



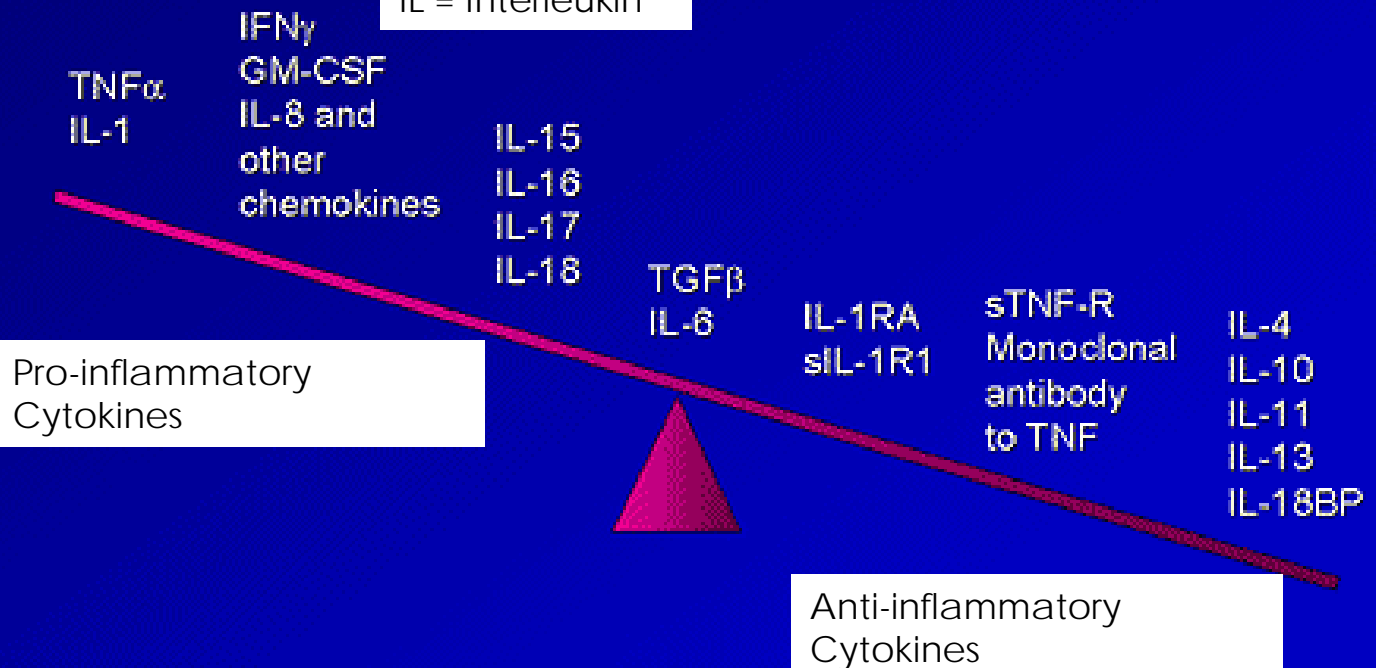
Biology of Mycoplasmas

Part 2: Interplay with Immune Defenses

Cytokines and Inflammation

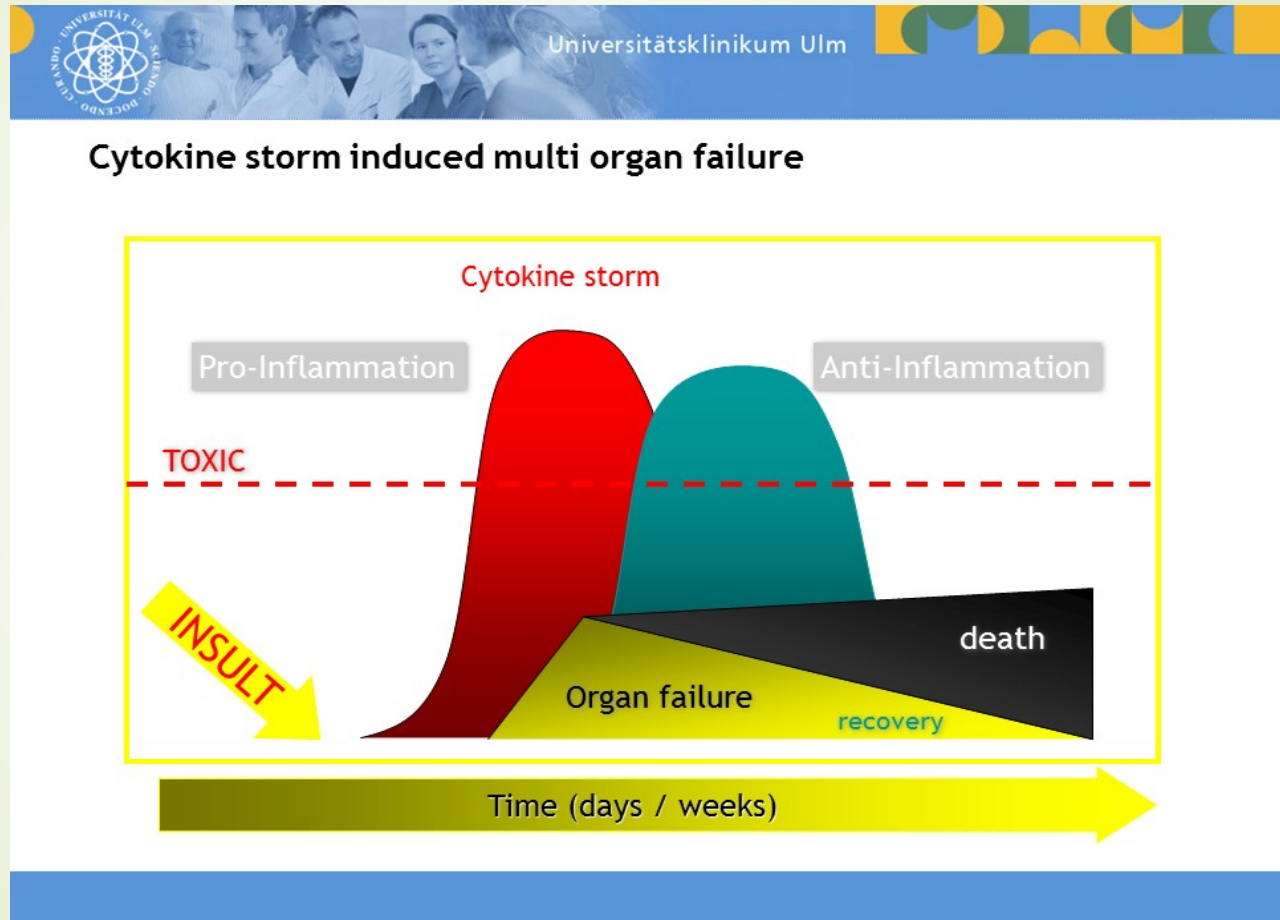
