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### Mouse study unlocks clues to 1918 flu mystery

A hyperactive immune response may be more to blame for the extraordinary virulence of the 1918 influenza strain than the direct effects of the virus itself, according to a new mouse study. Understanding the contribution of host response to the virulence of flu strains may allow researchers to better prepare for and respond to future pandemics.

The influenza pandemic of 1918–19 killed at least 50 million people worldwide, exhibiting a predilection for young, healthy individuals. Analysis of preserved autopsy samples has demonstrated extensive damage to the lung tissue, but the respective contributions of the virus and immune response to this pathology remain unclear.

Now, in the 5 October issue of *Nature*, John C. Kash of the University of Washington School of Medicine (Seattle, WA) and colleagues report the results of a study that may provide important clues. Kash's group intranasally inoculated mice with reconstructed 1918 virus (r1918), a contemporary seasonal flu strain, or one of two laboratory-made hybrid strains that incorporated two or five of the eight genes from the 1918 strain. Mice infected with r1918 lost the most weight, died soonest, and mounted a hastened immune response that was associated with the most severe lung damage. Moreover, microarray analysis of lung samples showed that infection by r1918 activated more proinflammatory and cell-death-related genes than the other strains, suggesting that an excessively strong immune response provoked by the 1918 flu strain may be the primary destroyer of host lung tissue.

### Mouse brain map completed

The Allen Brain Atlas, a web-based, three-dimensional map of mouse brain gene expression, is now complete. The Atlas is the first project completed by The Allen Institute for Brain Sciences (Seattle, WA), which was established and funded by Microsoft cofounder and philanthropist Paul Allen in 2001.

To create the cellular-resolution atlas, researchers stained brain slices from 8-week-old male C57BL/6J mice with probes specific to each gene. In compiling the atlas, they found that 21,000 genes, or 80% of the mouse genome, are expressed in the brain. Furthermore, very few genes are expressed only in one brain region.

The Atlas, which is available free-of-charge at http://www.brain-map.org, allows scientists to search for a specific gene and then view vertical and horizontal sections to visualize gene expression. Because humans share more than 90% of their genes with mice, the mouse brain map may prove a valuable tool for researchers seeking to better understand human brain disorders and diseases, such as Alzheimer's, Parkinson's, autism, and schizophrenia.

### The rebirth of tumor vasculature

A recent trend in cancer research is to attempt to cut off a tumor's nutrient supply by eliminating the blood vessels that nourish it, but a new study demonstrates that this therapy alone may be insufficient to stop the tumor's long-term growth.

The study, led by Donald McDonald at the University of California, San Francisco, investigated tumors treated with inhibitors of vascular endothelial growth factor (VEGF), a signaling protein involved in angiogenesis. McDonald injected one of two drugs that block VEGF into mice with pancreatic tumors for seven days (*J. Clin. Invest.*, October). As expected, both drugs used by McDonald markedly reduced the tumor vasculature, cutting blood vessel density by 50–60% and leaving only a matrix of empty basement-membrane 'sleeves.'

At this point, McDonald began his real experiment—to investigate what would happen to the vasculature after the drugs were withdrawn. Only seven days after treatment withdrawal, the vasculature had regrown completely, tapping into the circulation and achieving full function. Using immunoflourescent dyes, McDonald determined that the new vessels were apparently growing into the basement membrane sleeves, using them as a scaffolding of sorts. Researchers are hopeful that if they can develop a means for knocking out those empty sleeves of basement membrane, they may be able to prevent post-treatment vessel regrowth.