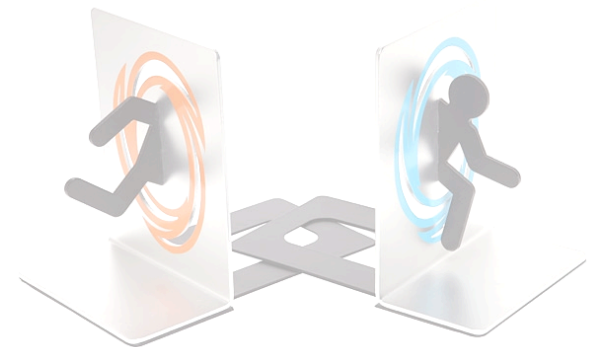
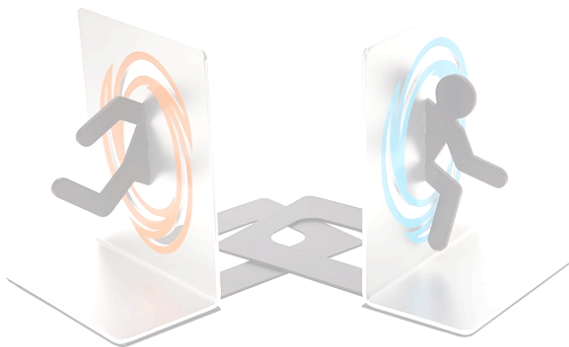
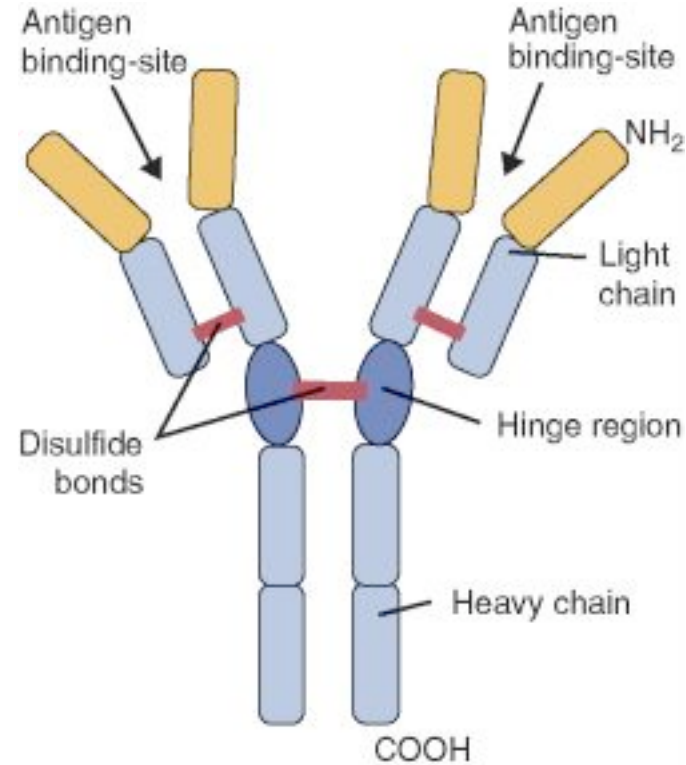
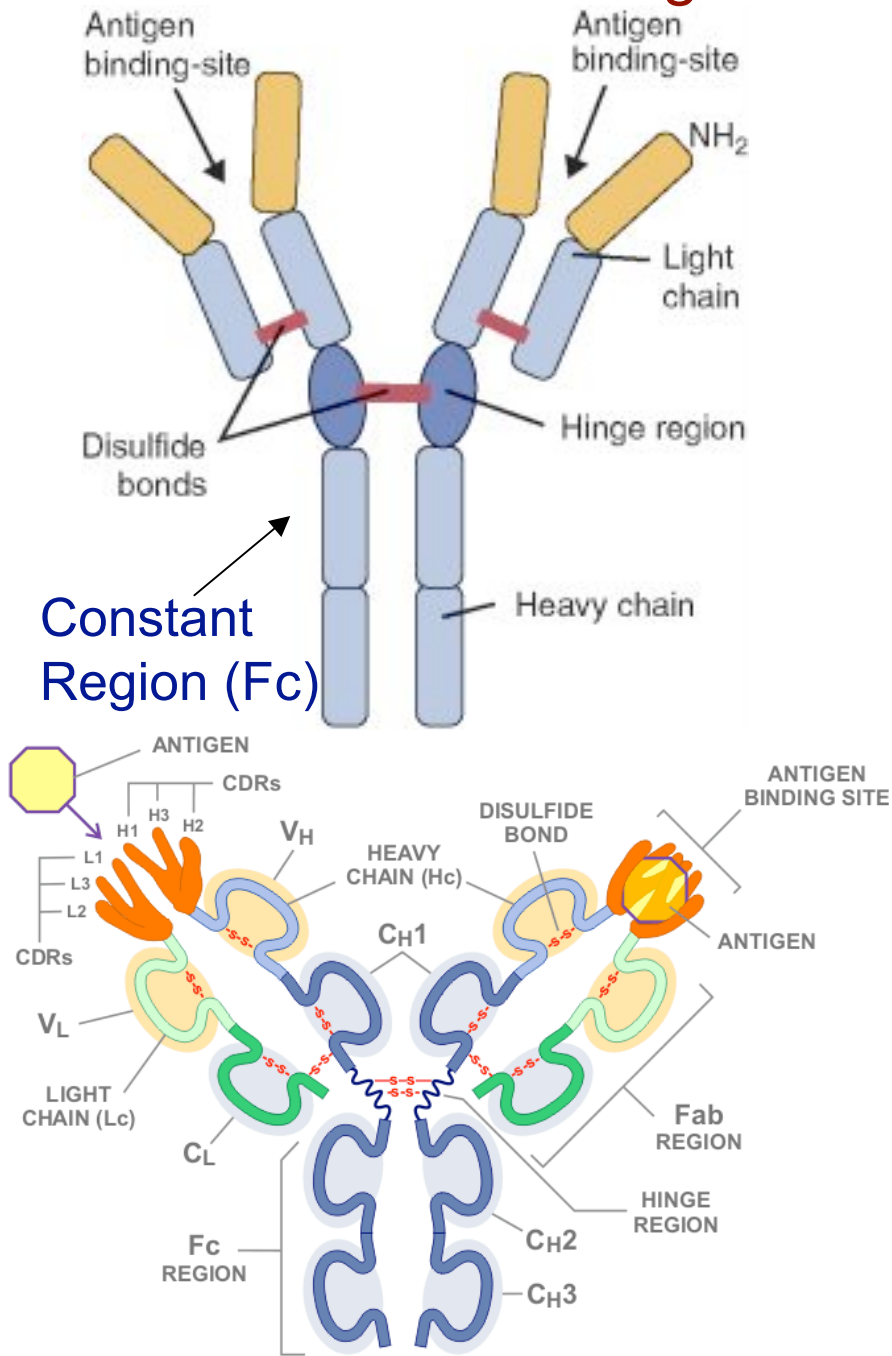


