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Knockout Mouse Project launched

On 7 September, the National Institutes of Health (NIH) kicked off its Knockout Mouse Project (KOMP) by granting a set of cooperative agreements totaling $52 million over five years. The goal of the project is to create a comprehensive open-access resource of knockout mutations for the ~20,000 protein-coding genes in the mouse genome.

As part of the KOMP, Regeneron Pharmaceuticals, Inc. (Tarrytown, NY) and a joint team from Children's Hospital Oakland Research Institute (Oakland, CA), the University of California, Davis, and the Wellcome Trust Sanger Institute (Hinxton, UK) will target genes in mouse embryonic stems cells (ESCs) and use them to create lines of knockout mice. A team at the Jackson Laboratory (Bar Harbor, ME) will collect and coordinate the data; two other teams will work to develop methods for high-throughput gene targeting or trapping in C57BL/6 mice. In 2007, the NIH will provide funding for the creation of a repository through which mutated ESC lines will be available to the research community.

Although many knockout mouse lines have already been published, they are not all readily available to the scientific community, necessitating that individual research groups spend time, money, and animals to recreate lines. The KOMP resource should facilitate access to these important mouse models of human disease.

Putting Lyme on the run

A small research victory in the war on Lyme disease, spearheaded by Mitchell Kronenberg and his team at the La Jolla Institute for Allergy and Immunology (La Jolla, CA), could lead to the conquest of this feared tick-borne scourge, which afflicted nearly 20,000 people in 2004.

Kronenberg and his colleagues study natural killer T (NKT) cells, unique among T cells in that they only recognize glycolipid antigens presented to them by a molecule dubbed 'CD1d,' whereas other T cells respond to peptide antigens found on class I or II major histocompatibilty complex molecules.

Unfortunately, until now, the list of glycolipid molecules known to activate NKT cells has been short and inconsequential. Now, Kroeneberg and his team have discovered that a glycolipid from *Borrelia burgdorferi*, the organism that causes Lyme disease, activates certain murine NKT cells *in vivo* and certain human NKT cells *in vitro* (*Nat. Immunol.* September).

The impact of this discovery could be staggering, as it evokes the possibility that differential susceptibility to Lyme disease may be caused by individual differences in NTK cell frequency or potency. Perhaps more importantly, the *B. burgdorferi* glycoprotein responsible for the NKT activation may prove useful in developing a safe and effective human vaccine.

Beating intestinal worms

New research on nematode infections sheds light on a previously unknown immune response to parasitic round worms. These promising results may provide insight into novel treatment modalities for human nematode infections, such as lymphatic filariasis and ascariasis.

In research described in the August issue of *Nature Medicine*, William Gause of the New Jersey Medical School (Newark, NJ) and colleagues investigated the chain of immunological events that leads to the expulsion of *Heligmosomoides polygyrus*, a murine intestinal parasite. If *H. polygyrus* larvae develop to adult parasitic worms, the infection becomes chronic; if, however, the larvae are expunged from the intestinal lumen, mice develop resistance to subsequent infection. *H. polygyrus* infection in mice induces a so-called T_H2 immune response, which is characterized by $CD4^+$ T cells; these cells promote the accumulation of another type of immune cell called 'alternatively activated macrophages' (AAMacs).

Gause and his team tested whether or not AAMacs mediate protection against secondary *H. polygyrus* infection *in vivo* by selectively depleting these cells from mice and then measuring the effectiveness of worm expulsion as compared to controls. As he and his colleagues describe in *Nature Medicine*, they found that "macrophages, activated by $CD4^+$ T cells, are an essential effector population in protective T_H2 responses, and their accumulation during the secondary response is required for parasite clearance."