Role of Cytokines and Cytokine Inhibitors in Chronic Inflammation

IL = Interleukin



Arend. *Arthritis Rheum* 2001.

Cytokines and Inflammation



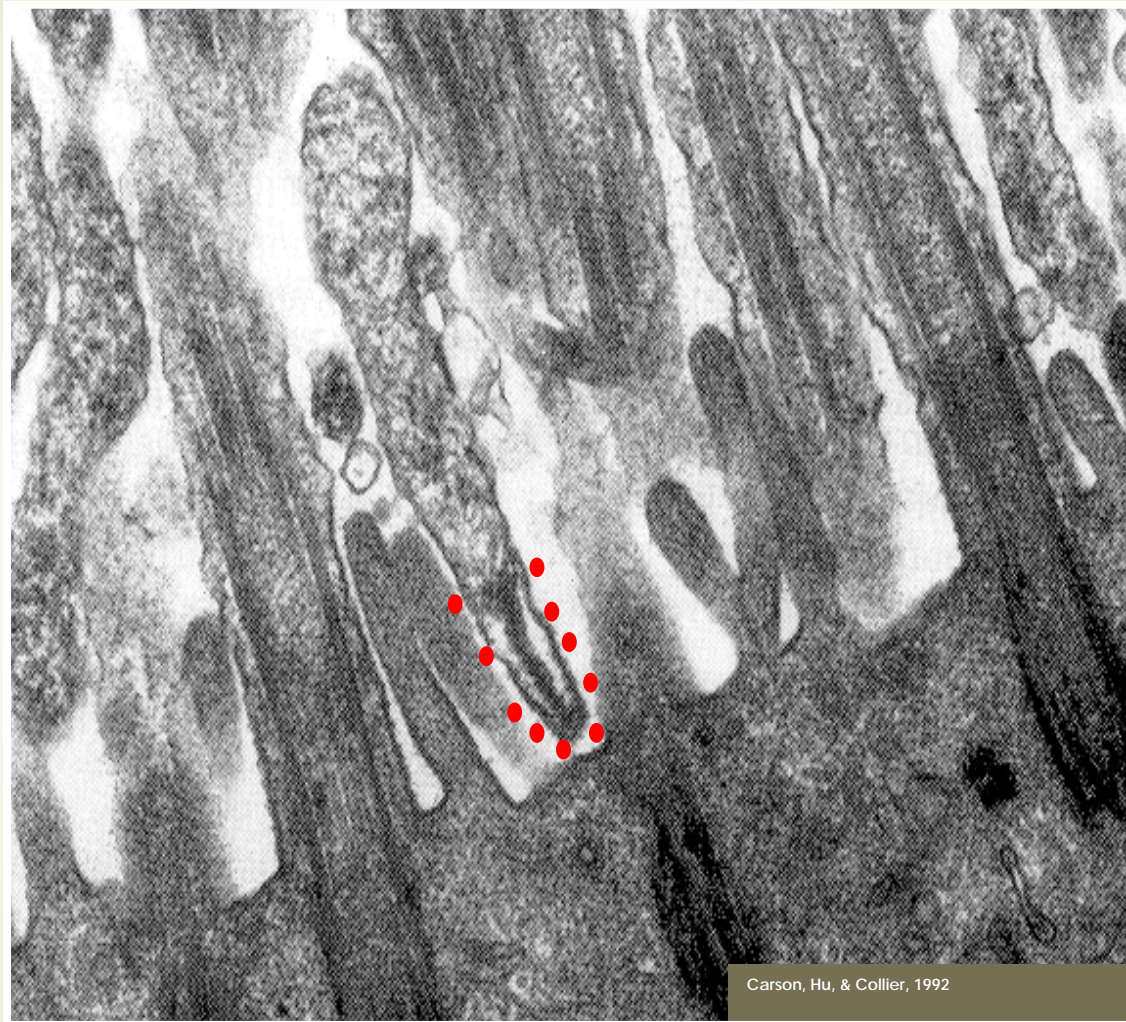
TB, shigellosis: cytokine storm mostly local

