IN THE NEWS

Botulism beaten

A drug that consists of recombinant oligoclonal antibodies has been developed by US scientists that could be mass produced to treat botulism.

The causative agent of botulism, and source of the botulinum neurotoxin, is the soil bacterium *Clostridium botulinum*. A recent report, highlighted by *The New Scientist*, claims that one gram of botulinum toxin could kill a million people if evenly dispersed and inhaled. Not surprisingly, this toxin is classified as one of the top six highest-risk bioterrorist weapons by the US Centers for Disease Control. However, if botulinum toxin was to be used in such an attack, there are currently no drugs available that could be produced rapidly in the required quantity to treat or prevent this disease.

Scientists from the University of California at San Fransisco, led by James Mark, have developed an effective drug that, as explained online by *HealthScoutNews*, consists of "recombinant oligoclonal antibodies — three laboratory-manufactured molecules that bind to the deadly toxin created by the botulism bacterium, rendering it harmless". Mark told *HealthScoutNews* that the drug will protect against the botulinum toxin within one or two hours and is effective if given up to two days after exposure, and that the protection will last for three to six months. He also said that, "The drug neutralises the toxin better than the most potent natural immune response. The procedure could be scaled up to mass produce and stockpile the drug to be used to prevent or treat botulism", as reported by *BBC News* online. This work is published online by *The Proceedings of the National Academy of Science* (DOI 10.1073/pnas.172229899).

Jenny Buckland

ANTIGEN PRESENTATION

MHC class II trafficking

T-cell activation requires many interactions with peptide–MHC complexes on antigen-presenting cells, such as dendritic cells (DCs). Two reports in *Nature* now show that DCs might be able to enhance the probability of productive interactions with T cells by the directed trafficking of peptide–MHC complexes along tubules that extend towards the sites of contact with T cells.

MHC class II molecules are assembled in the endoplasmic reticulum, then are transported through the endocytic pathway, where they acquire peptides that are derived from exogenous proteins. Peptide–MHC class II complexes are retained in late endosomes and lysosomes in immature DCs — when DCs are activated, the complexes are transported to the cell surface. These two studies looked at the transport of peptide–MHC class II complexes in live cells.

Boes and colleagues generated knock-in mice that express enhanced green fluorescent protein (EGFP)-labelled MHC class II molecules. The tagged MHC molecules behave in the same manner as wild-type molecules when assessed for peptide loading and transport. DCs were generated from the knock-in mice by stimulating bone-marrow cells with interleukin-4 and granulocyte–macrophage colony-stimulating factor. The DCs were pulsed with hen-egg lysozyme or ovalbumin peptides and exposed to antigen-specific T cells or control T cells; then, the trafficking of MHC class II complexes in the DCs was analysed using time-lapse confocal microscopy. Extensive tubule formation from the MHC class II compartments — sometimes of more than 50 μm in length — was observed, with tubules extending directly towards the contact area between the DC and antigen-specific T cell. When several T cells interacted with a single DC, tubules extended towards each of the T-cell contact areas.

Chow and colleagues expressed GFP-tagged MHC class II molecules in live bone-marrow-derived DCs using a retroviral transfection system. After stimulation of immature DCs with lipopolysaccharide, but in the absence of any T-cell interactions, the morphology of the MHC class-II-positive lysosomes was markedly altered — tubules developed and extended from late endosomes or lysosomes towards the plasma membrane. Using specific imaging techniques (epifluorescence and total internal reflectance fluorescence microscopy) the authors were able to observe the tubules fusing with the plasma membrane.

Together, these results show that DCs undergo marked morphological changes that result in the delivery of MHC class II complexes to the cell surface, but the role of T-cell interactions in inducing this process seems more controversial. Boes *et al.* propose that the tubulation process might maximize the delivery of peptide–MHC complexes to the site of interaction with T cells, and thereby enhance the generation of productive DC–T-cell interactions.

Elaine Bell

References and links

ORIGINAL RESEARCH PAPERS Boes, M. *et al.* T-cell engagement of dendritic cells rapidly rearranges MHC class II trafficking. *Nature* **418**, 983–988 (2002) | Chow, A., Toomre, D., Garrett, W. & Mellman, I. Dendritic-cell maturation triggers retrograde transport of MHC class II molecules from lysosomes to the plasma membrane. *Nature* **418**, 988–994 (2002)

FURTHER READING Hiltbold, E. M. & Roche, P. A. Trafficking of MHC class II molecules in the late secretory pathway. *Curr. Opin. Immunol.* **14**, 30–35 (2002)

WEB SITES

Hidde Ploegh's lab: http://www.hms.harvard.edu/pathol/ploegh/

Ira Mellman's lab: http://info.med.yale.edu/cellbio/Mellman.html