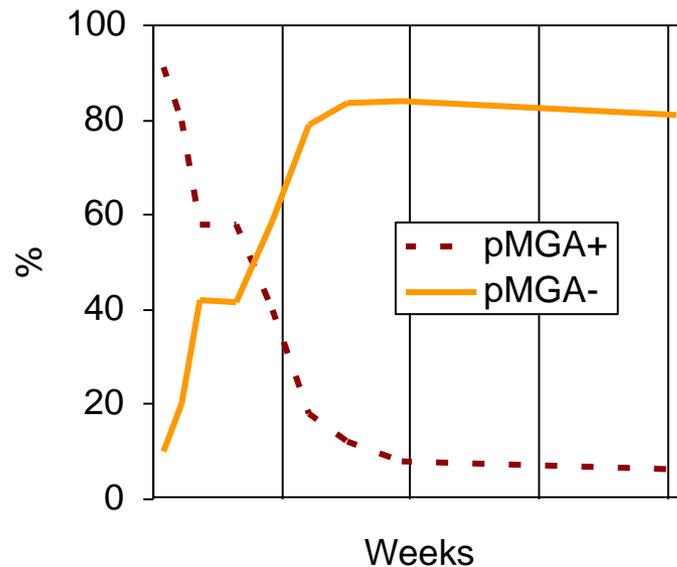
vlhA Family in *M. synoviae*



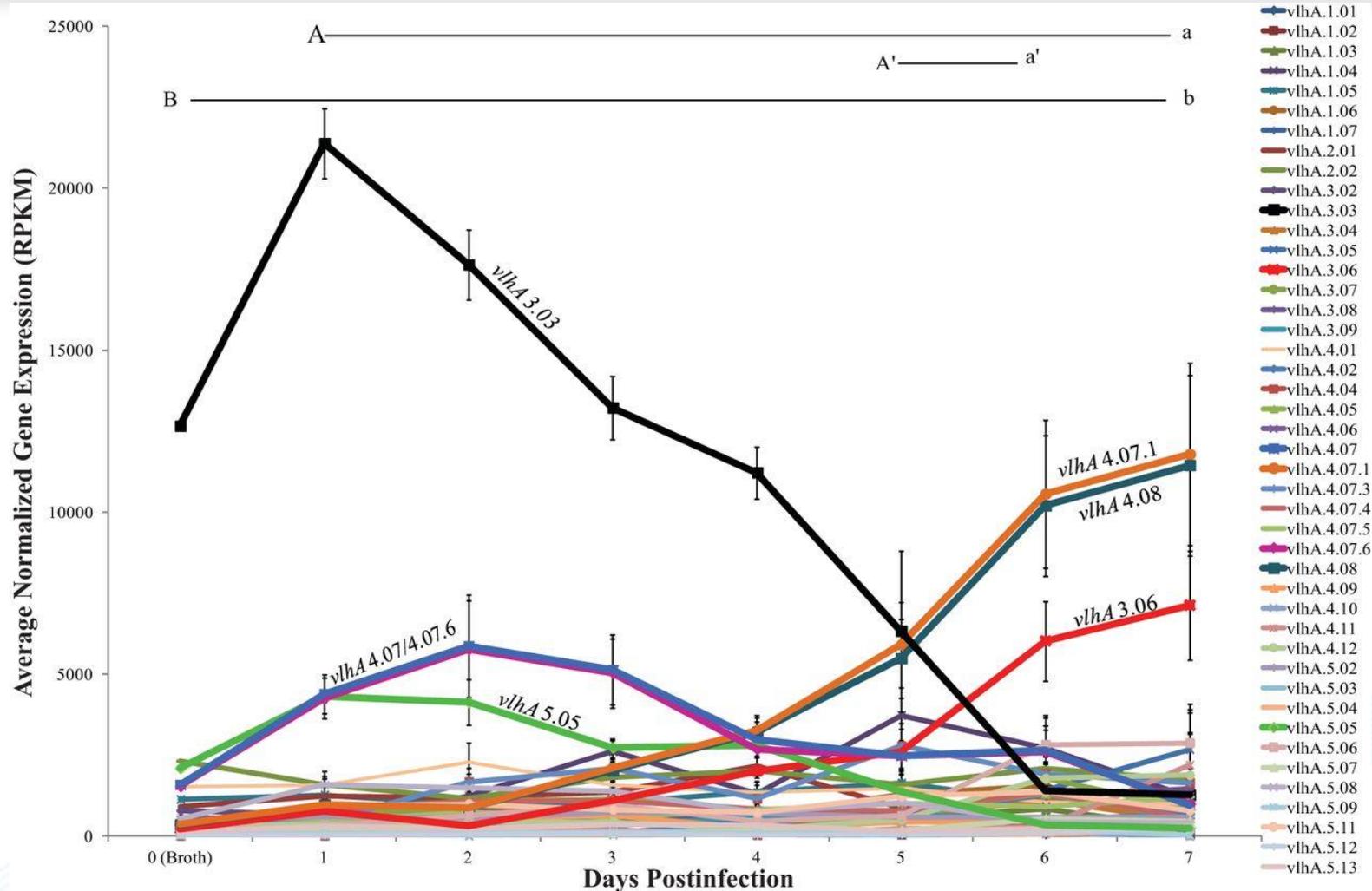
Total possible variants: 609,840

Expression of VlhA in *M. gallisepticum*

- Expression of pMGA1.1 rapidly ceases
- Most of population apparently pMGA- within 1 week



Antigenic Variation After Infection

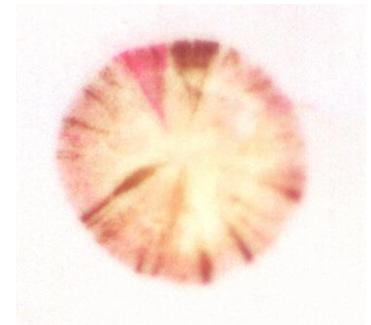
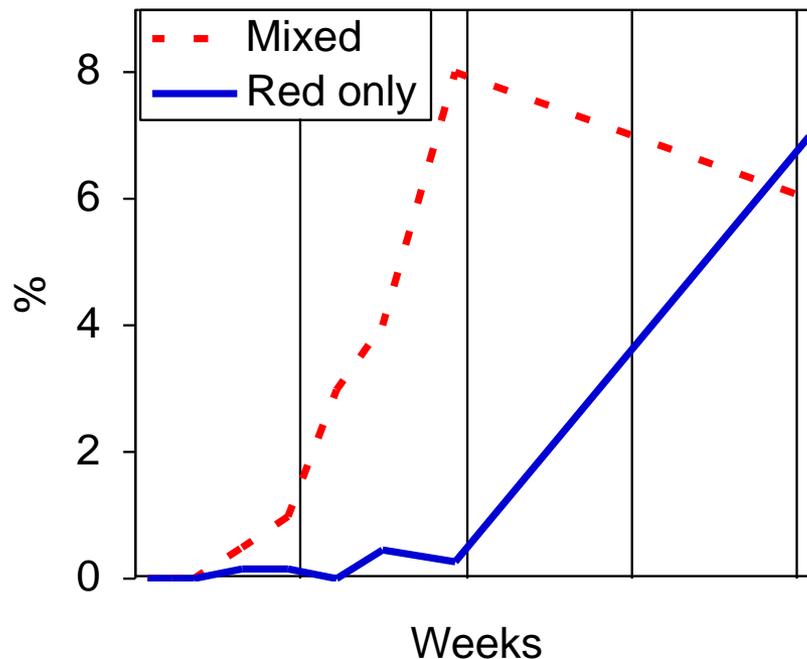


- Acute response
 - Early influx of CD8⁺TCR⁻ lymphocytes (probably NK cells)
 - Rapid induction of release of proinflammatory cytokines and chemokines from macrophages
 - Lesions peak at 2 to 3 weeks
 - CD8⁺ increasingly TCR⁺, most CD4⁺TCR2⁺
 - Few B cells until 3 weeks