Bookend 1: FcRN



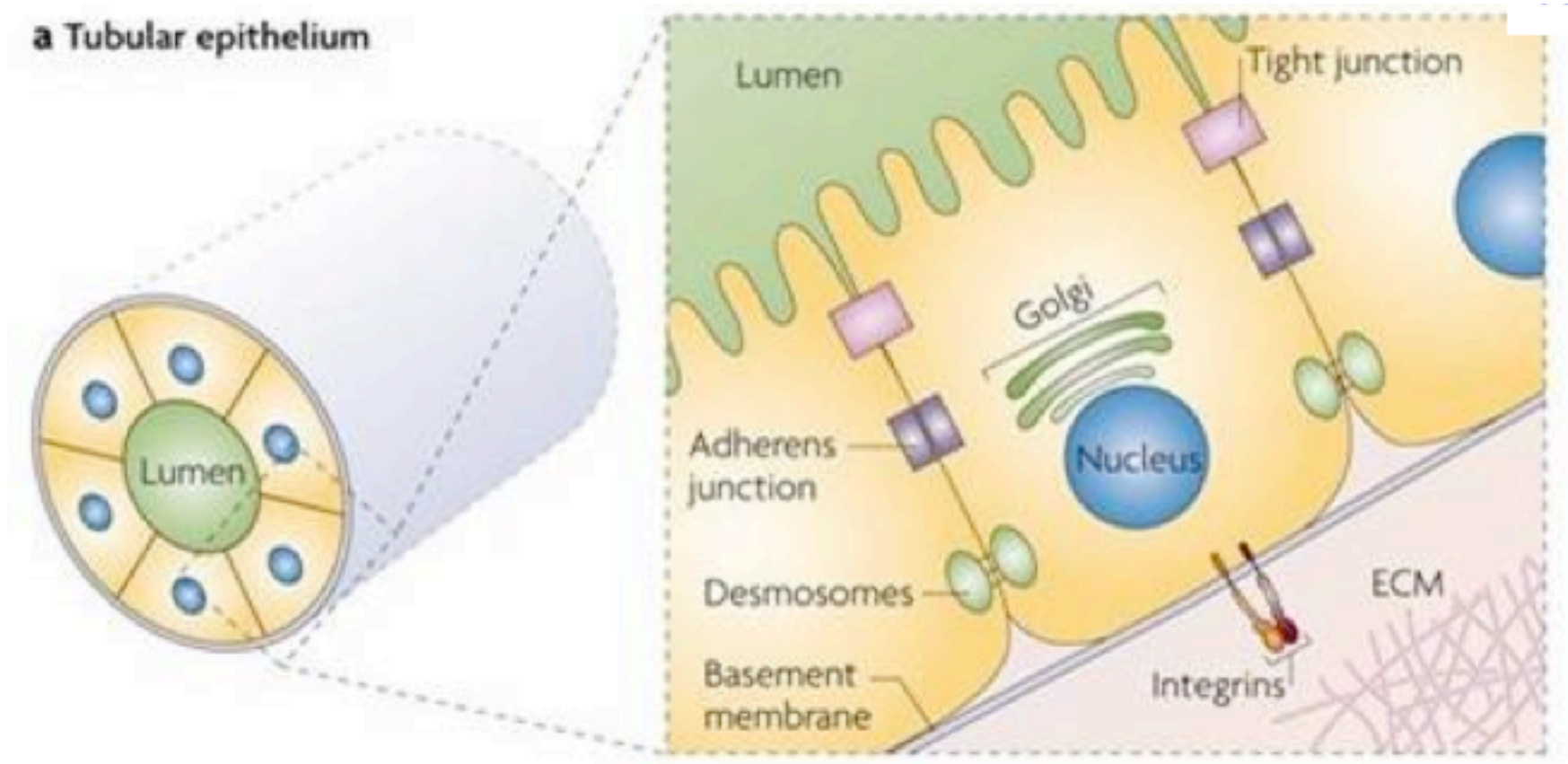
IgG structure and FcRN



FcRN looks like MHC

But groove collapsed so no peptide

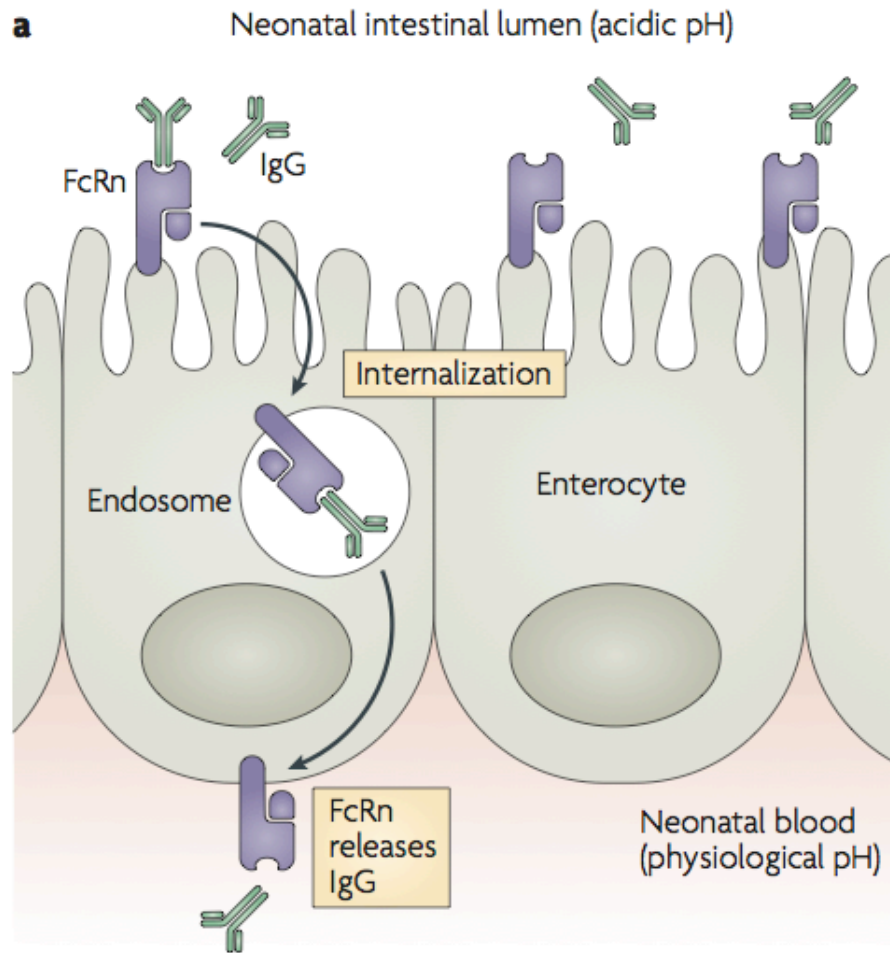
Polarized Cells



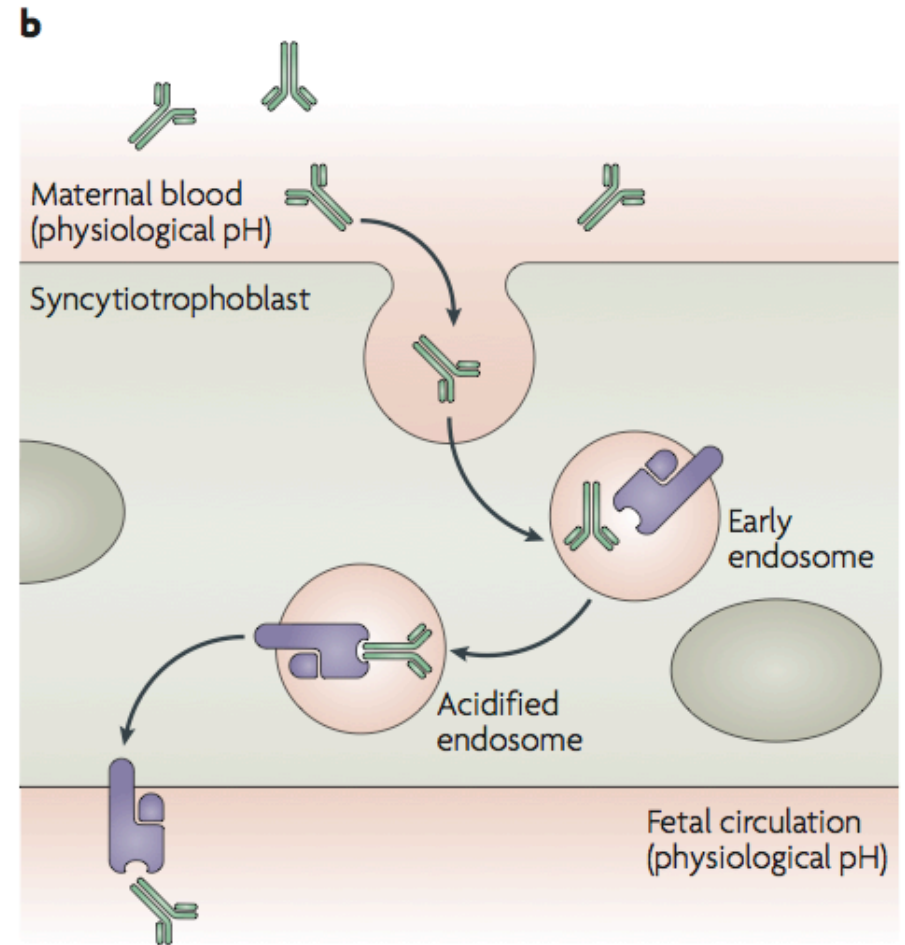