Flu, Dengue, typhoid fever: cytokine storm is systemic



Adaptive Defenses to *M. pneumoniae* Infection

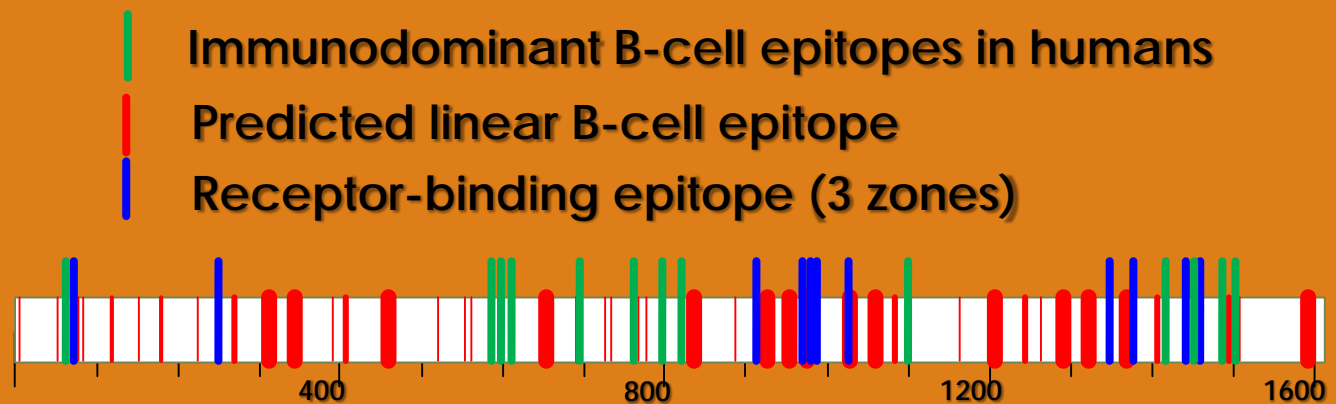
- ▶ Acute vs convalescent antibodies
- ▶ How antibodies protect
 - ▶ Aggregate
 - ▶ Opsonize
 - ▶ Activate complement
 - ▶ Block receptor binding
- ▶ Adhesin protein P1 is a primary target of humoral response
 - ▶ Serum antibodies
 - ▶ Secretory IgA in airways
- ▶ Anti-P1 convalescent antibodies ineffective



Carson, Hu, & Collier, 1992

P1 is a “Moving Target”

- Natural and experimental infections elicit strong but ineffective antibody response
- P1 mABs CAN block adherence / disrupt gliding
- Biological mimicry vs. sequestered epitopes



However:

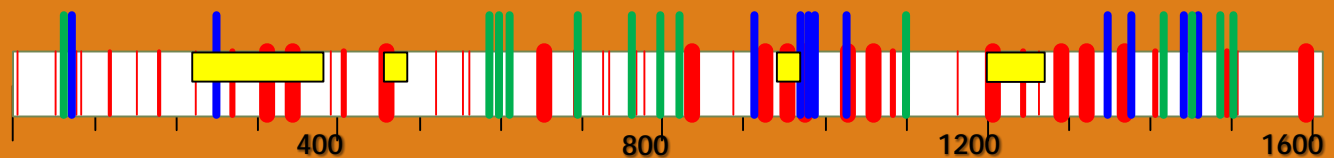
- Antigenic variation is limited
- *M. pneumoniae* genome is relatively stable
- Two major and a few minor genotypes

