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Resource

An Atlas of Genetic Variation Linking Pathogen-Induced Cellular Traits to Human Disease

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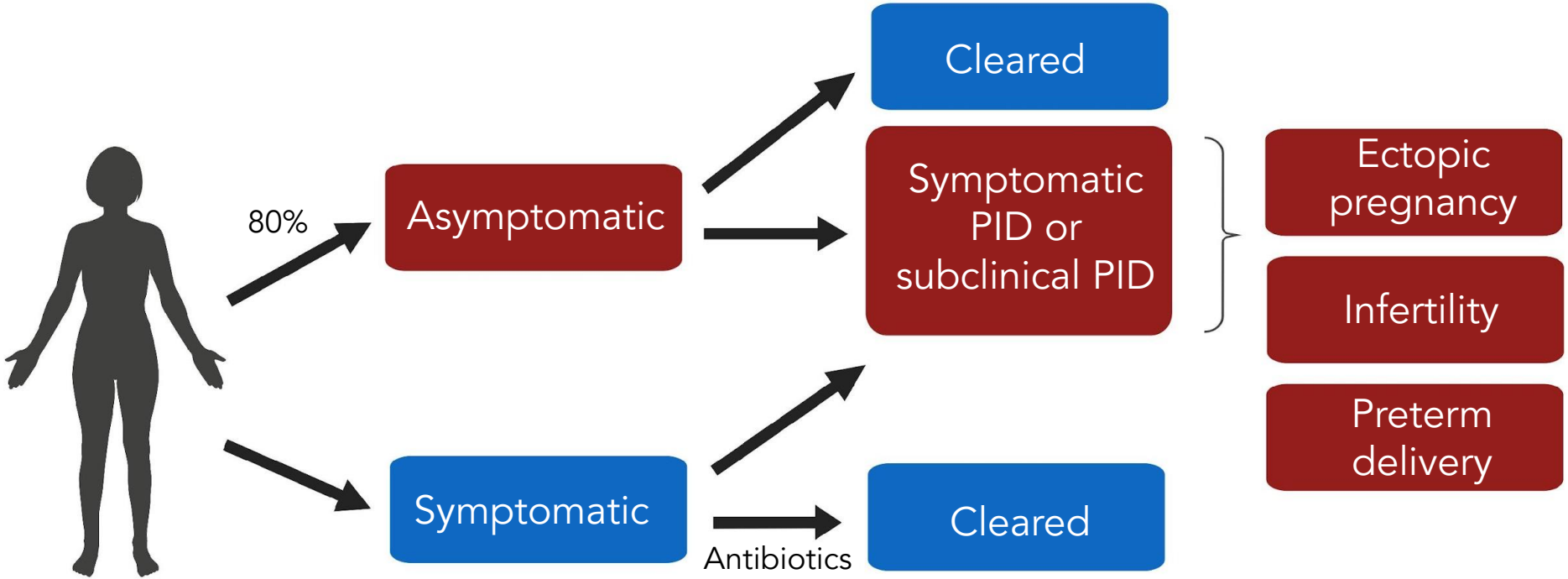
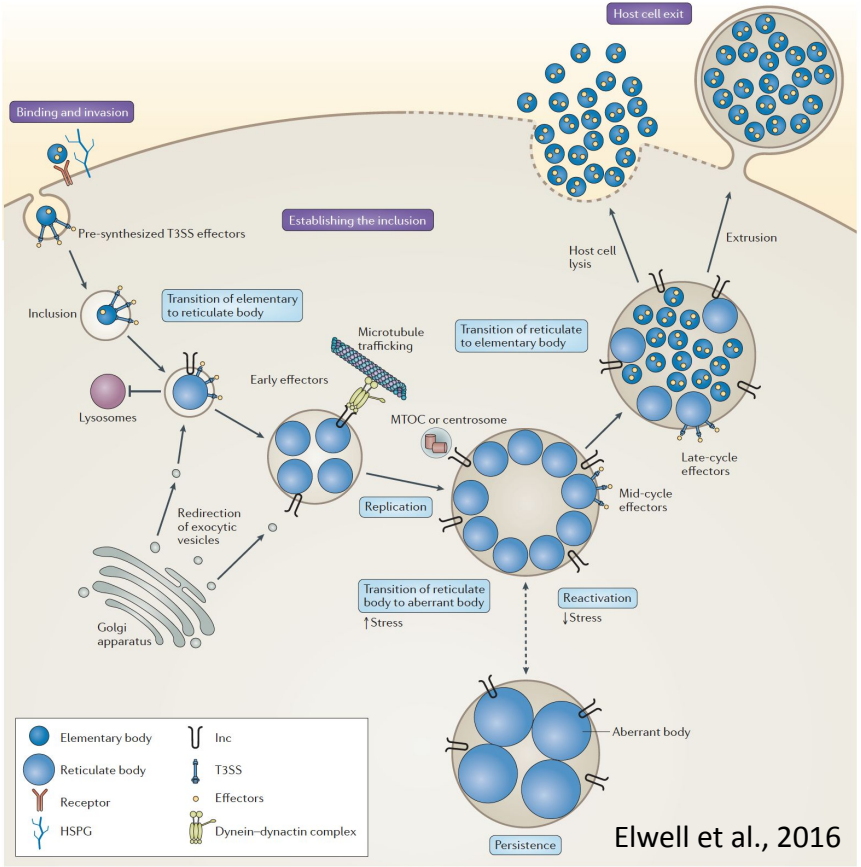
Data Expedition by
Rylee Hackley and Benjamin Schott
April 7, 2022