Lumen side: **apical**

Blood side: **basolateral**

Two Primary Roles in Newborn and Fetus

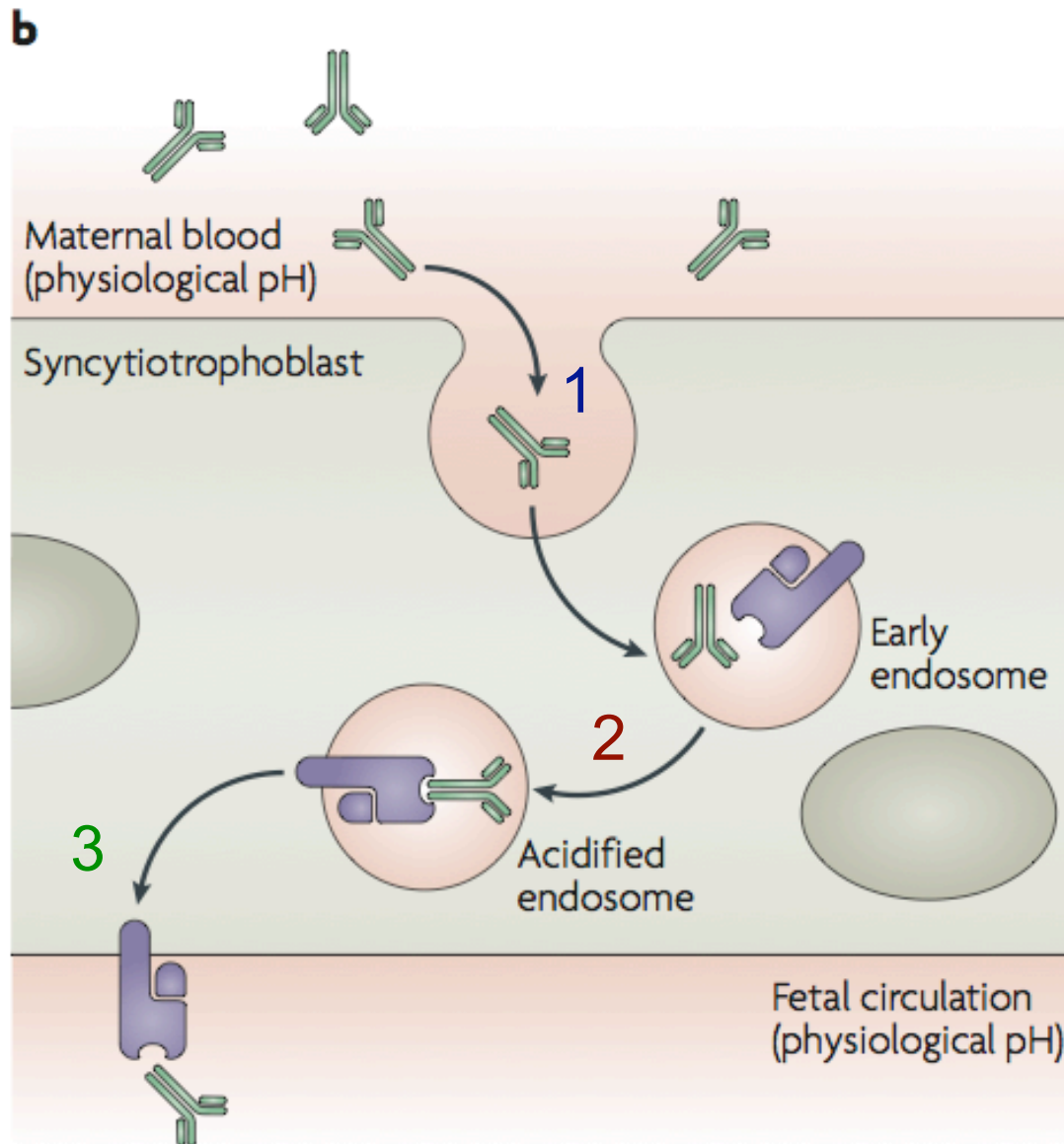


Rodents and Mammals



Humans

Steps in IgG passage through placenta