■ Sequence-variable regions

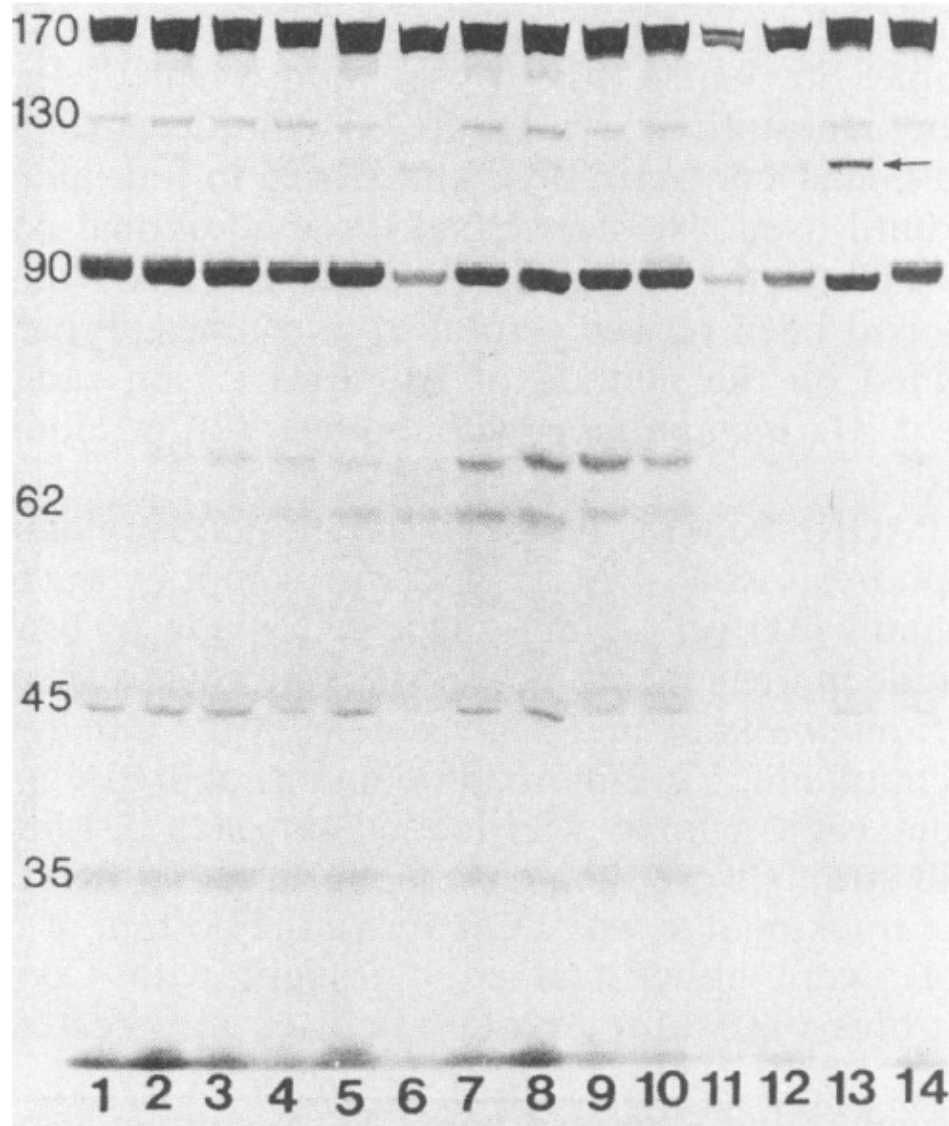
■ Immunodominant B-cell epitopes in humans

■ Predicted linear B-cell epitope

■ Receptor-binding epitope (3 zones)