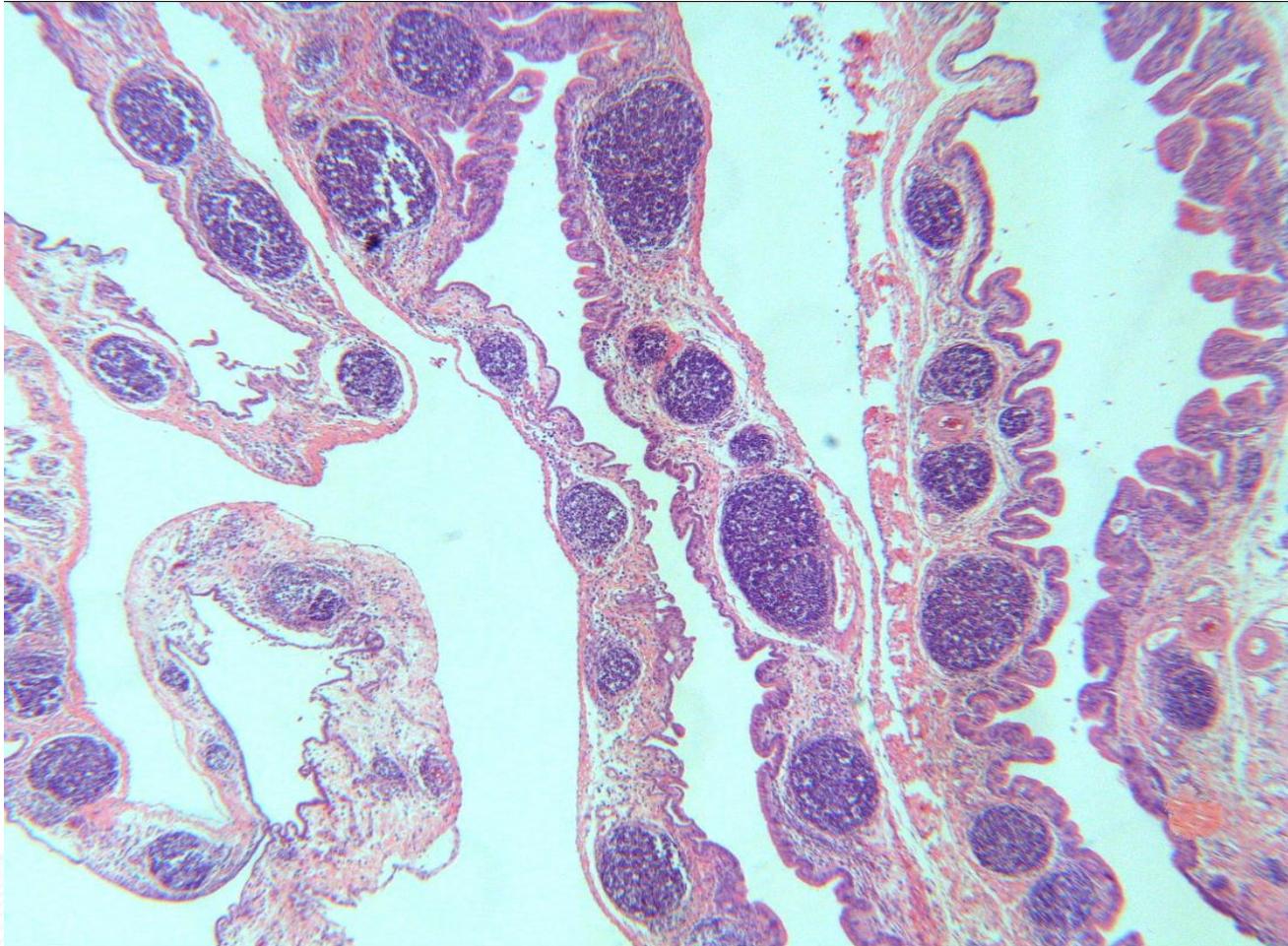
- Control of Infection
 - NK cells?
 - Cytotoxic cells?
 - B cells?
- Stimulus for Immune Response
 - Intracellular infection?
 - Membrane fusion?
 - Macrophage response to lipoproteins via TLR-2

