Micro 204

Flipped Classroom Session

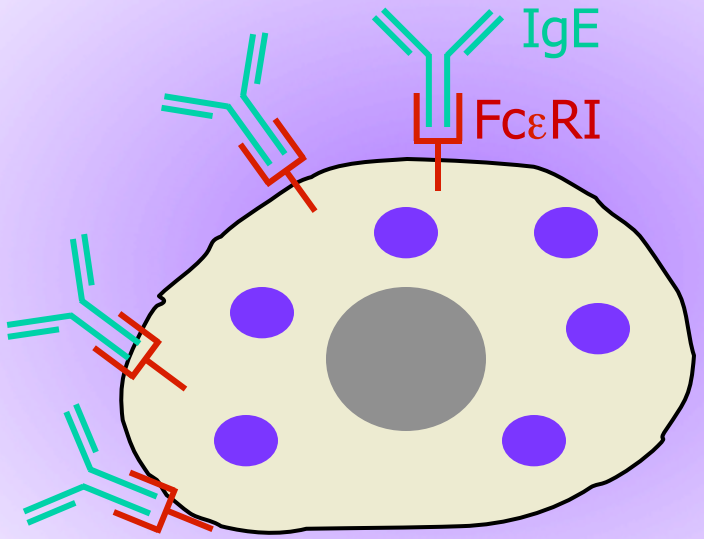
Antibodies

IgE and IgA

Chris Allen
Tony DeFranco

IgE Antibody Function

Parasitic worm



mast cell or basophil

mediators

including

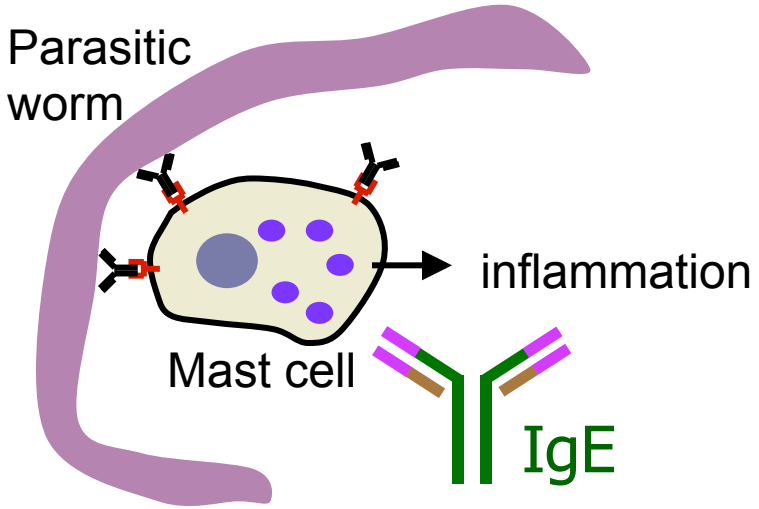
histamine

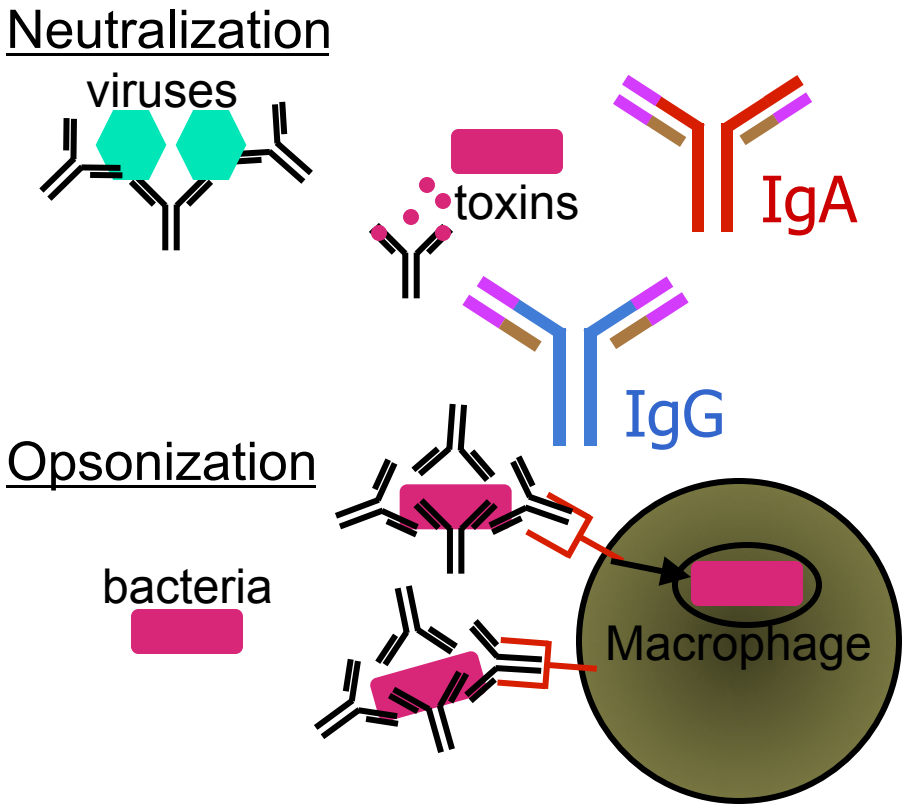
chemokines

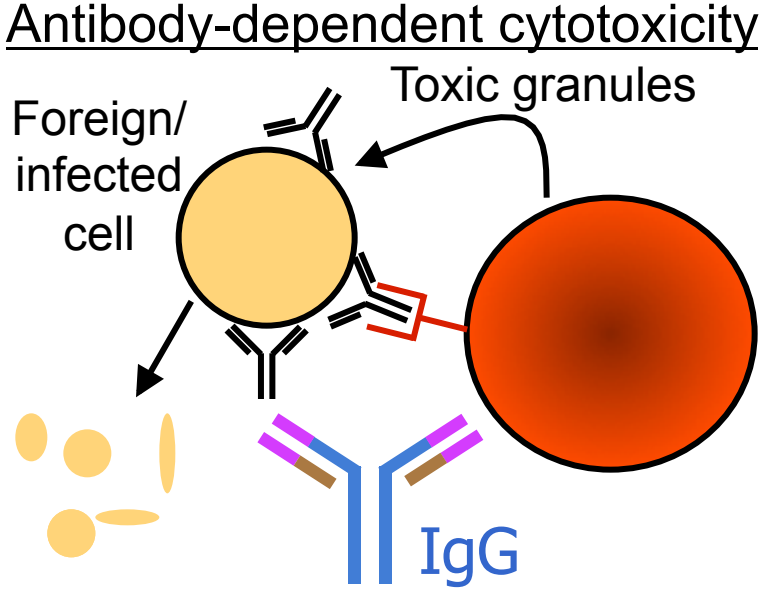