Chlamydia infection outcomes range from asymptomatic to severe



Chlamydia trachomatis is an obligate intracellular pathogen



Elwell et al., 2016

› Cell Microbiol. 2016 May;18(5):761-75. doi: 10.1111/cmi.12549. Epub 2016 Jan 17.

The Chlamydia trachomatis Ctad1 invasin exploits the human integrin β1 receptor for host cell entry

Sonja Stallmann [1], Johannes H Hegemann [1]

› Biochem Biophys Res Commun. 2018 Jan 1;495(1):353-359. doi: 10.1016/j.bbrc.2017.11.005. Epub 2017 Nov 3.

Chlamydia pneumoniae exploits adipocyte lipid chaperone FABP4 to facilitate fat mobilization and intracellular growth in murine adipocytes

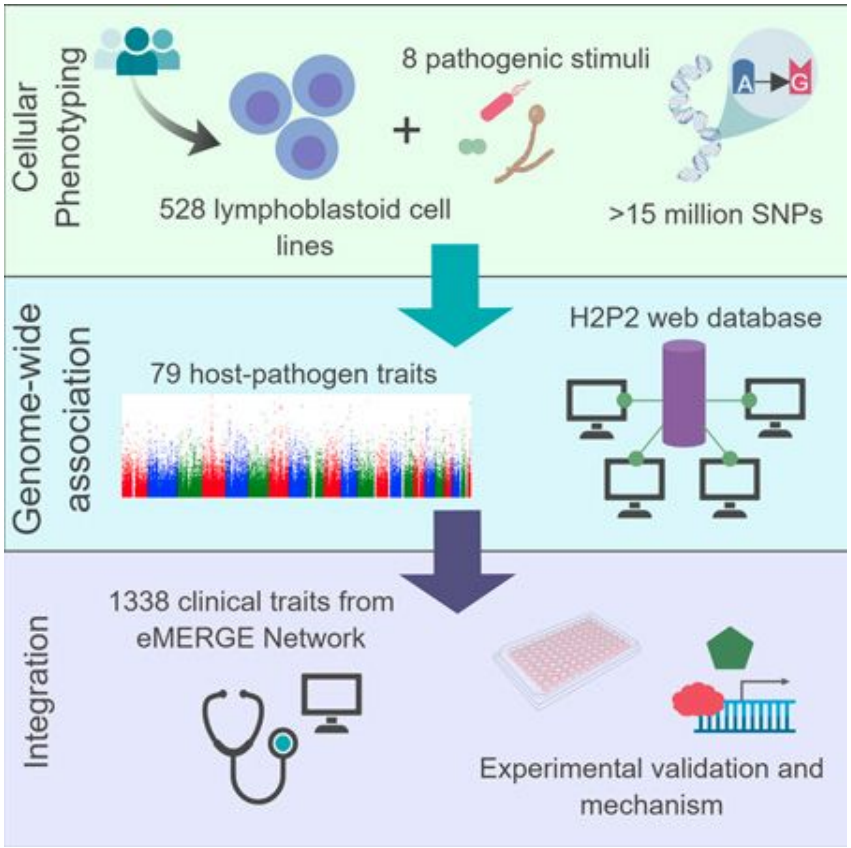
Nirwana Fitriani Walenna [1], Yusuke Kurihara [2], Bin Chou [2], Kazunari Ishii [2], Toshinori Soejima [2], Ryota Itoh [2], Akinori Shimizu [2], Takeshi Ichinohe [3], Kenji Hiromatsu [4]

