Hi Ron,

In class yesterday a question was raised that I can't answer: How does antibody + complement lyse a bacterium, given that there is a cell wall between the tissue fluids and the membrane that gets lysed? Is the cell wall permeable to large proteins? Every source I've found seems to ignore this question. Do you know the answer?
Thanks,
John

Hi John,

I'm not a complement expert, but ran this by a couple of the complement jocks over here (I am working in Ed Janoff's lab for a few months) and it seems to be ok.

First, recall that most bacteria fall into one of two broad, structurally distinct groups- Gram-negative and Gram-positive. The two types differ in the structure of their cell walls. The Gram positives (Staph, Strep, Clostridium...) have a thick peptidoglycan layer covering the cell membrane. This PG layer is an effective barrier that keeps the MAC from forming in/on the plasma membrane. The Gram negatives (E. Coli, salmonella, Neisseria*...) have two lipid membranes in their cell envelope. The plasma membrane is on the inside of the envelope, and is surrounded by a comparatively thin PG layer. Surrounding this unit is a second lipid membrane, the "outer membrane". (For your reference, bacterial LPS is the lipid constituent of the outer leaflet of the outer membrane). The Gram-negative bugs that are the ones that are susceptible to complement-mediated killing (MAC, etc). The outer membrane is "exposed" on the outer surface of the cell, and MAC can disrupt the integrity of the OM. With that said, many Gram negatives are resistant to complement (often referred to in the literature as "serum resistance") because they have stuff surrounding the OM, blocking access of the C'. For example, the long carbohydrate side chains of LPS on some bacteria are protective. Complement may still be "fixed" but the C3b is out on the sugar side chains and too far from the OM to allow functional assembly the the MAC. Capsules (polysaccharide "slime") that surround the cell are another protection mechanism.

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*You may remember we said in class that people with widely disseminated *Neisseria* infections (meningitis, gonorrhea) may have defects in one component of the membrane attack pathway, C6 to C9. *JJC*