cytokines

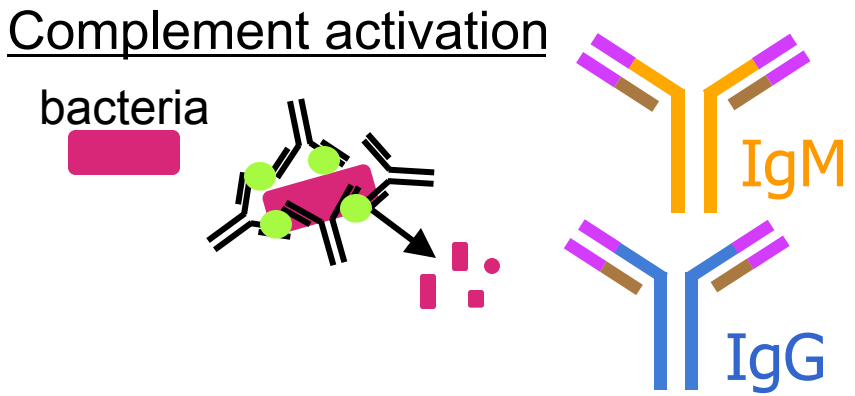
inflammation

Normal Functions of Antibodies

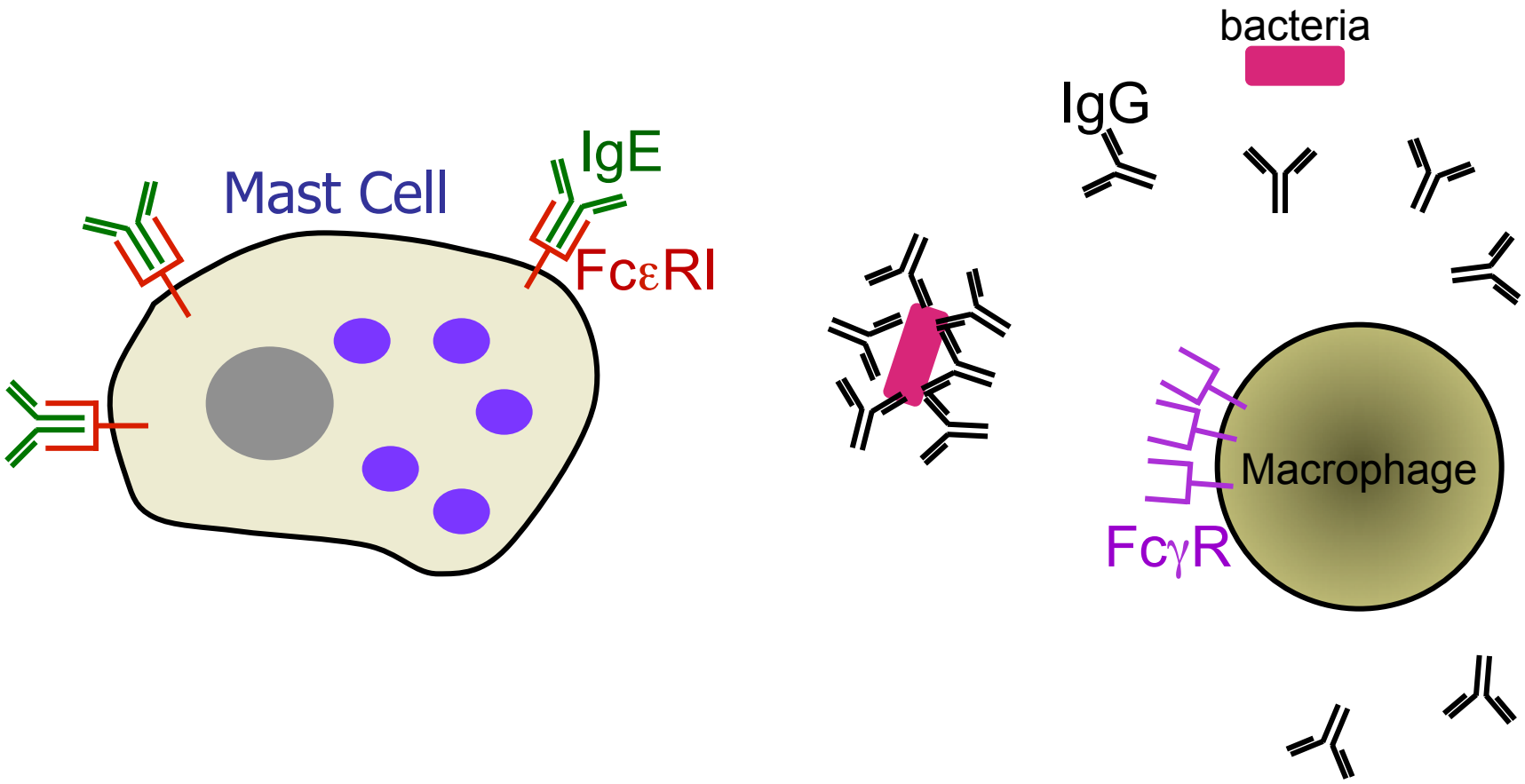




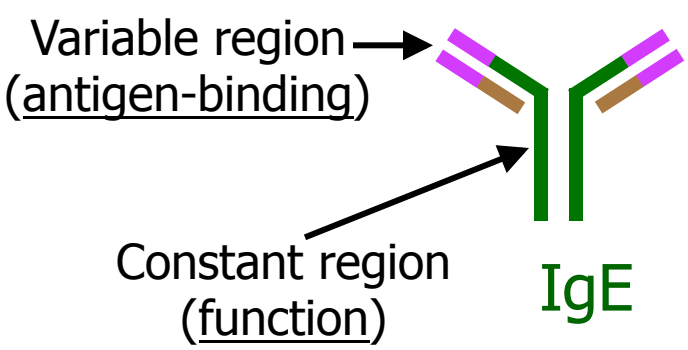




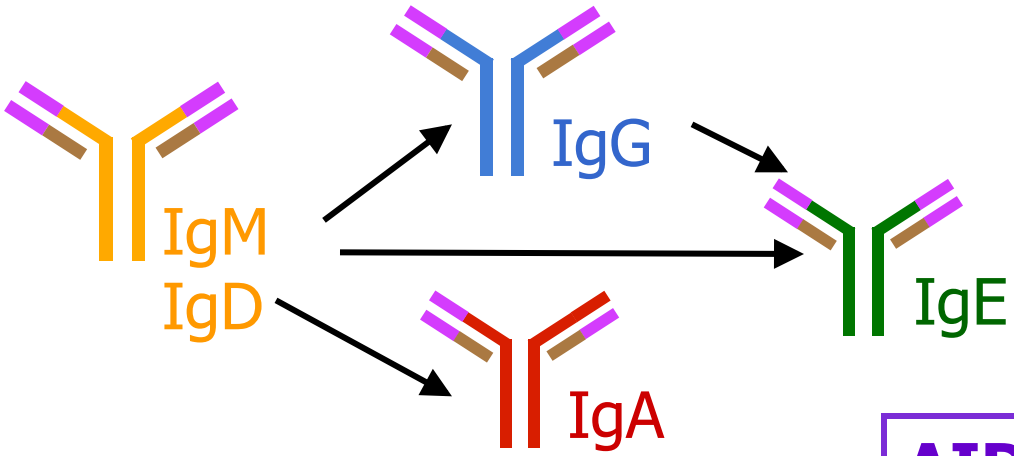
Differences in Fc Receptors



Changes in Antibodies

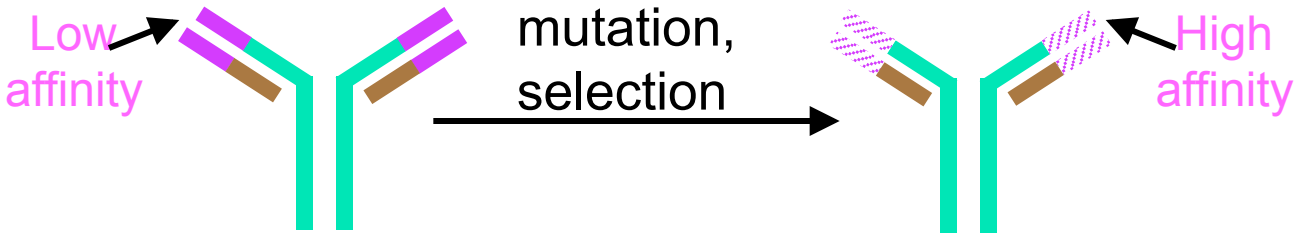


- Class switch recombination