Step 1: endocytosis

Step 2: acidification and binding

Step 3: exocytosis

Step 4: recycle

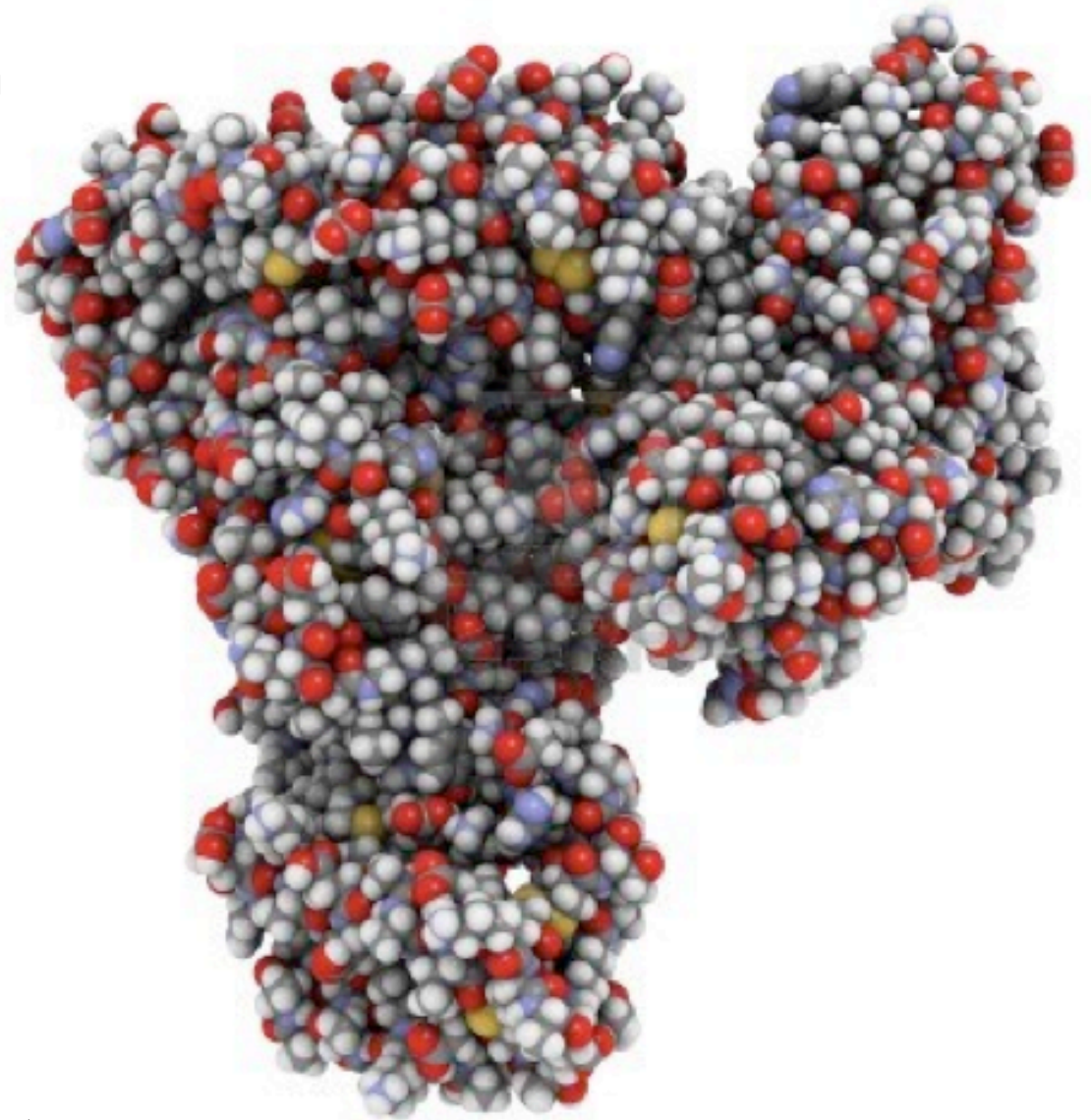
FcRN roles in the Adult

1 & 2) Extend $t_{1/2}$ of IgG
and albumin

3) Defend against
intestinal infections