Expression of Alternative pMGA Genes

- Increasing propensity to express alternative pMGA genes

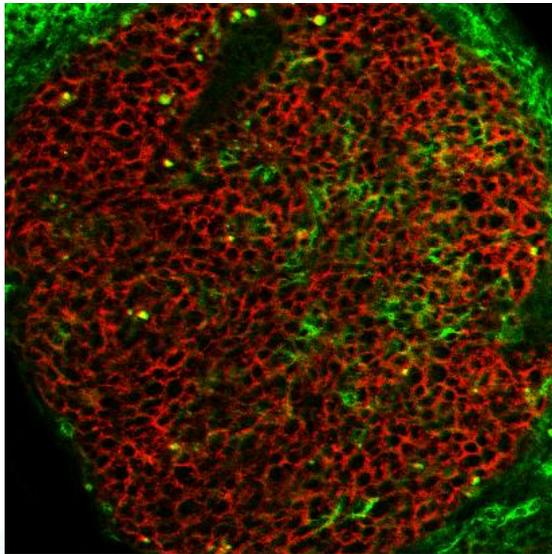


Follicles in Chronic Phase

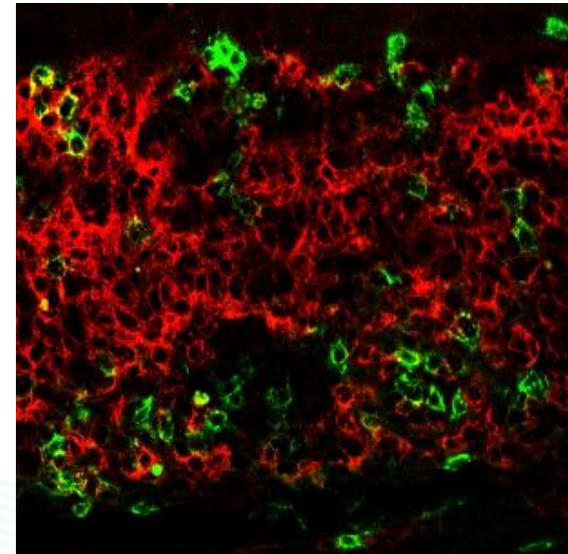


Chronic Immune Responses

- CD4+TCR3+ cells predominate
- CD8+TCR3+ cells also seen
- B cell follicles become prominent