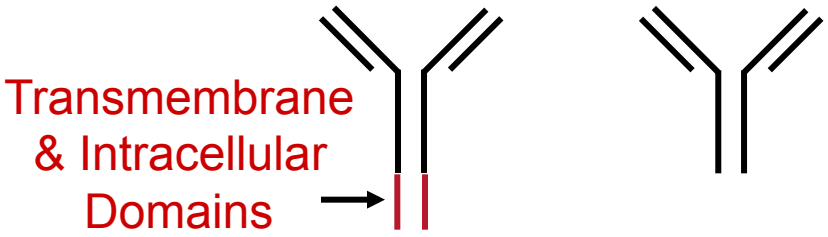


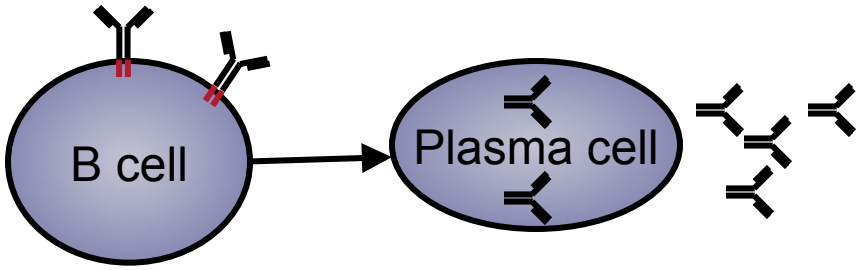
AID

- Affinity maturation

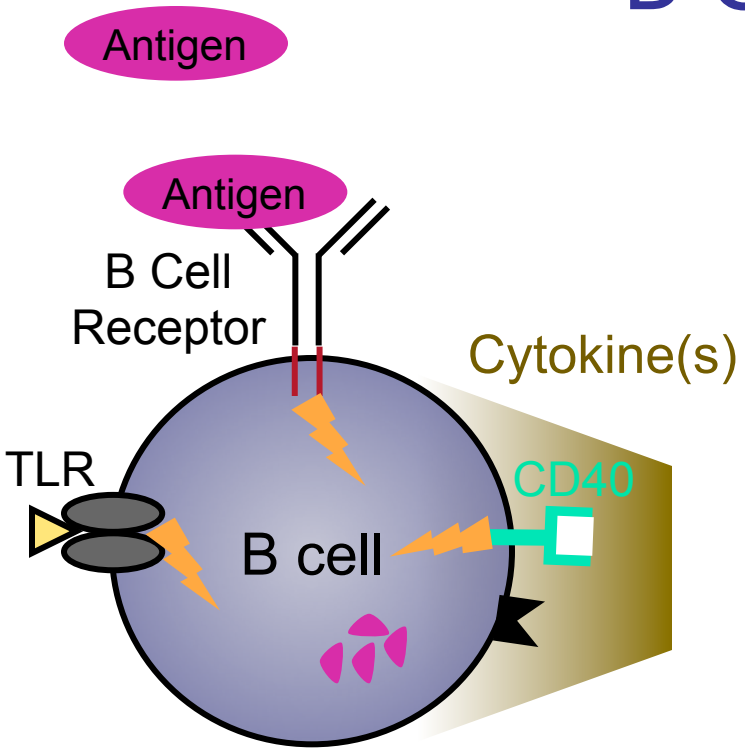


- Membrane vs secreted



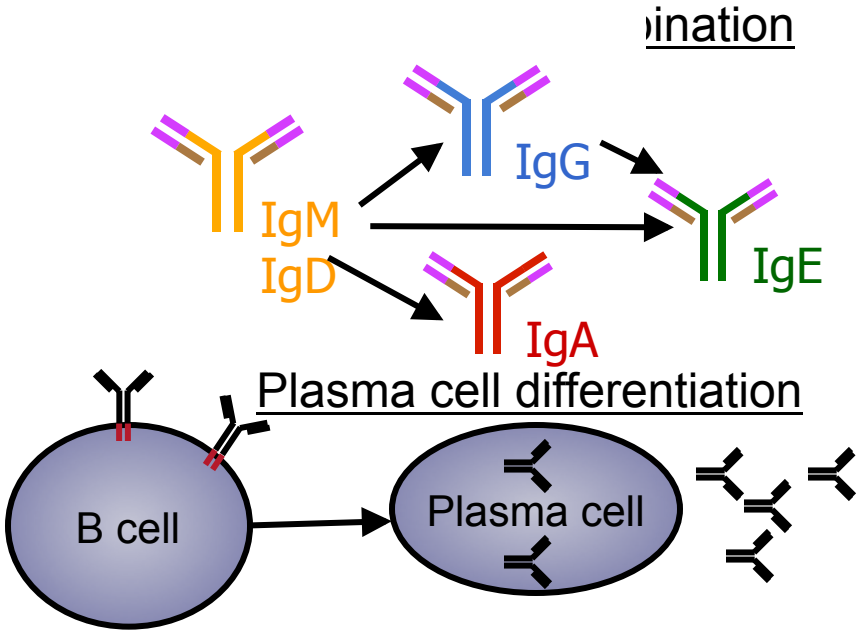


B Cell Activation

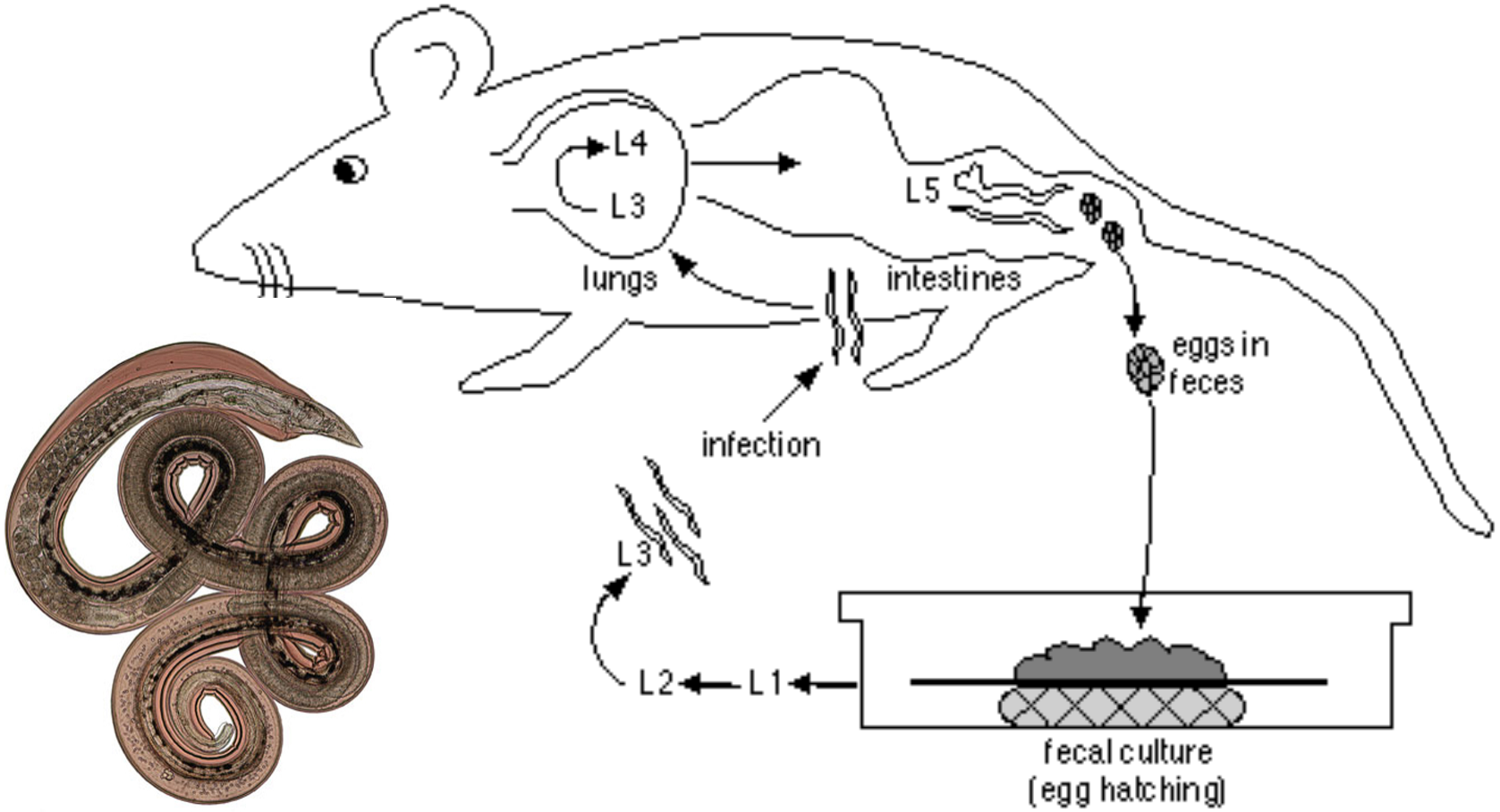


Signaling steps

1. B Cell Receptor (BCR)
2. Innate receptors (e.g. TLR)
3. CD40
4. Cytokine(s)