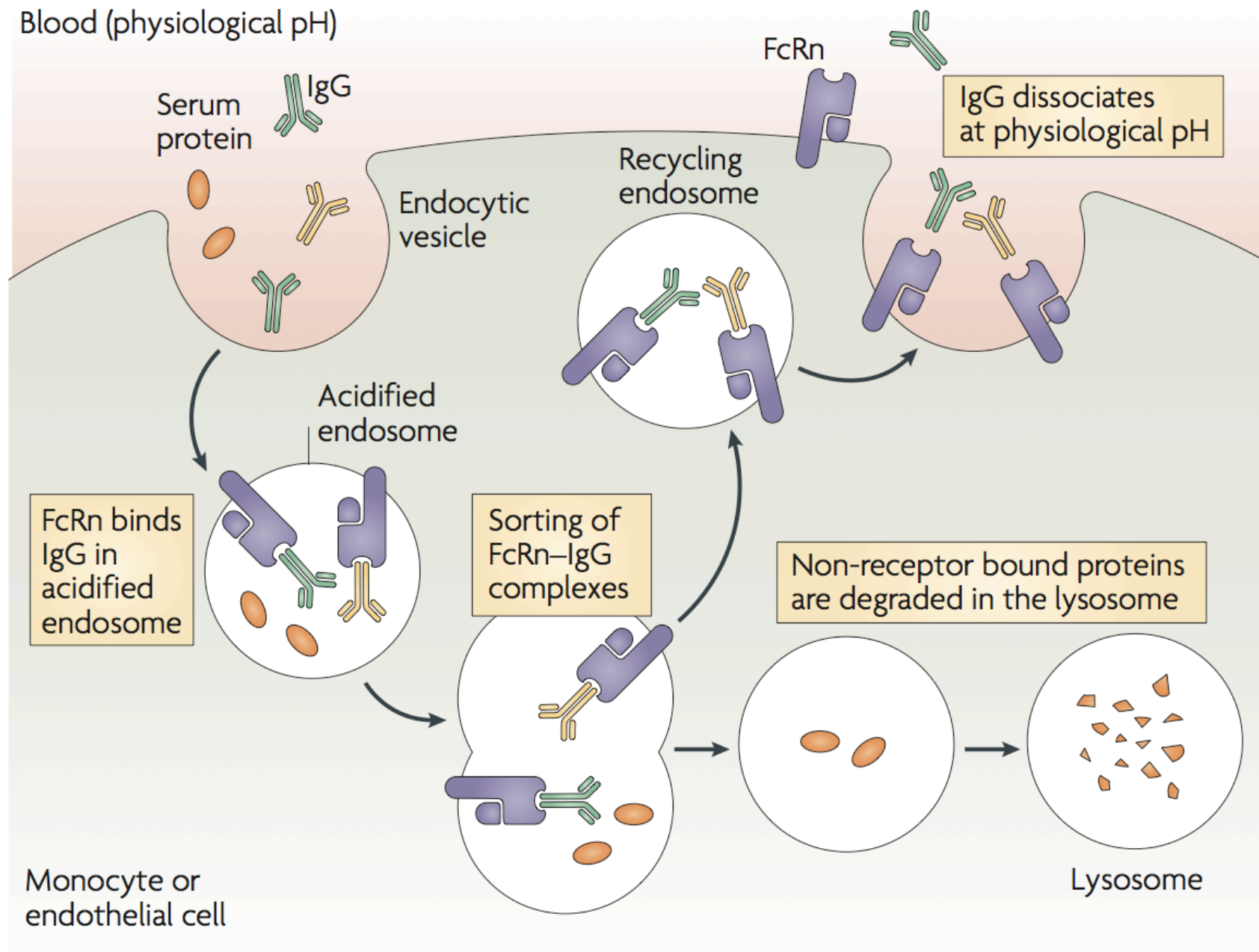
4) Maintain immune
privilege in CNS

5) Clear kidney filter system

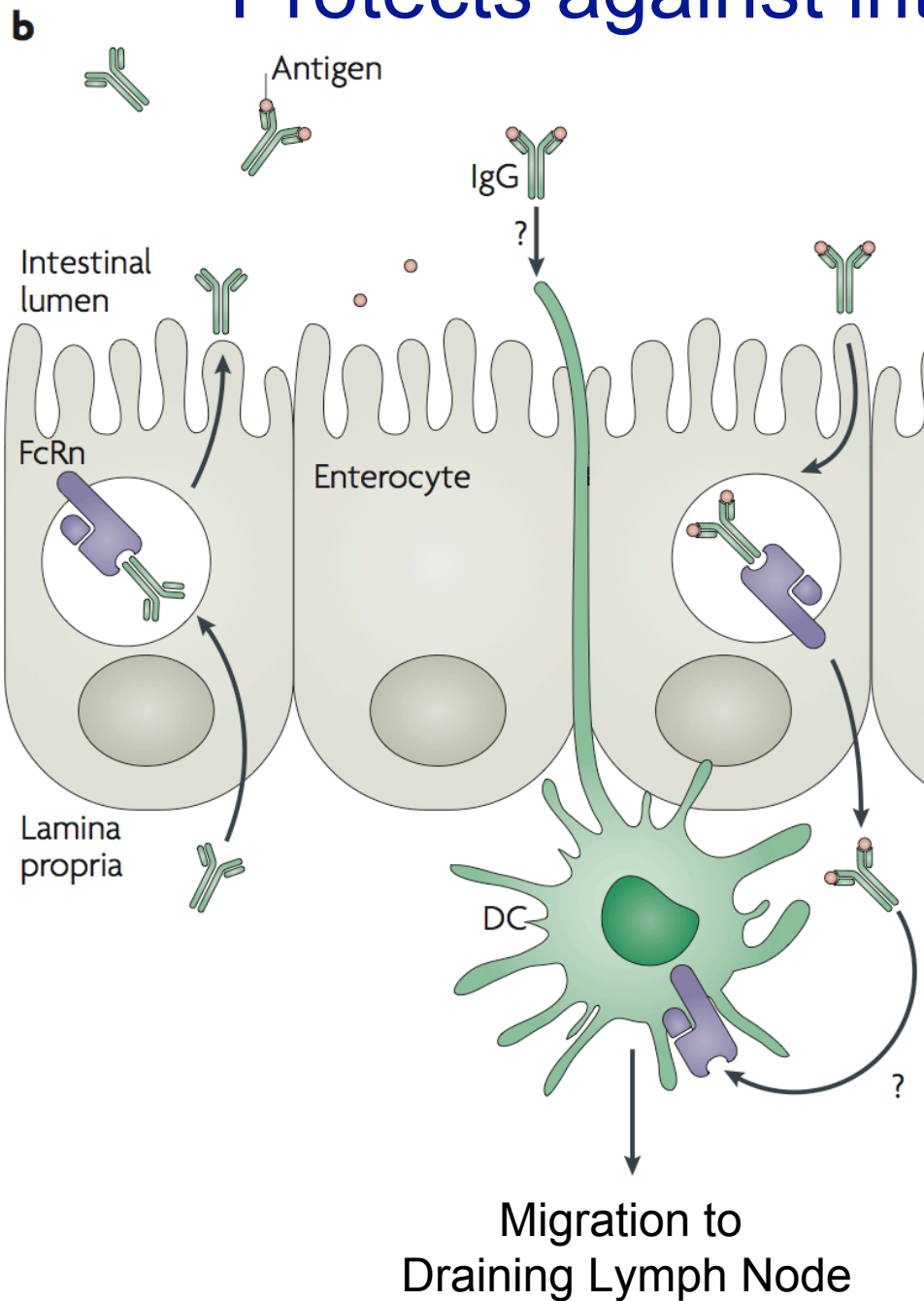


albumin

Extension of IgG $t_{1/2}$ by vascular endothelial & APCs