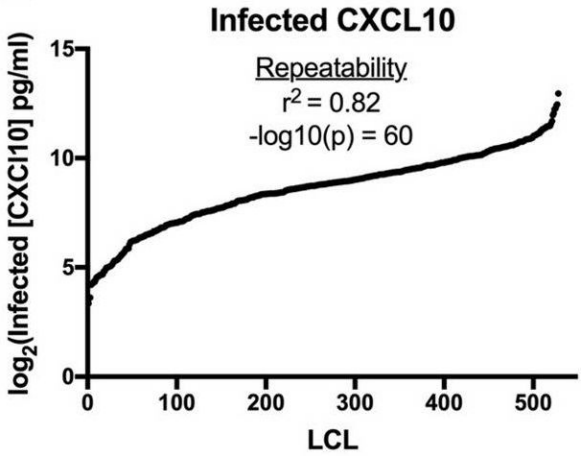
Review › Drugs Today (Barc). 2006 Mar;42 Suppl A:75-81.

Innate immunity in defense against Chlamydia trachomatis infections

J A Severin [1], J M Ossewaarde

Cellular models and this screen





Advantages:

- Quantitative phenotypes instead of Case-Control
- Experimental platform

Disadvantages:

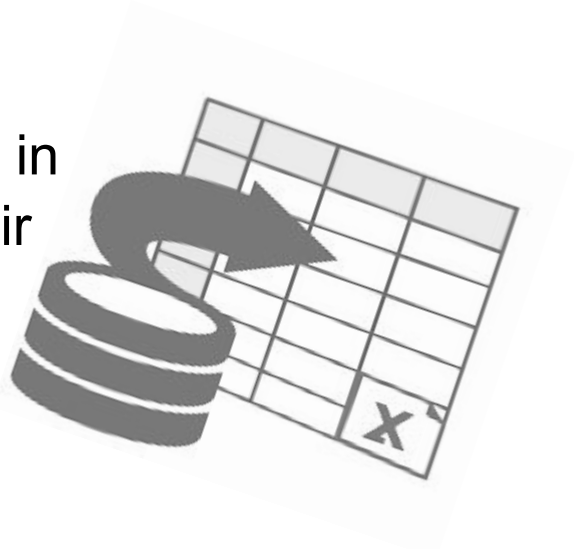
- Possible detection of cell-type-specific phenomena
- Bad assumptions about molecular correlates of disease

Today's Question:

What, if any, host genetic variants affect CXCL10 protein levels?