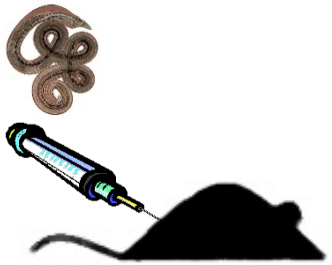


Helminth parasite model: *Nippostrongylus brasiliensis* infection

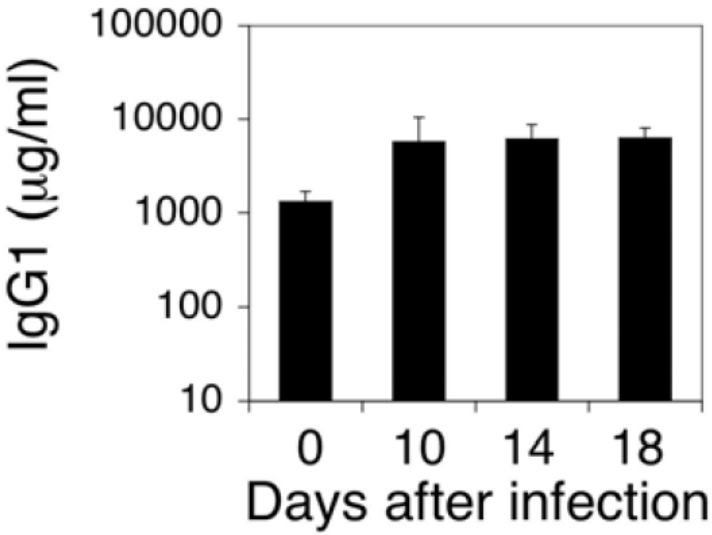


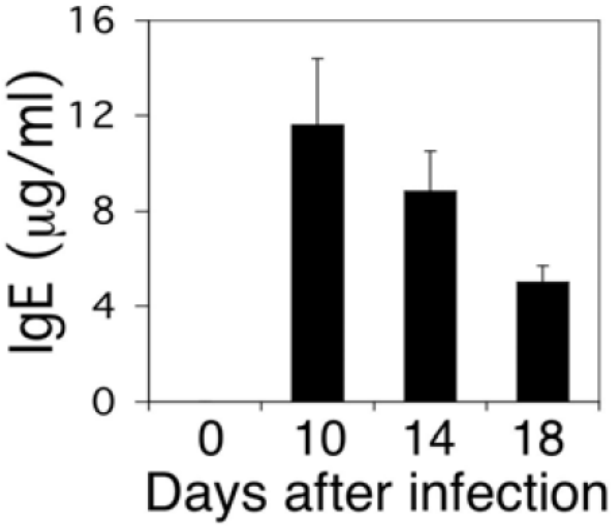
Differences in Kinetics of Antibody Responses

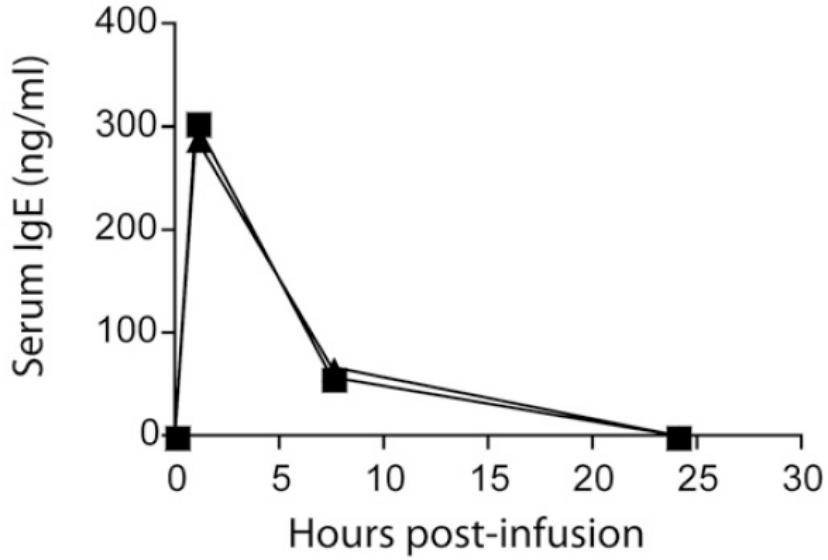
Infection
N. brasiliensis
L3 larvae



Erazo A. *et al. Immunity* 2007, 26:191-203.