Western blot of strains collected over 10-year period



P1

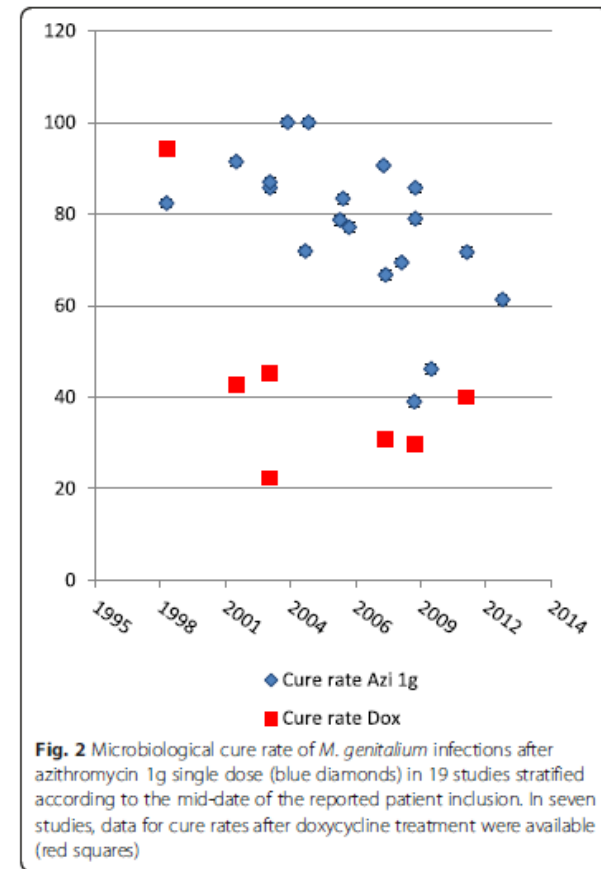
P90 / B

Mycoplasma genitalium Infections

- Closely related to *M. pneumoniae*
- First isolated in 1980 from men with urethritis (NGU)
- Extremely difficult to culture from clinical specimens (PCR detection)
- Associated with:
 - Urethritis in both men and women
 - Prostatitis
 - Pelvic inflammatory disease; Endometritis; Cervicitis; Tubal factor infertility
- Prevalence ~ 2% in low-risk and 7% in high-risk groups
- May increase HIV transmission

M. genitalium Infections – cont'd

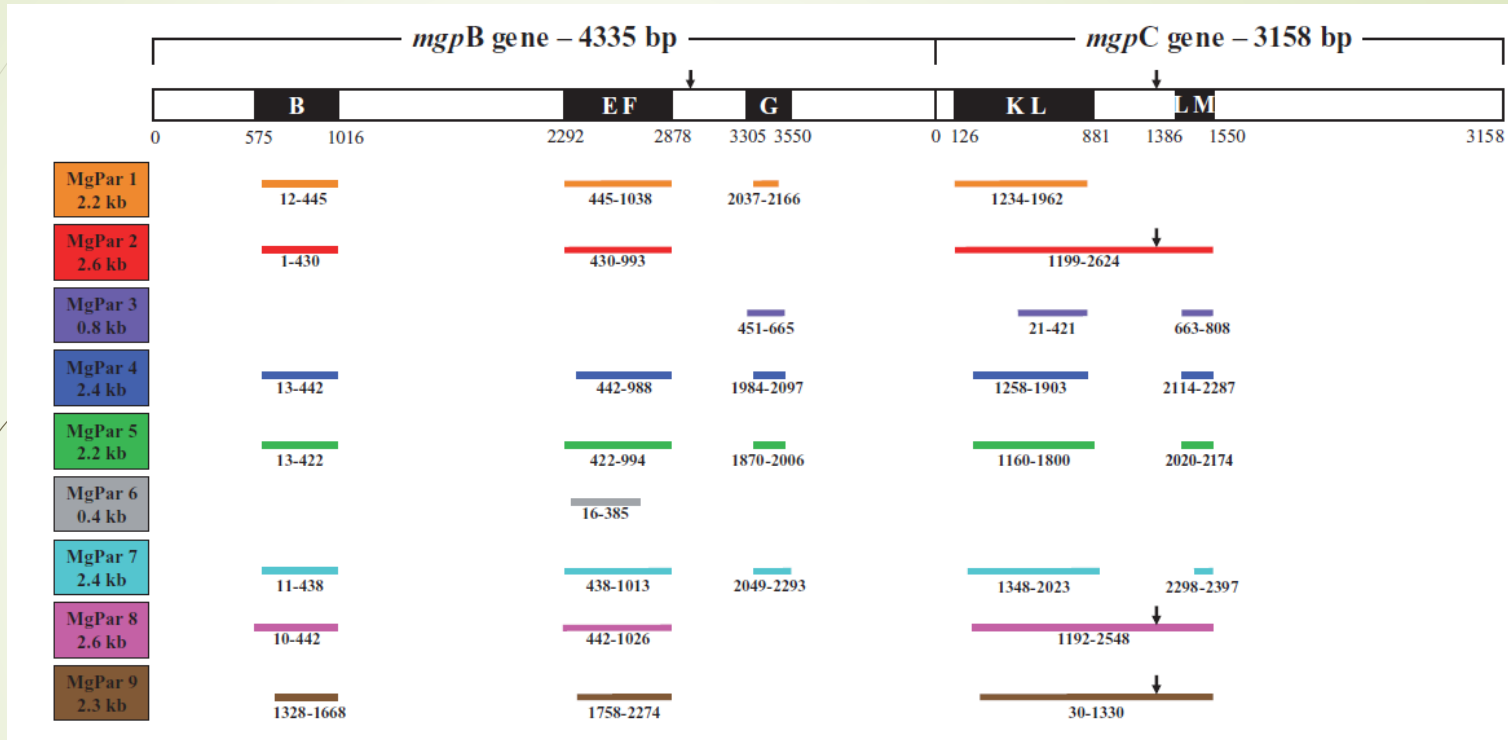
- Infections may persist for > 2 yrs
 - Documented in human infections and animal models
 - Antibiotic treatment failures
 - Persisters vs Resisters
 - Immune evasion – HOW?