B and CD4+ cells

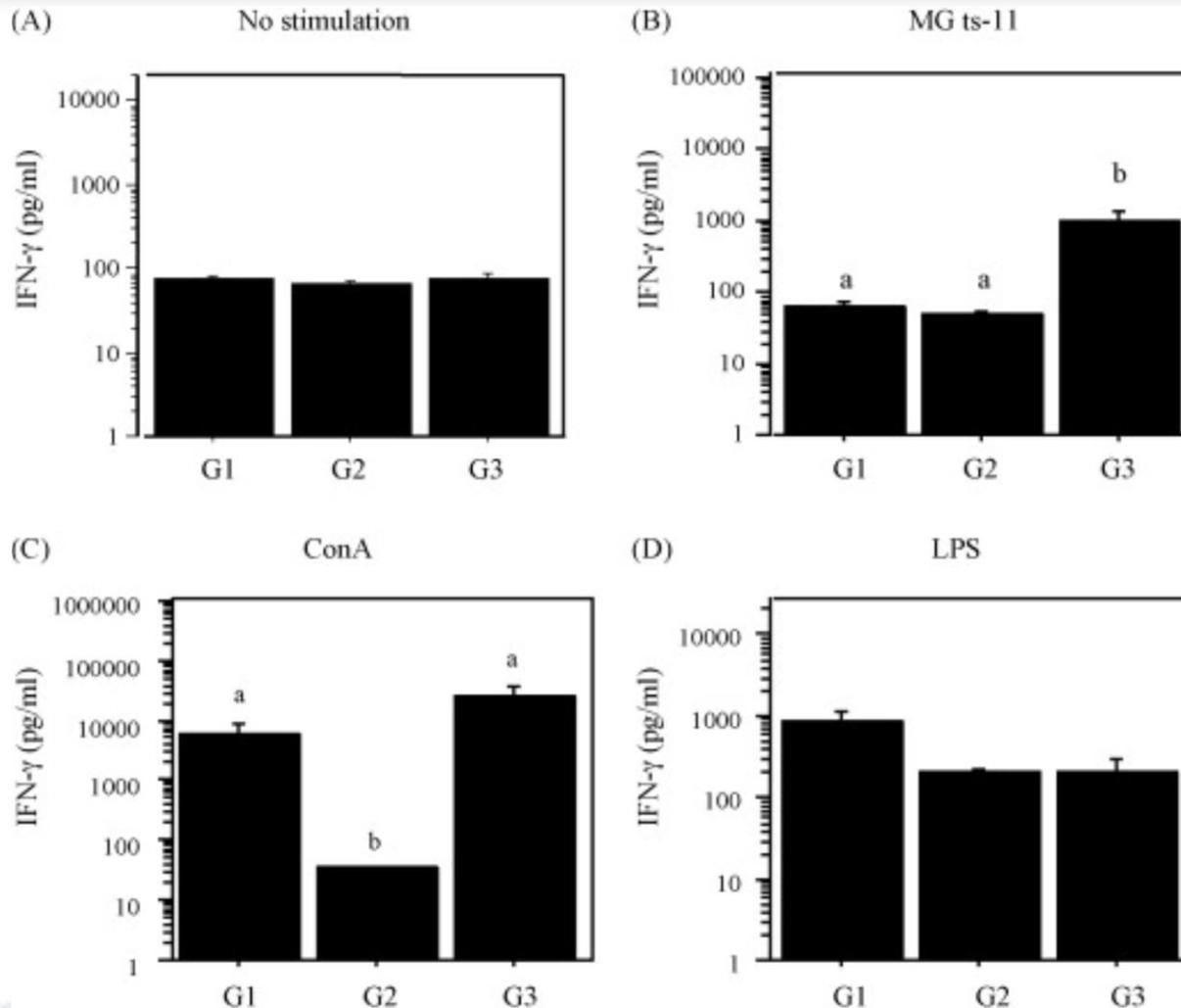


B and CD8+ cells

Interactions in Chronic Phase

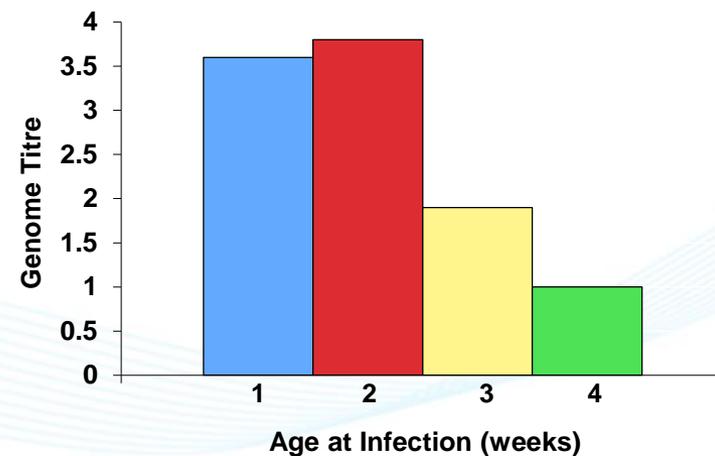
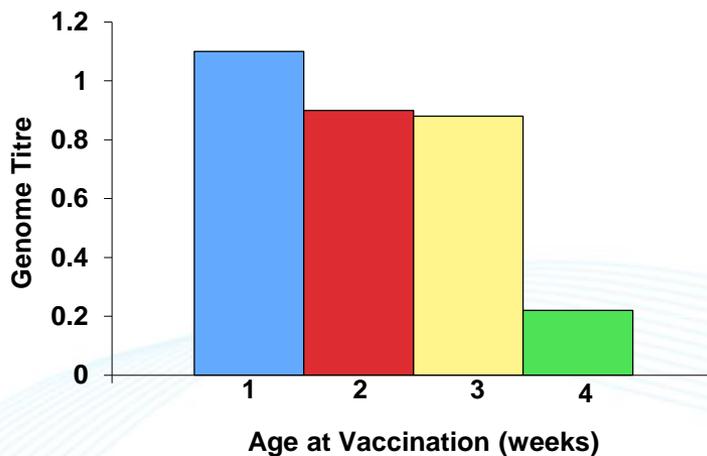
- Proliferative humoral response
- Increasing antigenic variation
- Continuing stimulation of B cell follicles by novel variants?
- Control but not elimination by antibody response

Systemic Immunosuppression



G1 – Unvaccinated
G2 – ts-11 vaccinated
G3 – ts-11 expressing
IFN-gamma

- Lesions more severe in young birds
- Higher titres of *M. gallisepticum* in trachea
- Vaccination less effective in young birds



Susceptibility of Younger Birds

- Higher concentrations of mRNA for inflammatory cytokines
- No discernible difference in T cell populations
- Severity of disease due to a greater, but less effective, immune response

Maturation of T Cell Populations

- Third wave of thymic emigrants at 3 weeks
- More TCR3+ cells
- Suggests a role for later thymic emigrants?

Conclusions

- Host-pathogen relationship actively evolving throughout infection
- Rapid alterations in adhesin expression
- NK cells recruited but not very effective
- Control of acute phase associated with TCR2+ cells
- Chronic phase due to continuing antigenic variation and proliferative B cell response
- Infection both immunostimulatory and immunosuppressive
- Susceptibility of younger birds due to relative lack of TCR3+ cells?

Immunity Against *M. gallisepticum*

- No evidence of interference by maternally acquired antibody in infection
- Serum IgG concentrations not correlated with protection
- Little evidence of correlation between tracheal IgA and protection
- Correlations between tracheal IgG and protection
- Conflicting evidence about the role of T and B lymphocytes in protection

Immunity against *M. gallisepticum*

- Some protection shown with a variety of inactivated vaccines
- Better protection seen when initial intramuscular vaccination boosted by intratracheal vaccination than by an intramuscular boost, suggesting local immune responses are needed

What Might Be Needed for Effective Vaccination?

- Mucosal immunity in the respiratory tract with local IgG secreted onto the mucosa
- Cell-mediated immune responses
- Broad response against a variety of cell surface antigens

Why Might Attenuated Vaccines Perform Better?

- Induce local mucosal immunity at the site of colonisation
- Persist in the respiratory tract and present a broad range of surface antigens
- Induce cell-mediated immune responses, especially locally

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