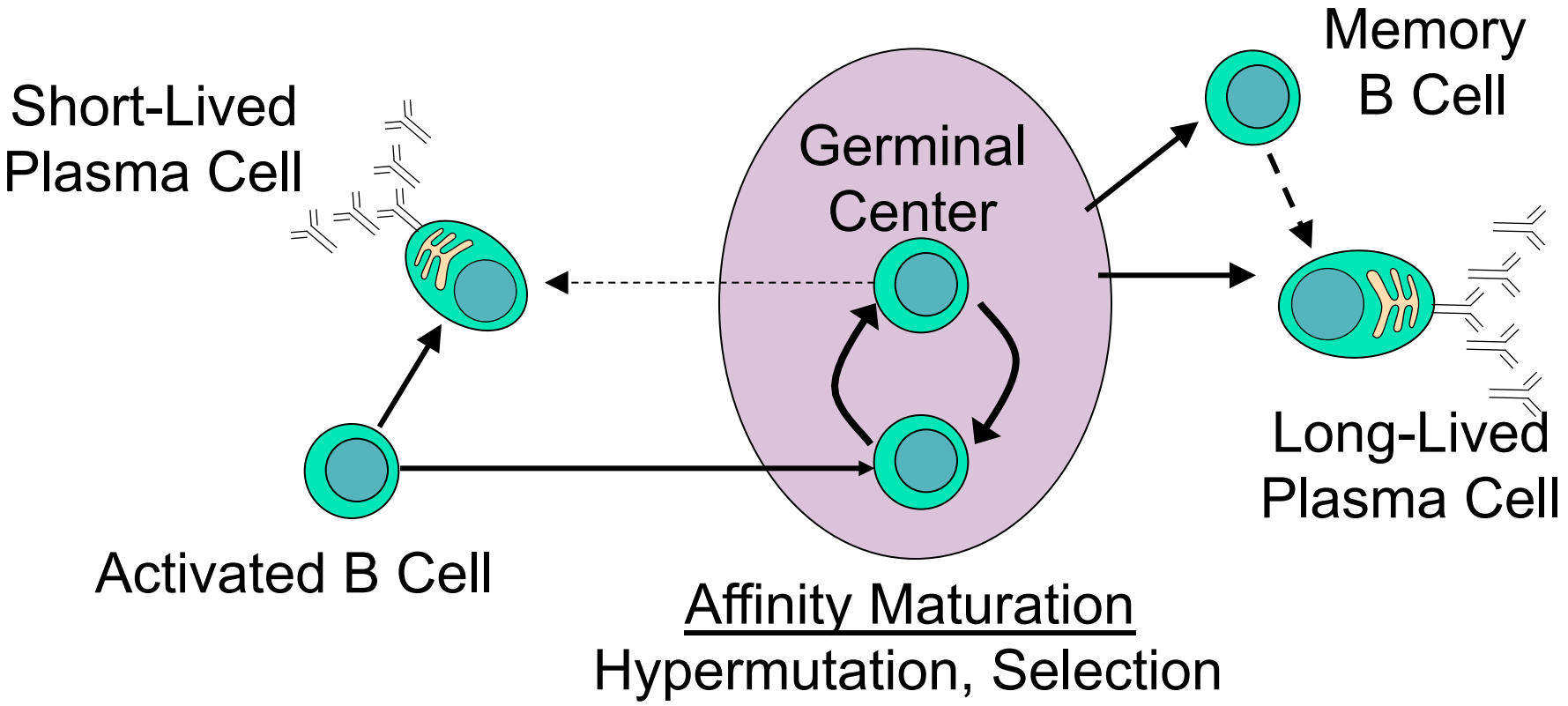




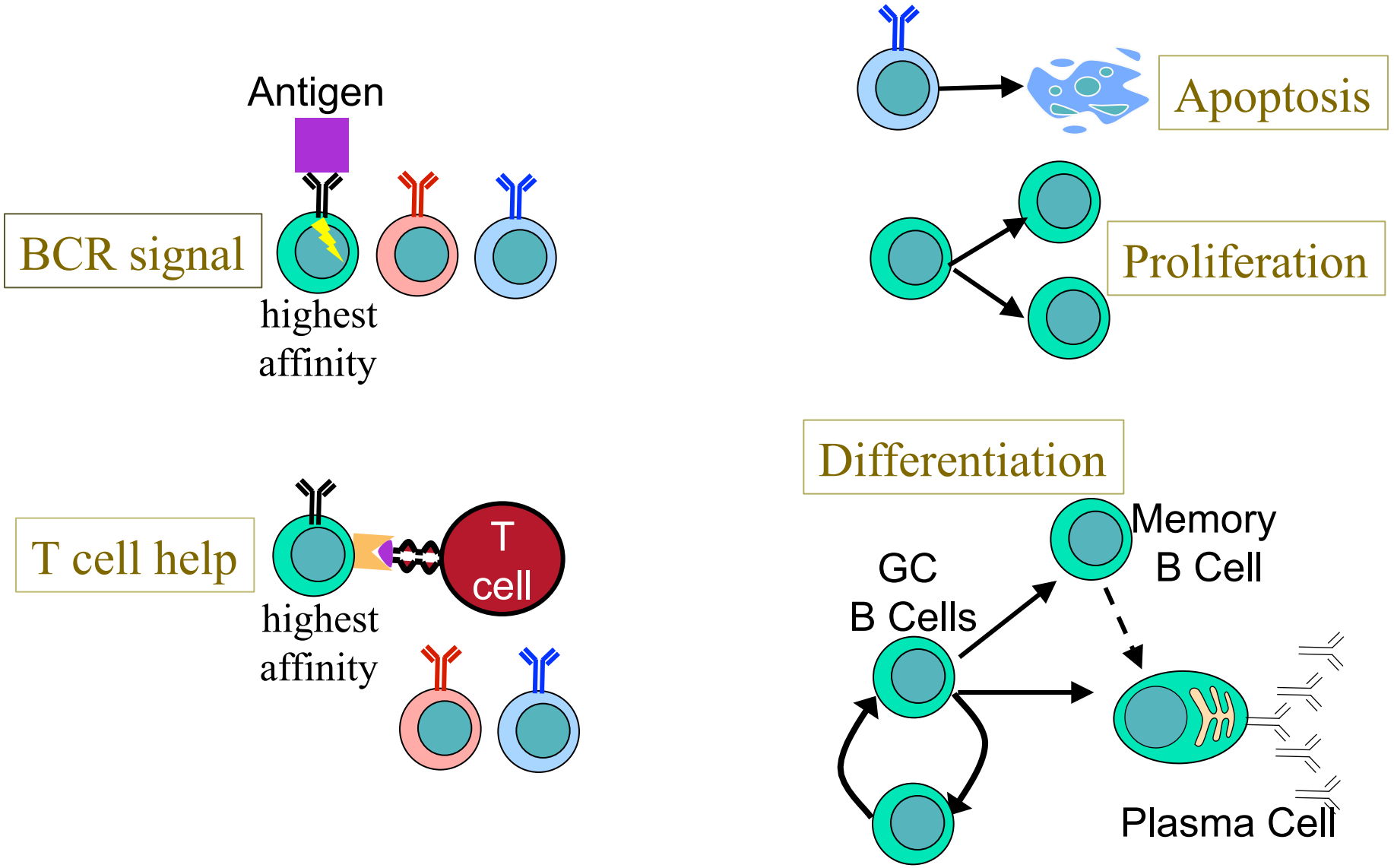


Cheng L.E. *et al.*
J Immunol 2010,
185:5040-5047.

