Herpes simplex virus 1 interaction with Toll-like receptor 2 contributes to lethal encephalitis

Kurt-Jones, et al

Tips for understanding the paper:

This paper relates to the section of your textbook reading "Virus induced immunopathology" on page 335, and to the chapter on innate immunity.

Ligands of **Toll-like receptors**:

- TLR2 peptidoglycan, herpesviruses (agonist unknown)
- TLR3 dsRNA
- TLR4 (+MD2) LPS
- TLR6 (+TLR2) LPS
- TLR9 unmethylated CpG dinucleotides (which are found in bacterial or viral DNA, but rare in vertebrates)

moi = multiplicity of infection

MD2 protein is required for optimal signaling of TLR4.

The cytokine **IL-1β** activates the NF-κB promoter.

i.p. = intraperitoneally

Peritoneal exudate cells include a large percentage of macrophages and B cells.
You can see how they are extracted here: http://www.jove.com/video/1488/isolation-of-mouse-peritoneal-cavity-cells

The following passage (from Zhang et al, Curr Protoc Immunol. 2008 Nov; Unit–14.1.) describes them: *The peritoneal cavity provides an easily accessible site for the harvesting of moderate numbers of resident, nonmanipulated macrophages. These cells have been thoroughly studied, and most of our understanding of resident tissue macrophages comes from the study of these macrophages. Usually, the number of macrophages present in the peritoneum under nonelicited condition is insufficient for extensive biochemical studies. To increase macrophage yield, sterile eliciting agents, such as Brewer's thioglycollate broth or protease peptone, can be injected into the peritoneal cavity prior to cell harvest. These agents increase monocyte migration into the peritoneum, and therefore increase macrophage yield.*

Thioglycollate is an inflammatory irritant.

IL-6 is a proinflammatory cytokine, secreted by T-cells and macrophages. It crosses the blood-brain barrier and induces fever, among other things.

MCP-1 is monocyte chemotactic protein-1, a chemokine which attracts monocytes and other leukocytes.

Perivascular cuffing is the accumulation of lymphocytes or plasma cells in a dense mass around a vessel. It is an indication of inflammation.