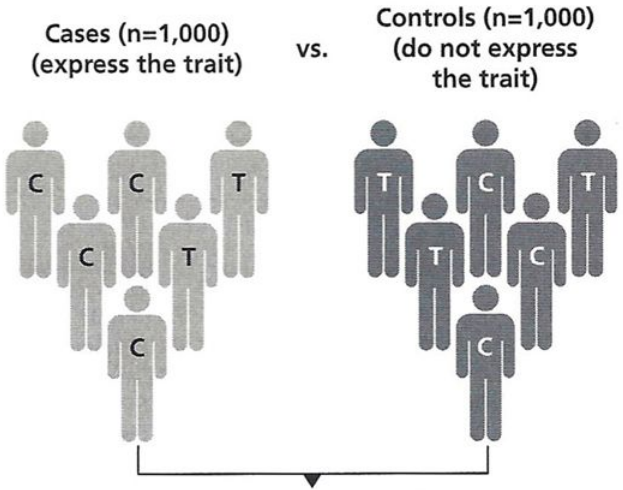
Today's Data:

The prevalence of variants within 2Mb of CXCL10 in 527 cells lines from 4 human populations, and their *association* with CXCL10/IP10 protein levels after Chlamydia infection.



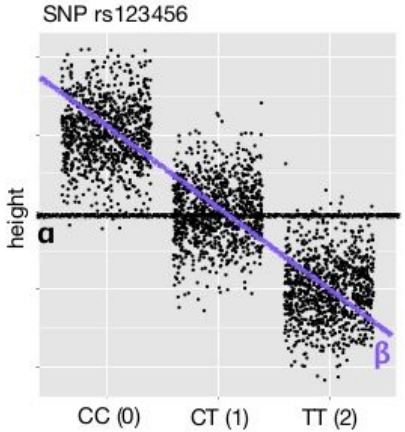
Genome-wide association testing seeks to link DNA base-pair differences with differences in a trait

Case-control study for genetic association



	C	T
Cases	62%	38%
Controls	49%	51%

Associating **One** SNP with ***Quantitative*** Trait
Linear Regression and Additive Risk Model