B Cell Differentiation Pathways

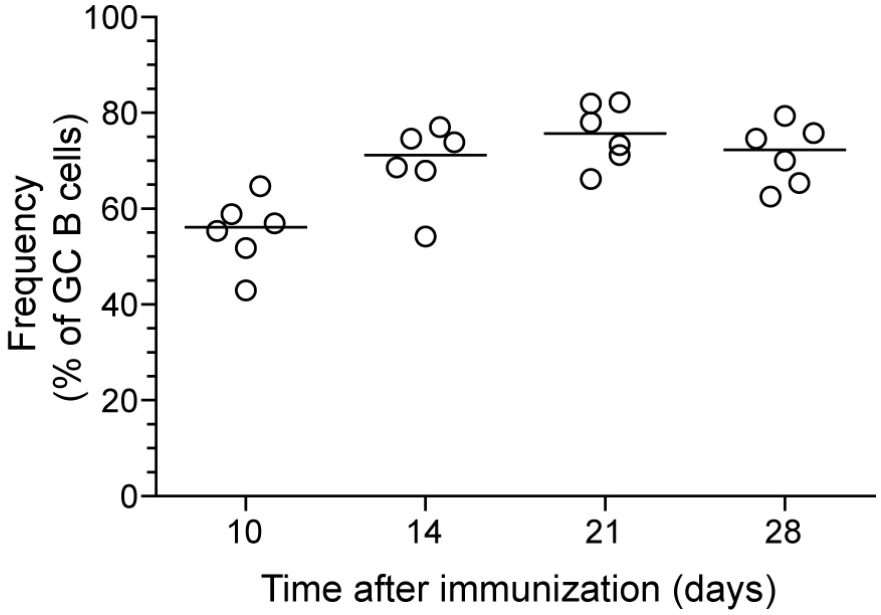


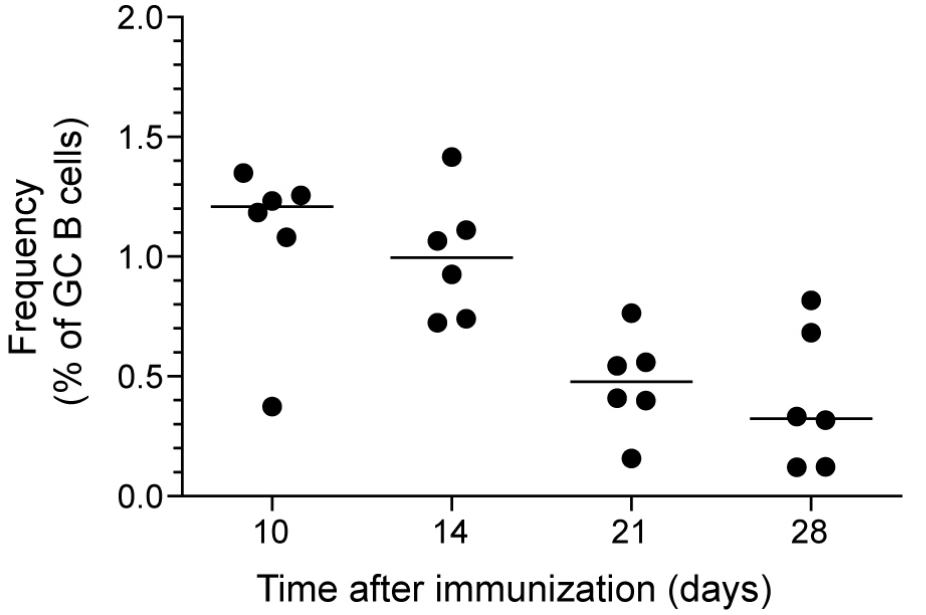
Germinal Center Selection



Differences in IgG1 vs IgE Germinal Center B Cell Responses

N. brasiliensis infection





Yang Z. *et al. Immunity* 2012, 36:857-872.

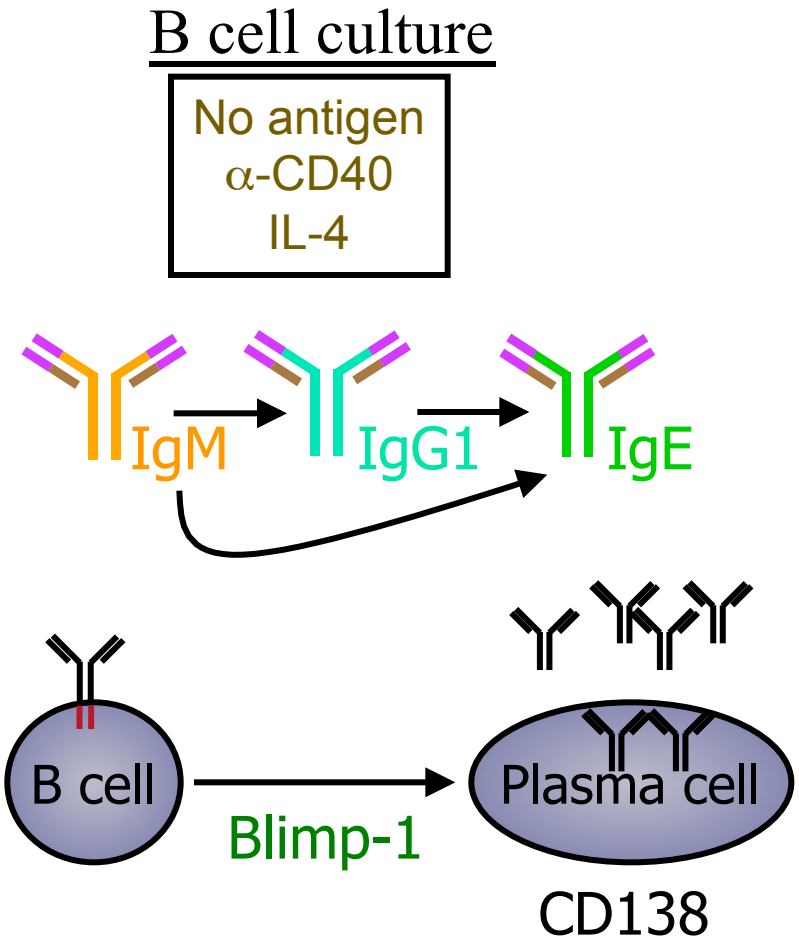
Similar data in: Talay O. *et al. Nat Immunol* 2012, 13:396-404.

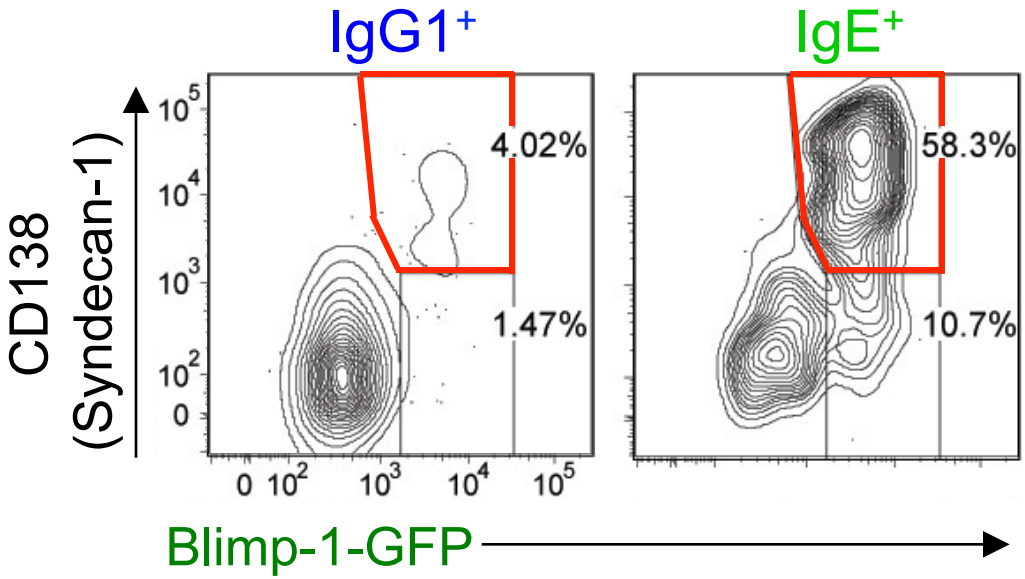
He J.S. *et al.* J Exp Med 2013, 210:2755-2771.

Questions

- Why do IgE^+ B cells disappear from the germinal center?
- What are the implications for the IgE antibody response?