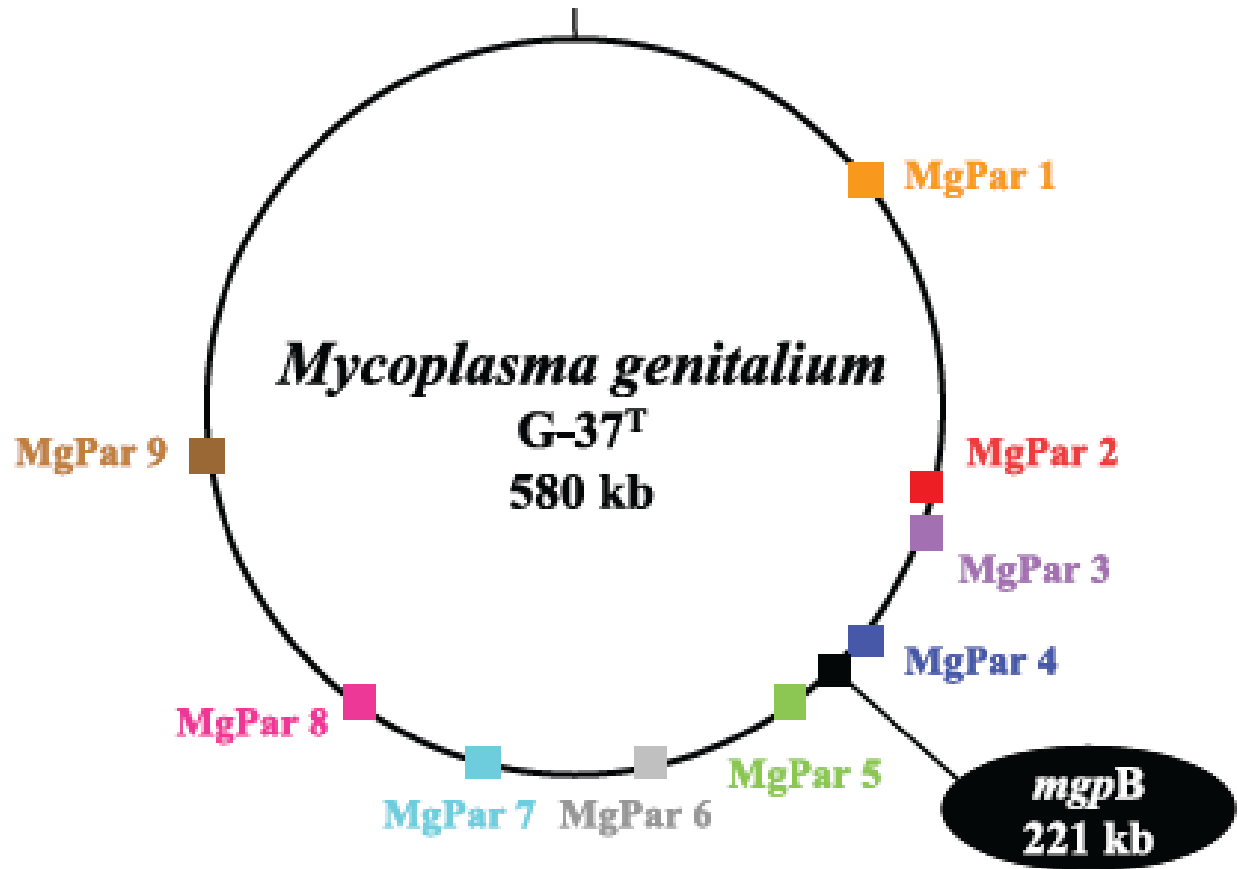


Genome sequencing reveals:

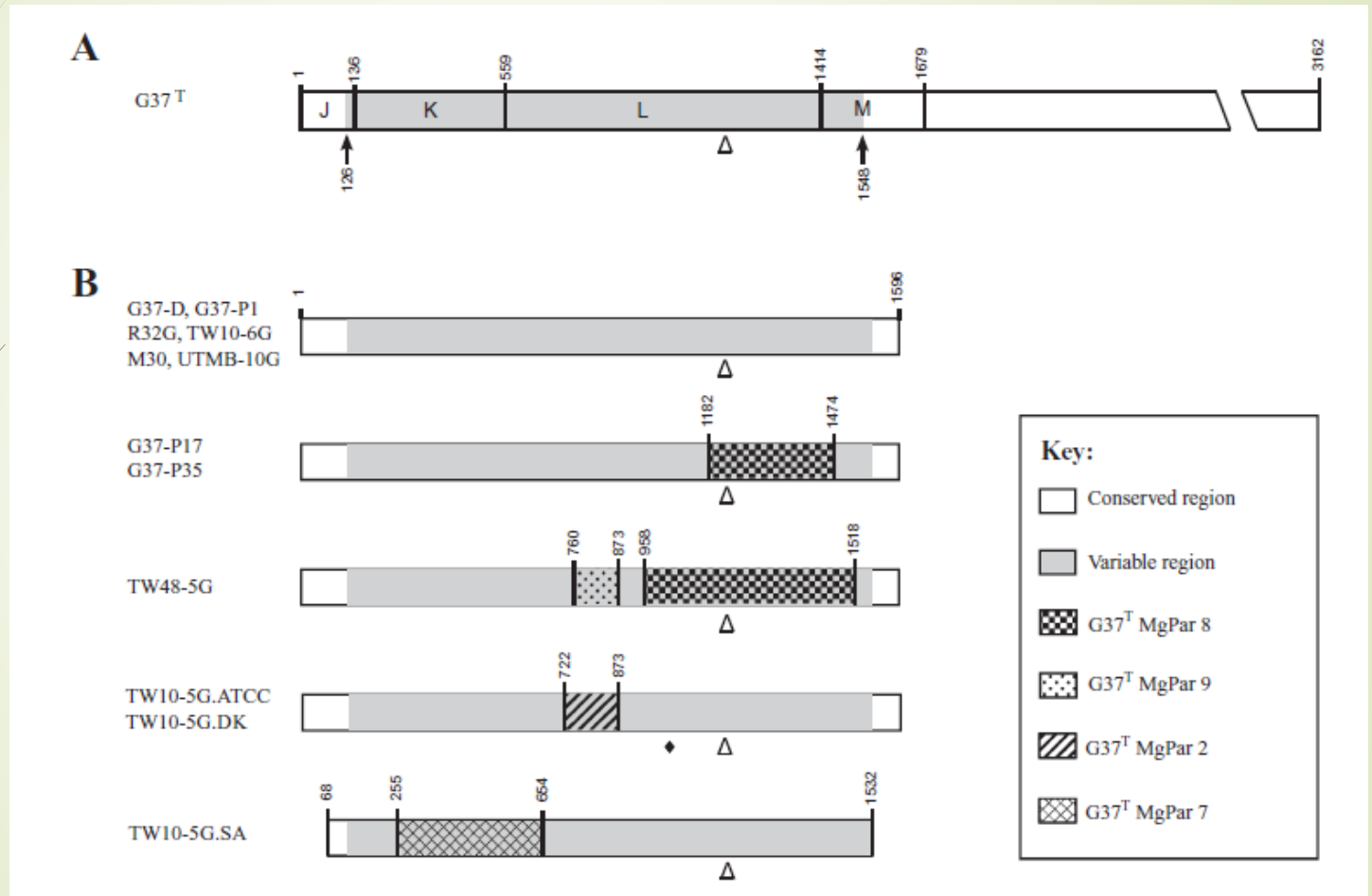
P1 homolog

P90-P40 homolog (B&C)