$y=\alpha+\beta x+\varepsilon$ T= risk allele

$x_{CC}=0$ if individual is CC

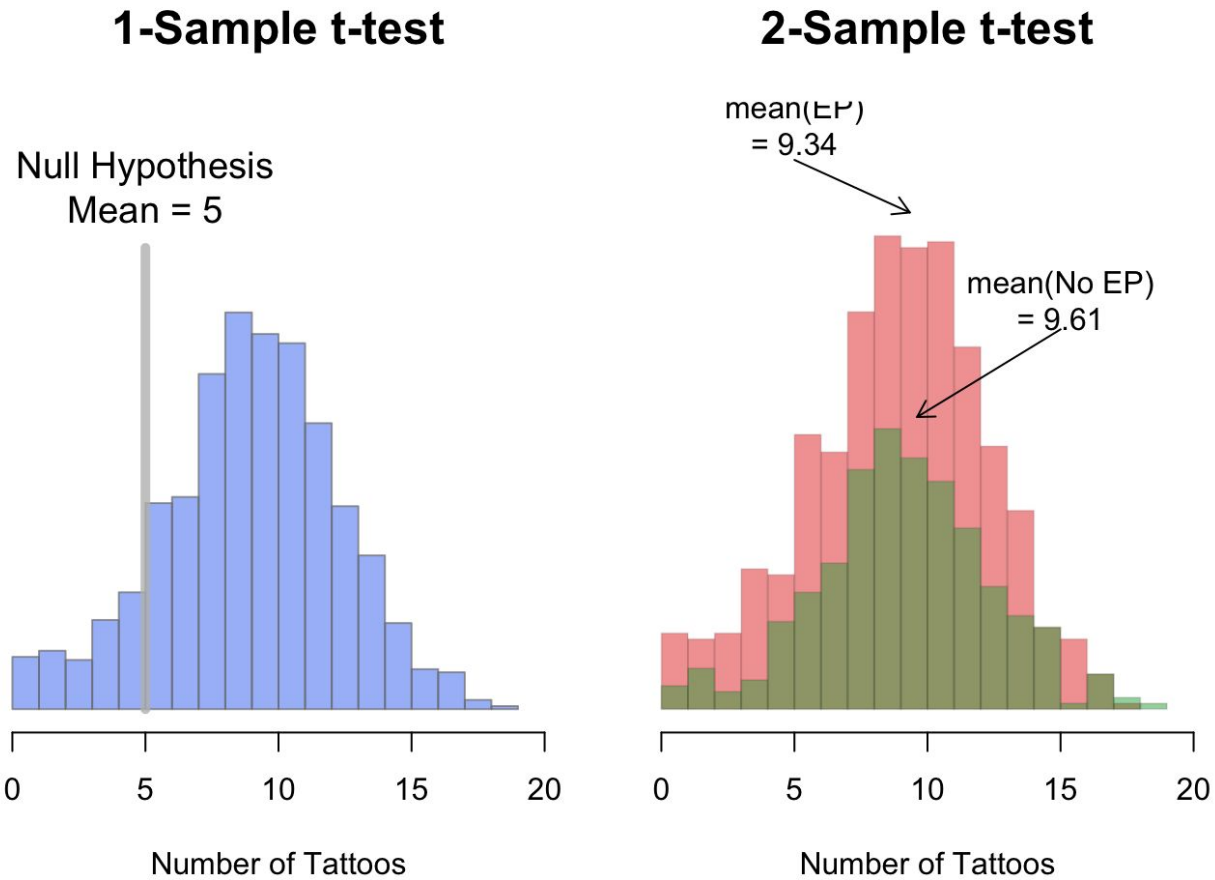
$x_{CT}=1$ if individual is CT

$x_{TT}=2$ if individual is TT

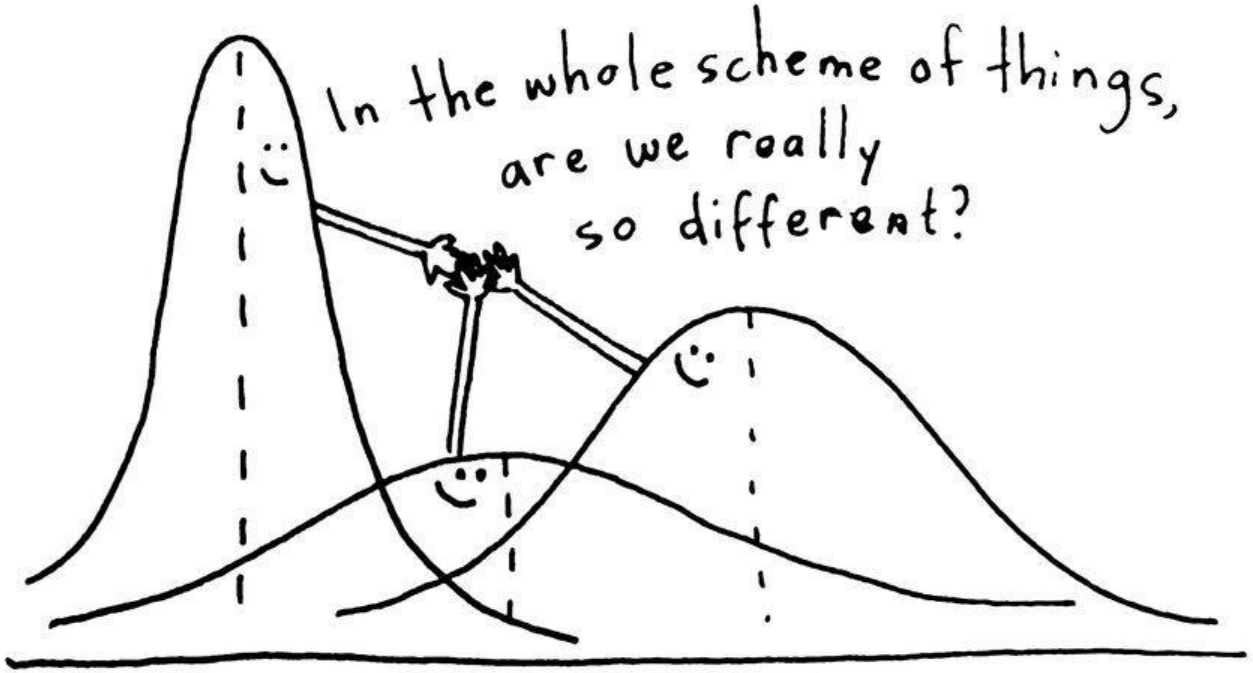
