› NEWS UPDATES

1918 influenza: puppeteer of the immune system?

In the last few years, scientists have been experimenting with the recently reconstituted 1918 'Spanish Influenza' virus in the hope that they can apply their findings to the H5N1 avian flu virus currently on the pandemic horizon. Now, a paper that appears in the 18 January issue of *Nature* reports that a large collaboration of researchers, led by Yoshihiro Kawaoka (University of Wisconsin-Madison, Madison, WI), has found evidence that an abnormal antiviral immune response may explain the deadliness of the 1918 flu virus.

Previous studies have described the effects of the 1918 virus on mice, but such results are not always indicative of the human condition. The *Nature* study is the first to evaluate the clinical pathology of the virus in nonhuman primates. The researchers infected cynomolgus macaques with either 1918 virus or conventional human flu virus, and then euthanized the animals for pathological analysis. They found numerous differences in the progression of the two viruses, most notably that the expression of some antiviral immune molecules was depressed in monkeys afflicted with the 1918 virus—an indication that the 1918 virus kills by tinkering with the immune system. Knowing the mechanism of that tinkering may help investigators combat similar viruses, like H5N1.

Muscles in the long run

Open a physiology textbook to the section on muscle fibers and you are likely to read about types I, IIA, and IIB. Unmentioned may be a fourth adult skeletal muscle fiber: type IIX. Long poorly understood, type IIX fibers have now been shown to increase the 'athletic ability' of mice enriched with these fibers—a finding researchers hope will aid in treating muscular dystrophies and similar conditions.

Type IIX fibers are a hybrid between the 'slow-twitch' type I and IIA fibers (good for endurance) and the 'fast-twitch' type IIB fibers (good for short, rapid activity). Mammalian muscles are an amalgam of different fiber types, but unlike other muscle fibers, type IIX fibers do not predominate in any of the body's muscles, which has been an obstacle for researchers studying these fibers.

In the January issue of *Cell Metabolism*, a group led by Bruce Spiegelman at Harvard University (Boston, MA) announced they had created mice that overexpress the transcription factor PGC-1β in skeletal muscle. To their surprise, these mice had skeletal muscles significantly enriched in type IIX fibers, suggesting that PGC-1β could be used therapeutically to modulate muscle fiber type. Spiegelman tested the transgenic mice in a treadmill exercise and found that they ran an average 230 meters farther than their counterpart controls—an encouraging result for those with muscle disabilities.

Impeding plague's progression

Washington University Medical School researchers have hit upon a protein responsible for the progression of pneumonic plague, a less common and deadlier manifestation of infection by the bacterium responsible for bubonic plague. Pharmacological inhibition of the protein may prove to have therapeutic value in managing outbreaks (natural or intentional) of plague.

Yersinia pestis, usually transmitted by the bite of a flea, can also spread between people. A few days after exposure, the individual unlucky enough to inhale *Y. pestis*-laden respiratory droplets develops severe respiratory symptoms. When caught early, pneumonic plague is treatable with antibiotics; unfortunately, the nonspecific symptoms usually result in a late diagnosis.

Now, a research team led by William E. Goldman report that inhibition of the plasminogen-activating protease Pla may be the key to increasing the timeframe during which antibiotic treatment is effective (*Science*, 26 January). Goldman's team infected mice with *Y. pestis* deficient in Pla, a protein that promotes the degradation of fibrin clots. These mice lived significantly longer than those inoculated with wildtype bacteria, and their disease course was characterized by decreased bacterial proliferation in the lungs, less severe lung edema, and less invasion of the lungs by pro-inflammatory cytokines. In a separate experiment, inhibition of Pla activity also delayed time to death.