Protects against intestinal pathogens

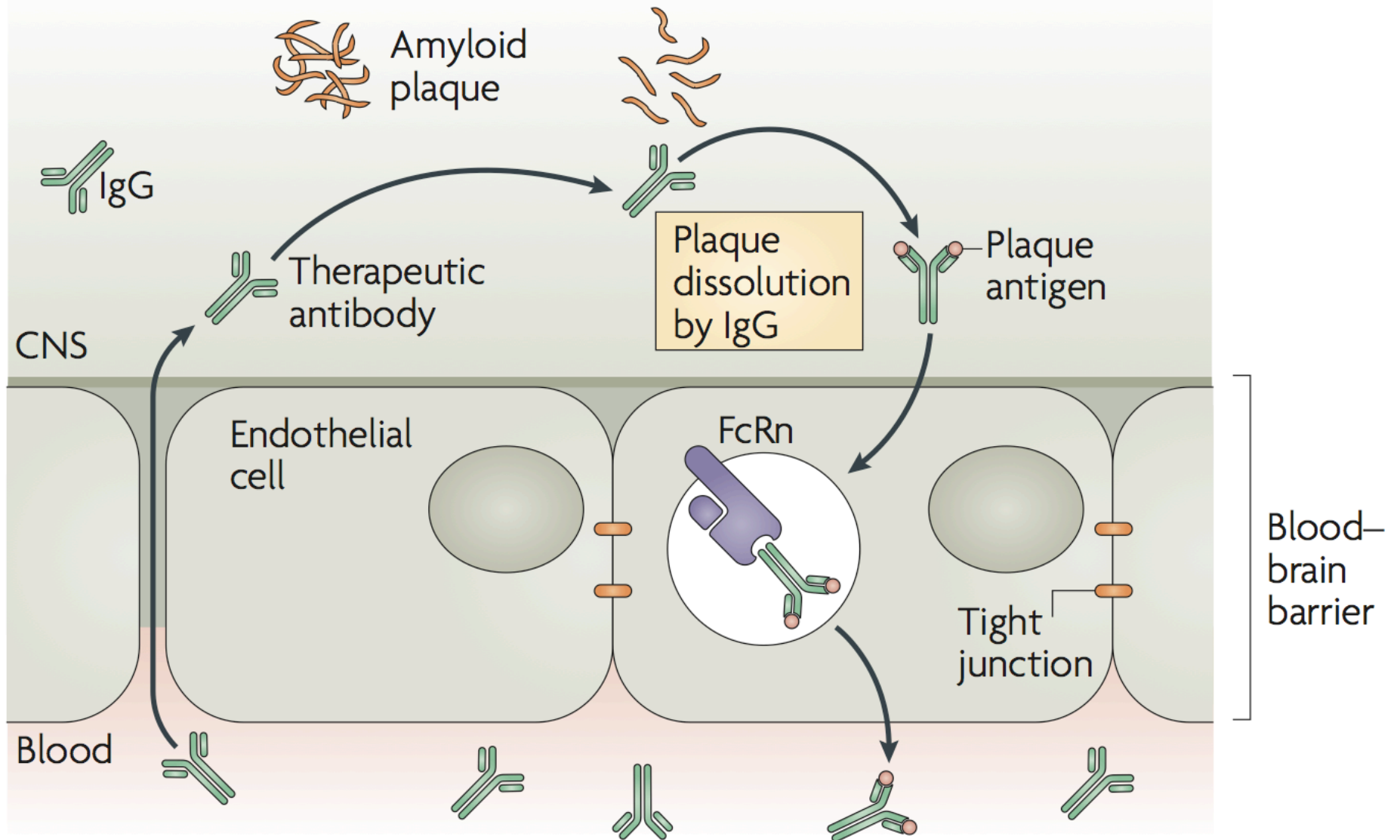


FcRN transports IgG from blood to intestinal lumen

Dendritic cells then might transport IgG/Ag complexes to lymph to stimulate immune response.