IgE+ B cells are biased toward plasma cell differentiation in cell culture without antigen

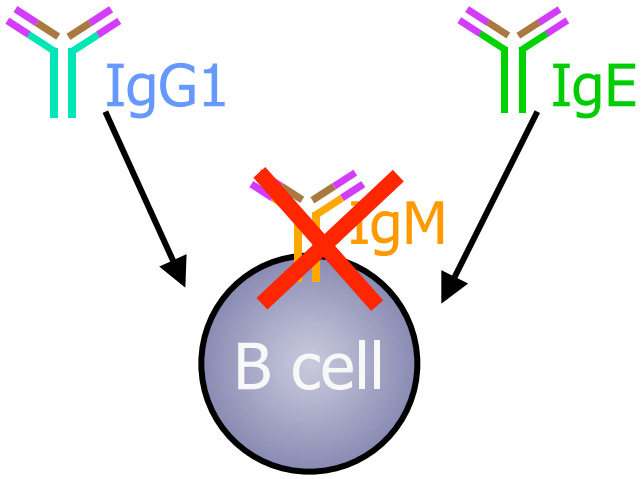




Yang, Z. et al. (2016) *eLife* 5:e21238
Similar to Haniuda, K. et al. (2016) *Nat Immunol* 17:1109

Ectopic expression of IgG1 vs IgE

<u>Retroviral transduction</u>



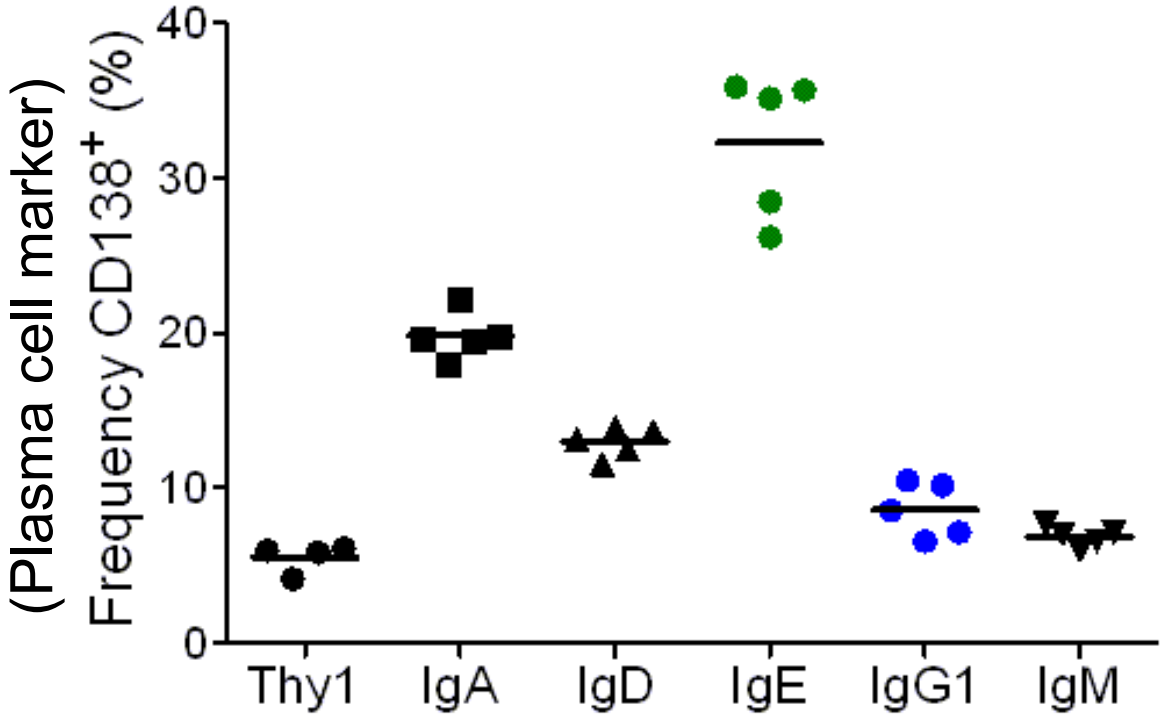
B1-8$^{flox/+}$ Cγ1-Cre

Haniuda, K. et al. (2016) *Nat Immunol* 17:1109

Yang, Z. et al. (2016) *eLife* 5:e21238

IgE Induces Plasma Cell Differentiation

without antigen