height = $\alpha+\beta x$

β: change in height for 1 risk allele

Student's T-test

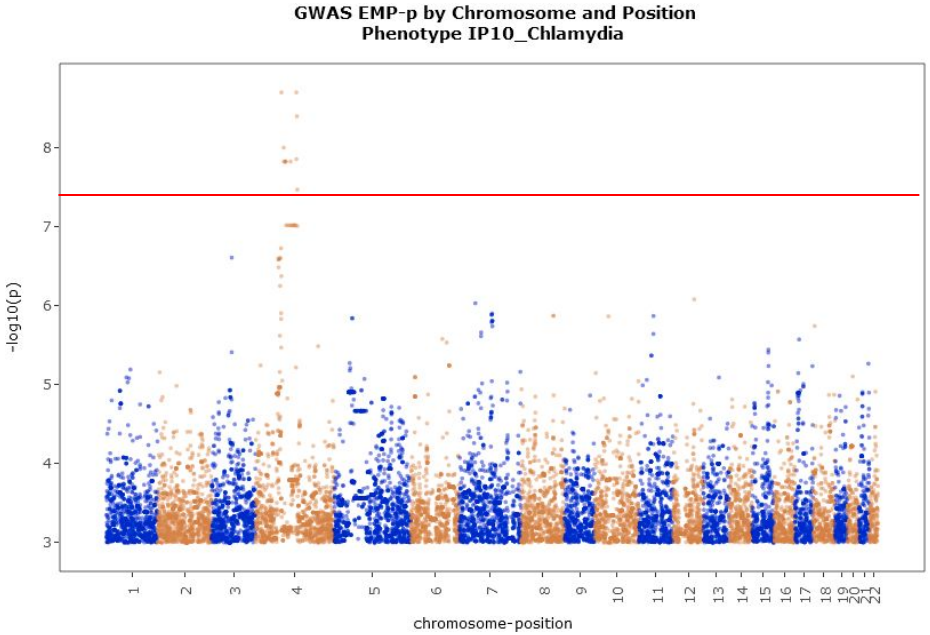


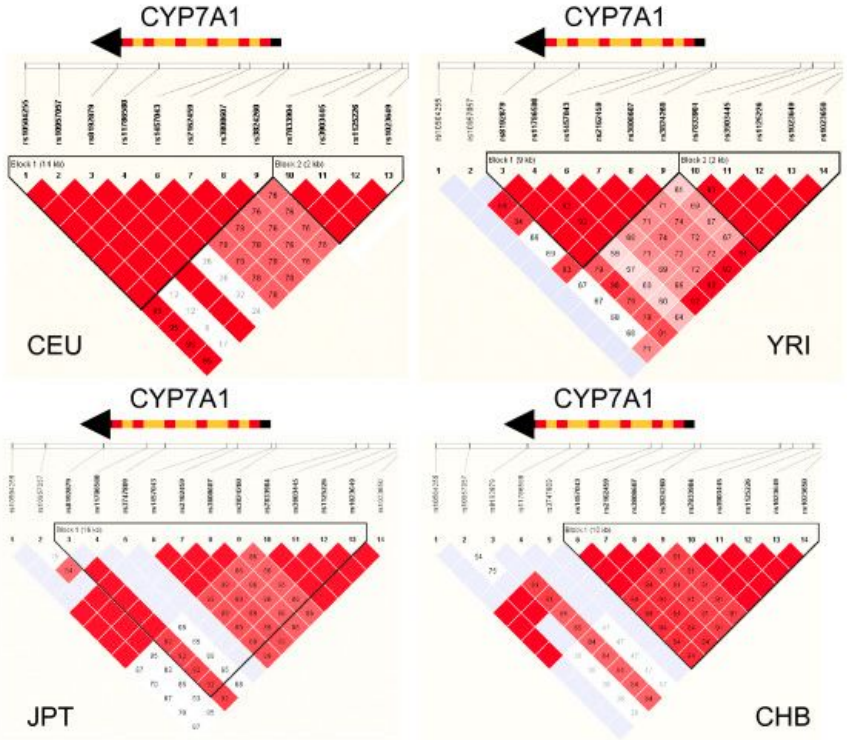
Analysis of Variance (ANOVA)