Removal of IgG from CNS

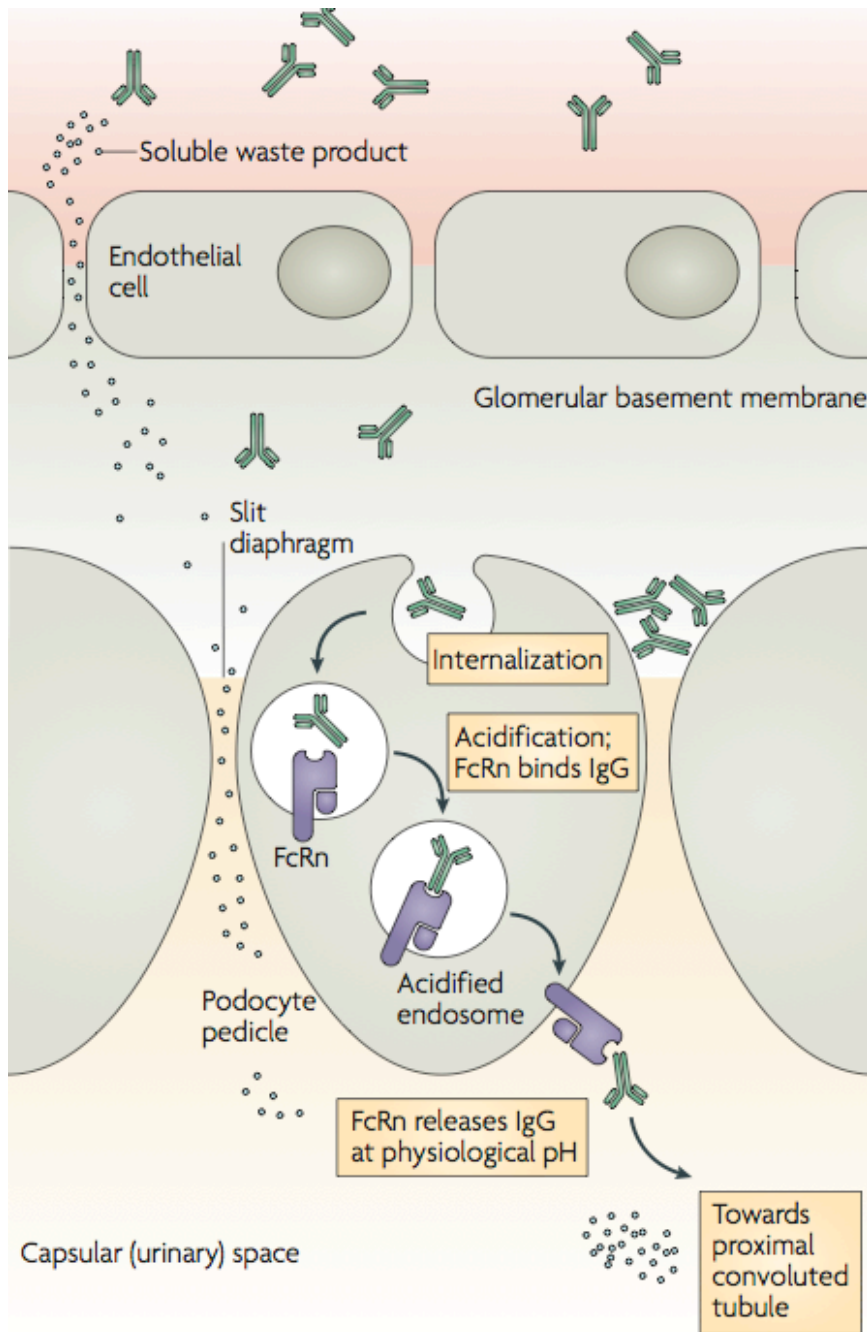
c



Removal of IgG from filter in kidney

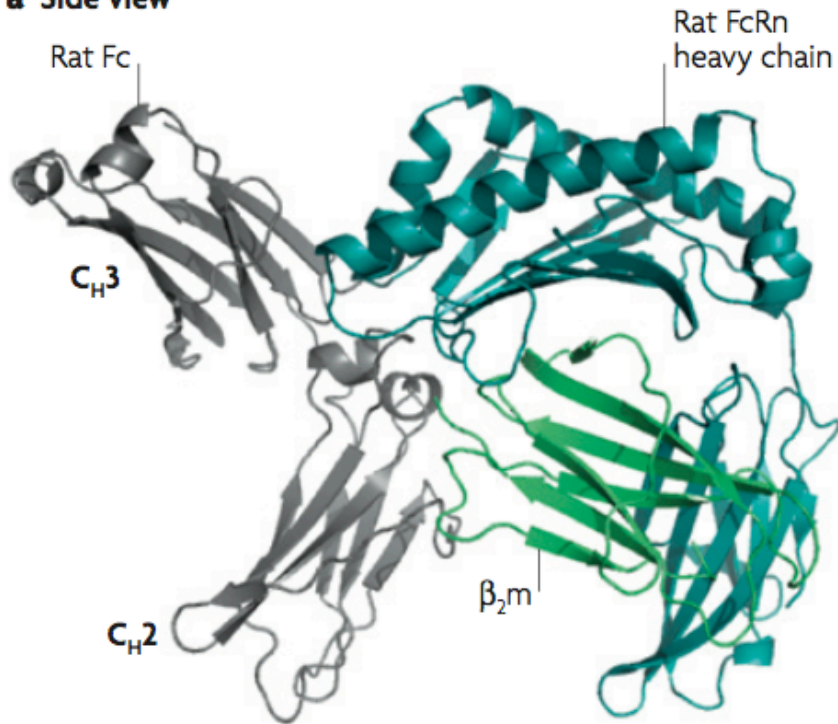
Filters macromolecules $>70\text{kD}$ preventing them from entering urine