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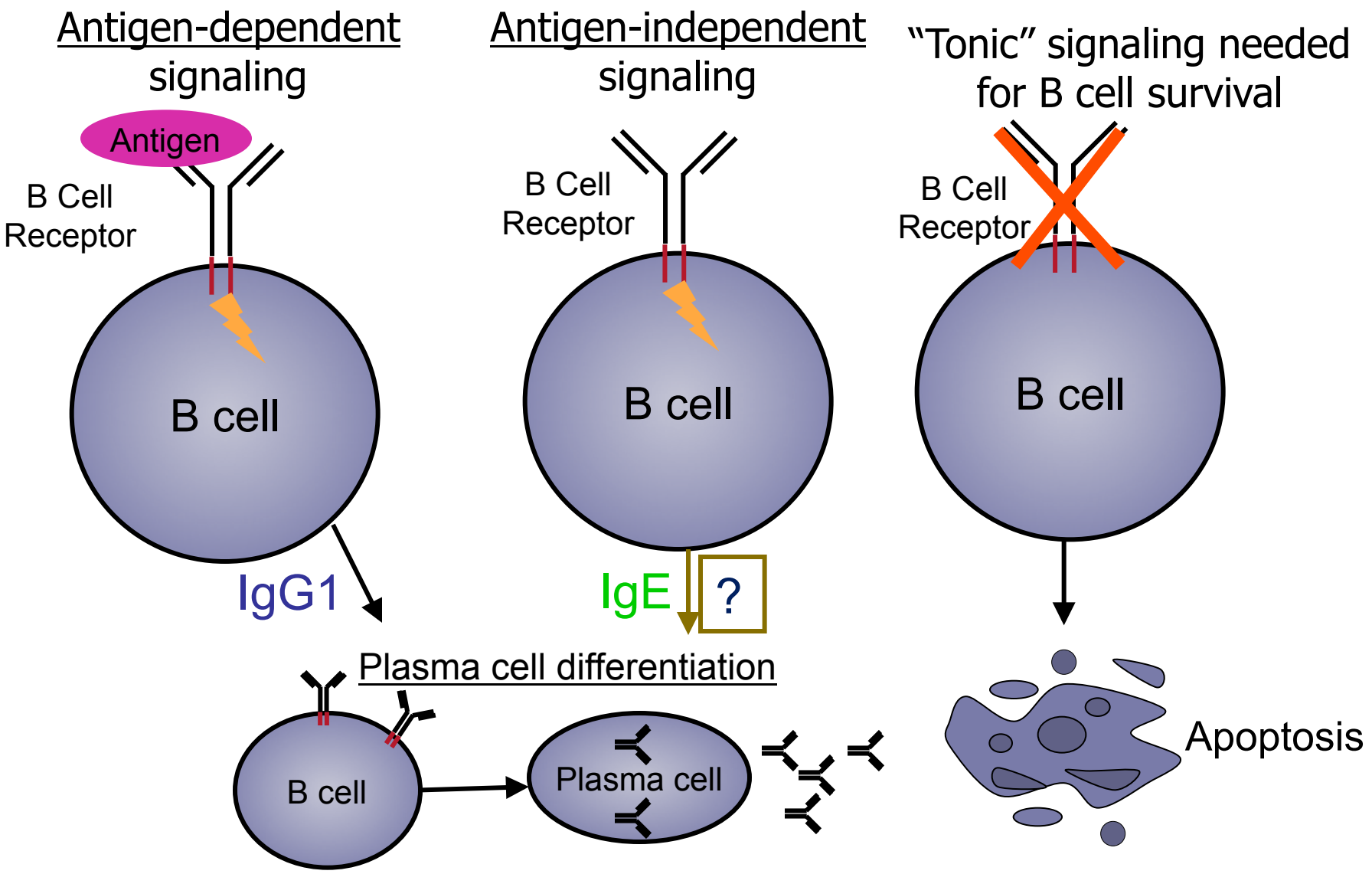
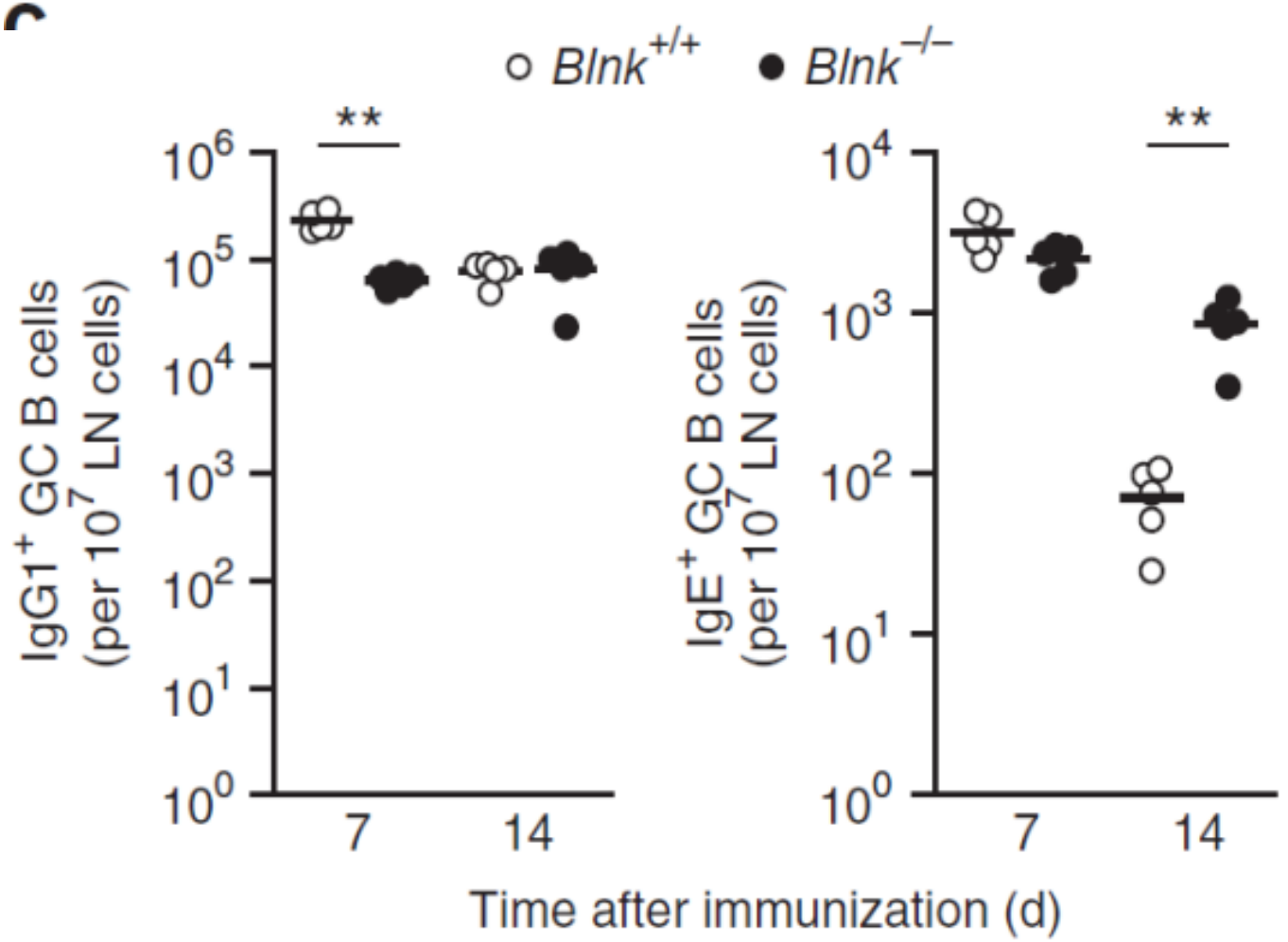
Antigen-dependent *vs.* independent B cell receptor signaling

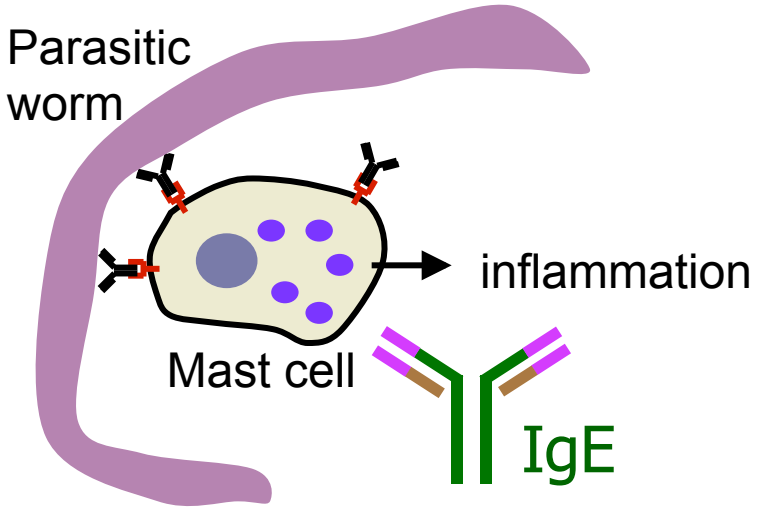


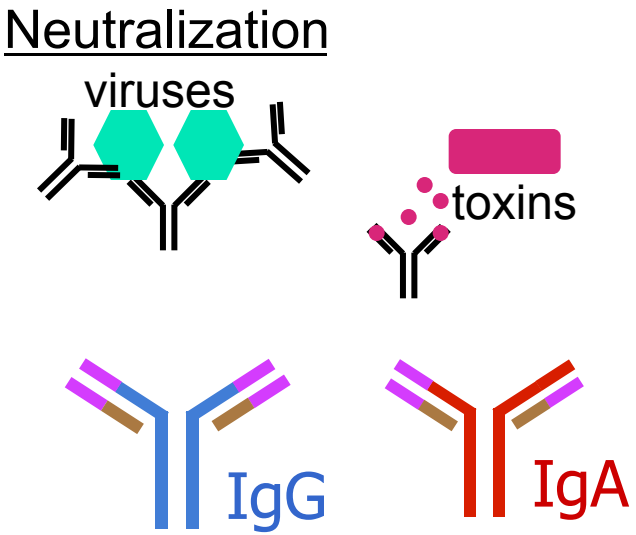
IgE GC B cells maintained with BCR signaling mutant



Haniuda et al. (2016) *Nat Immunol* 17:1109
Similar to: Yang, Z. et al. (2016) *eLife* 5:e21238

Why IgE B cell lifespan and affinity may be limited





Systemic IgE activation