Is the between group variation greater than the within group variation?

Why is the threshold for genome-wide significance so high?

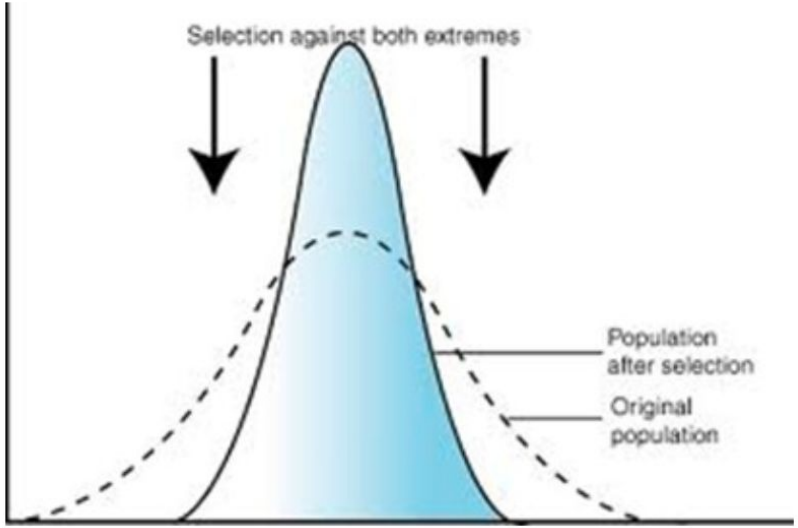




Is high CXCL10 protective? And if so, why is the polymorphism maintained?

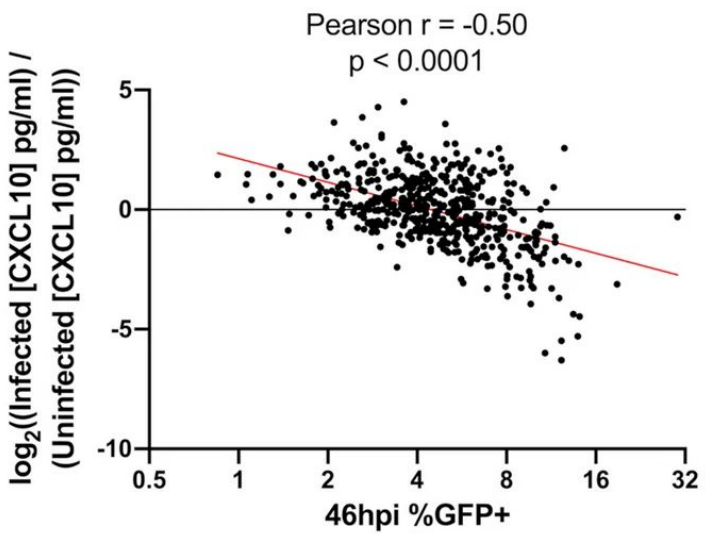
High CXCL10 -> protection from infection, predisposed to inflammatory disorders (IBS)

Balancing selection



The pathogen fights back:

Chlamydia has evolved a protease, CPAF, which actively degrades host proteins including CXCL10



https://forms.gle/UZfRBxPJCJwEnZU48