So IgG and Albumin might clog the kidney filters if not removed by the podocyte

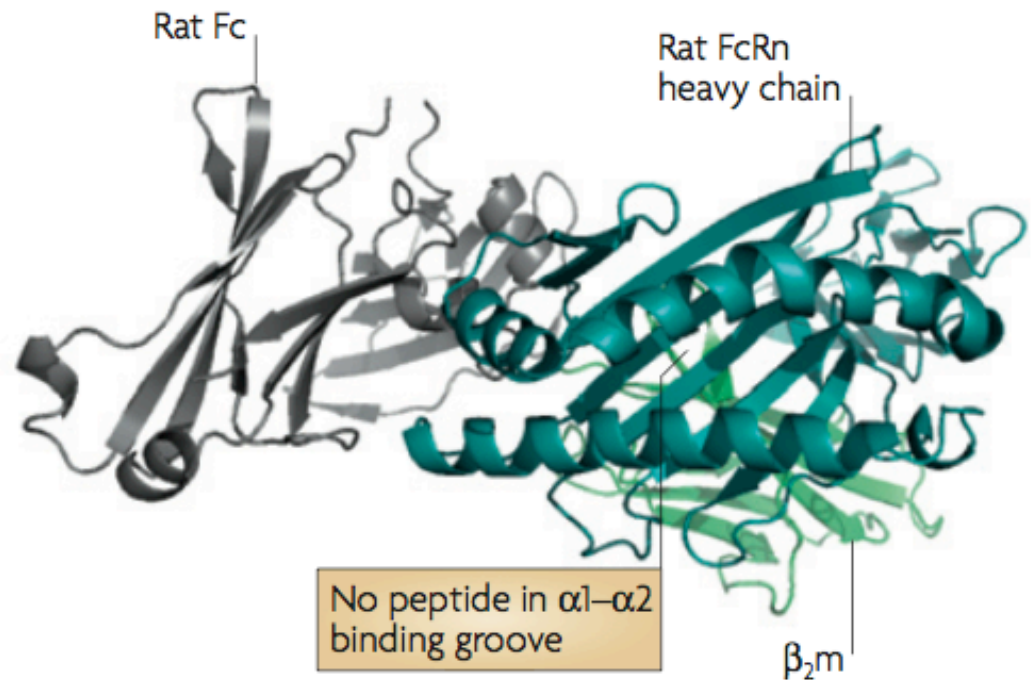


FcRN binds Fc at C_H²/C_H³

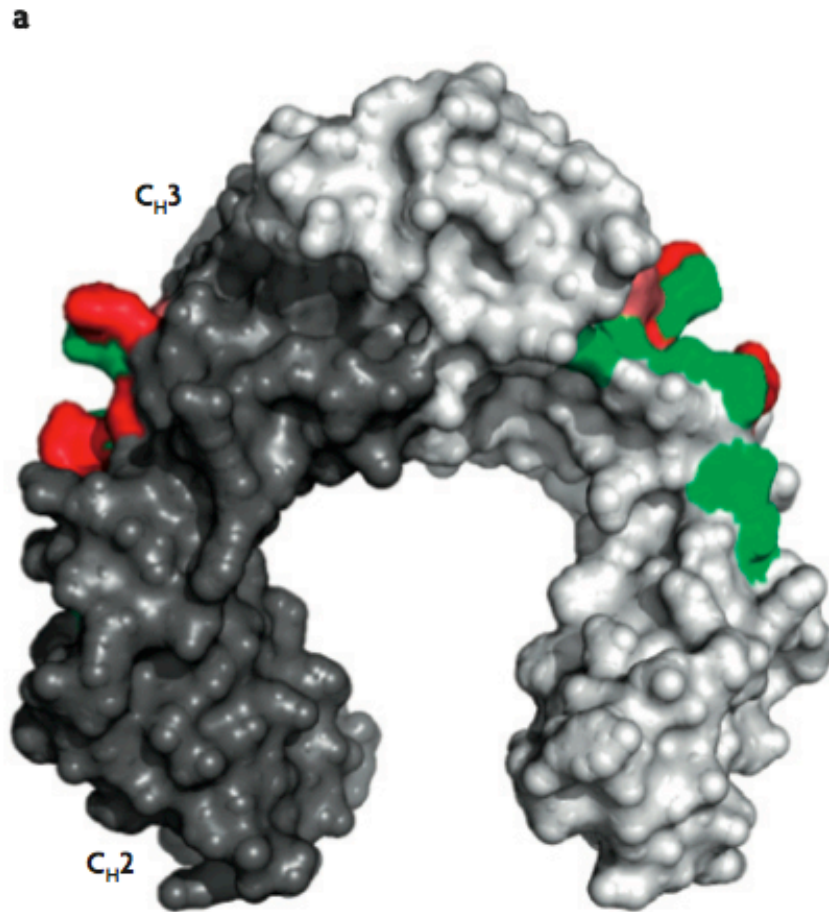
a Side view



b Top view



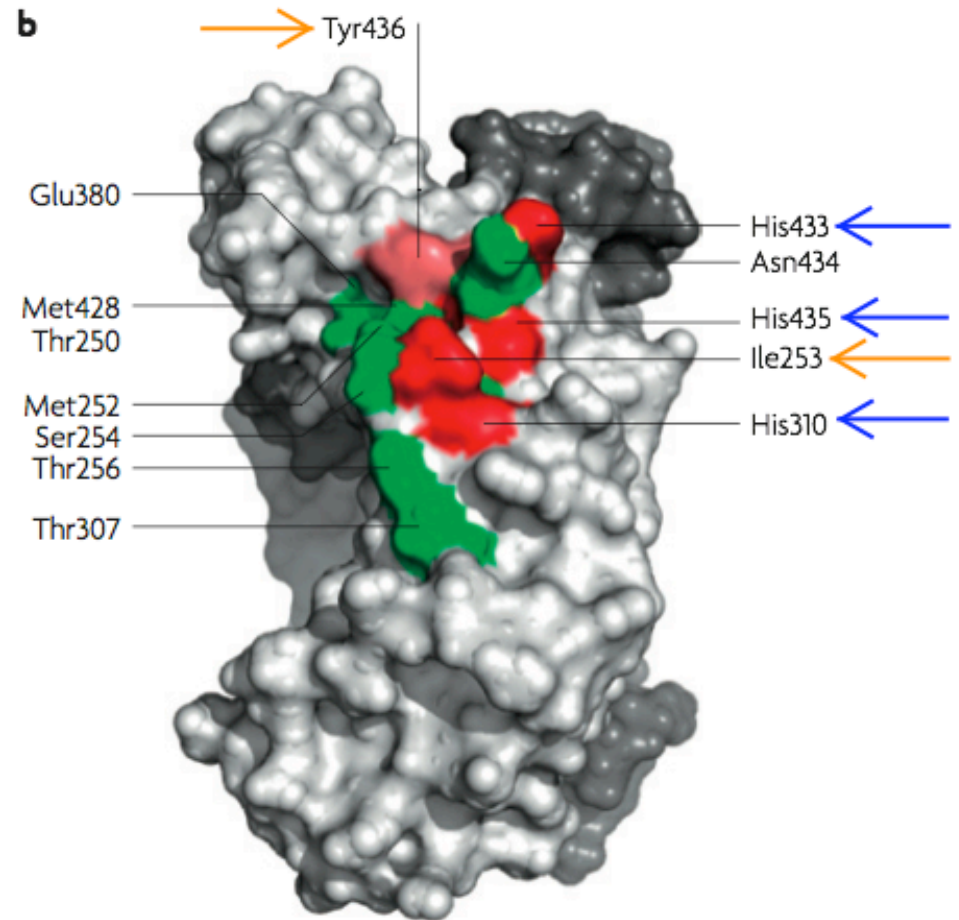
IgG residues important for FcRN binding



On FcRN:

Glu 117, 132, 135

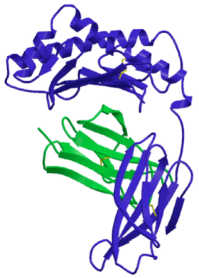
Asp 137



Mutations:

Red: reduce affinity for FcRN

Green: increase affinity for FcRN



FcRN Therapeutics



A) Extending life of therapeutic Ab

Engineer Ab so that bind FcRN with higher affinity

But if increase affinity too much, wont let go at pH 7.4

B) Decreasing life of pathogenic Ab

1) Competition with xs IgG

2 & 3) FcRN/IgG binding with Ab to beta or FcRN

4) XS engineered Ab that binds FcRN w high affinity