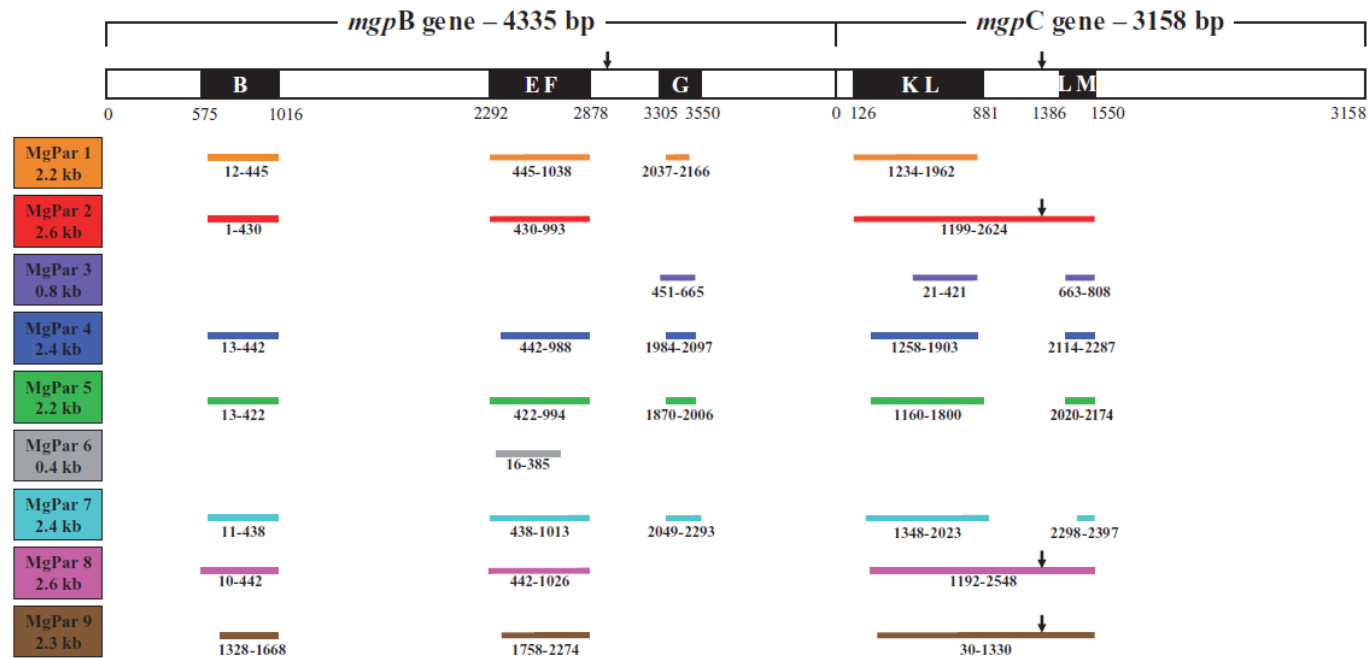
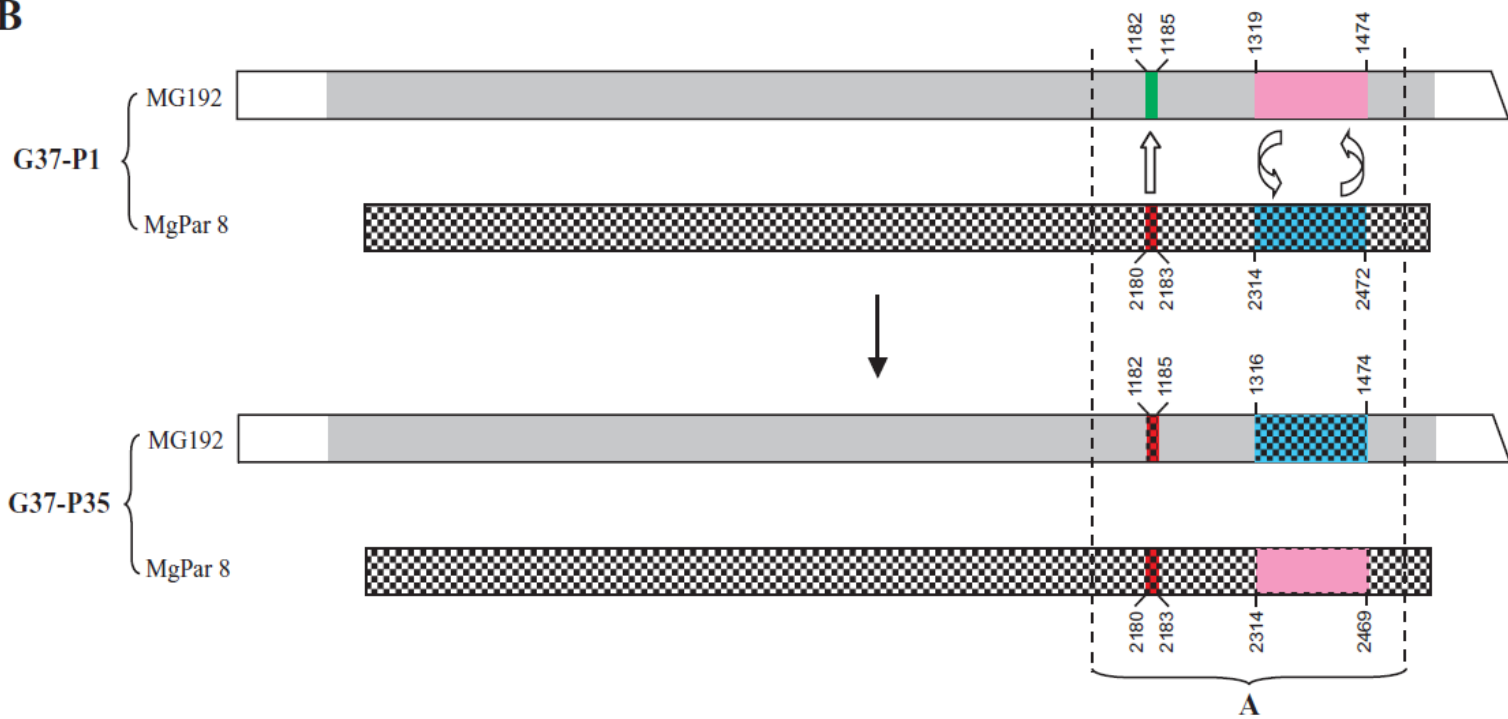


M. genitalium Genome Plasticity During Culture



(Homologous recombination and site-specific recombination)

B



M. genitalium Genome Plasticity During Infection

