arthritis," says Lee. Although mast cells riddle arthritic tissue, no one knew how they contribute to the disease, in part because the cells are difficult to study in humans. So the team took advantage of two strains of mice, one prone to inflammatory arthritis and another lacking mast cells. The mice are "a very nice model to elegantly show the involvement of mast cells. Previously, it was guilt by association," says rheumatologist Maripat Corr of the University of California, San Diego.

In rheumatoid arthritis, the two prongs of the immune system cooperate. One, known as innate immunity, immediately pounces on pathogens with cells that devour germs and inflame tissues. The other, called adaptive immunity, forges antibodies to fight invaders it has encountered. Going astray in arthritis, they destroy the synovium, a cushion wedged between bones in joints. Researchers think the disease begins when antibodies are somehow generated against a protein in the synovium. These so-called autoantibodies orchestrate the collapse of the joint lining by drawing in inflammatory immune processes. The inflamed cushion swells and eventually hardens to make joints distinctively gnarled. Until now, no one had determined how the autoantibodies muster up inflammation.

Lee's team examined whether mast cells spur the interaction between antibody-based and innate immunity. The researchers suspected the cells in part because they have receptors for both autoantibodies and inflammation-inducing proteins known as complement. What's more, mast cells can release inflammatory molecules called cytokines.

To test this idea, the team turned to so-called K/BxN mice, which have a genetic mutation that causes them to spontaneously develop inflammatory arthritis. Serum taken from these animals and injected into mice of almost any other strain will cause the receiving mouse's paws to swell. The researchers injected K/BxN serum into mice that lack mast cells as well as littermates with normal immunity. As expected, the normal mice acquired full-blown arthritis within 10 days of injection. However, mice without mast cells never manifested the disease. The team also transplanted mast cells into the mastless mice; if then injected with K/BxN serum, their paws flared with inflammation. When the researchers examined arthritic tissue, they saw that the mast cells had spewed their cytokines and other inflammatory chemicals within 2 hours of serum injection.

The researchers suggest that mast cells residing in synovial tissue are a cellular link between the free-floating autoantibodies and inflammation. Autoantibodies and complement bind to mast cells, the team proposes, which prompts them to dump their cytokines and other inflammatory chemicals, thus calling in the inflammation brigade. Rheumatologist Cornelia Weyand of the Mayo Clinic in Rochester, Minnesota, says the "beautiful study" clearly shows that "mast cells are the key effector cells in translating adaptive immunity to inflammatory disease. When you read the paper, it leaves you very satisfied."

How the study translates to human disease isn't as clear, however. Rheumatologist Joseph Craft of Yale University says that mast cell involvement will be hard to verify, because such experiments can't be done in humans. However, the mouse result might explain data showing that a cytokine named TNF-α that is released from mast cells "serves as such a dominant force" in human disease. The most recent therapy developed for rheumatoid arthritis targets this cytokine. The rheumatologists agree that the paper will cause a surge of interest in mast cells—as if the ornery rabble-rousers don't get enough attention from the allergists. –MARY BECKMAN

Mary Beckman is a writer in southeast Idaho.

CREDIT: SCOTT CAMAZINE/PHOTO RESEARCHERS

Inflammatory ruckus. Mast cells might be the missing link necessary for arthritis.

SCIENCE BUDGETS

Japan's Ministries No Longer Call the Shots

TOKYO—When Japan's ministries last week unveiled their budget requests for the fiscal year beginning next April, they revealed eye-popping increases in science-related spending. The Ministry of Education, Culture, Sports, Science, and Technology wants to boost its budget for research in four economically strategic fields by 36%; the Ministry of Economy, Trade, and Industry wants 44% more money for the same areas.

In past years, the ministries could be confident that they would end up with close to what they asked for. Not this year. The prime minister's cabinet office will now cut and shape the ministries' requests, putting its own stamp firmly on the priorities by deciding which projects actually get increases while holding overall science spending flat. Researchers fear this will further tilt the scales toward economically strategic areas. "I am strongly protesting the fact that funding will be available only when a

ScienceScope

Banking on Stem Cells The United Kingdom's plans for a stem cell bank are expected to take concrete shape next week. The Medical Research Council (MRC), which will oversee the cell repository, will announce details of the bank's location and operation at an 11 September symposium in London.

According to a plan strongly endorsed last February by a House of Lords special committee on stem cell research, the bank will hold both embryonic and adult stem cell lines and distribute them to academic scientists in the United Kingdom and abroad. Any new human embryonic stem cell lines derived in Britain must be deposited in the bank.

The planned announcement made headlines in the United Kingdom last week as several newspapers questioned the meeting's timing on the anniversary of last year's terrorist attacks, charging that MRC hoped any potential controversy stirred by the meeting would go unnoticed. But an MRC spokesperson says the date was chosen for logistical reasons—and noted that both the press and opponents of stem cell research have been invited.

Splitting Cells Australia's quest for national legislation regulating human embryonic stem cell research has hit another speed bump. The House of Representatives last week voted to split the proposed legislation (*Science*, 30 August, p. 1461) into two bills—passing one that bans human cloning for reproduction but delaying a vote on the other, which allows researchers to use and derive certain human stem cell lines for research. Lawmakers are expected to revisit the issue later this year, but researchers worry that opponents of stem cell research will use the time to organize.

Prime Minister John Howard, meanwhile, has ordered a review of the government's $25 million commitment to a new stem cell research center in the wake of a controversy sparked by researcher Alan Trounson of the Monash Institute of Reproduction in Melbourne. Trounson, head of the new Center for Stem Cells and Tissue Repair, admitted to misrepresenting a video of a crippled rat he showed to Parliamentarians. He claimed that the rat had regained partial muscle function after being treated using rat stem cells; in fact, researchers had used other kinds of human fetal tissue. Howard said he was "disturbed" by the incident, but he supports stem cell research.

Contributors: Robert F. Service, Gretchen Vogel, Leigh Dayton

project will produce immediate results," says Norio Kaifu, director-general of the National Astronomical Observatory in Tokyo.

The new procedure represents a significant change in the way Japan crafts its research budget. In the past, when ministries submitted funding requests at the end of August, they expected the numbers to be shaved a little by the time the budget was finalized in December, but the overall science spending trend and the fate of particular programs would be set. In early August, however, the Council on Economic and Fiscal Policy, which is chaired by Prime Minister Junichiro Koizumi, centralized the priority setting.

Sink or swim? Funding for completing the derrick for this ocean drill ship could be among the initiatives swept away by Japan's efforts to trim government spending.

The council invited bureaucrats making proposals for a certain category of science spending—which provides most of the money for actual research but doesn't cover salaries or facility construction—to ask for up to 20% more than they are getting this year. "The requests will be squeezed [by the council] so science-related spending will be about the same as in the current year," says an Education Ministry official. An official on the staff of the Council for Science and Technology Policy, which is also part of the prime minister's office, explains that the administration wants "more flexibility in dramatically redistributing budget resources," something that was difficult when each ministry decided where money would go.

The budget requests already tilt heavily toward four fields the cabinet deems economically important: life sciences, information technology, the environment and energy, and nanotechnology and materials science. The Education Ministry's requested 36% increase, to $2.6 billion, for the priority fields compares to a proposed 13% increase, to $1.6 billion, for grants to individual researchers and a rise of only 2%, to $370 million, for operating large facilities such as accelerators. Kaifu argues that this rapid shift in priorities not only short-changes basic research but wastes money by pumping up funding in the priority areas faster than labs can increase staffing and facilities to absorb it.

Just how wide the disparities between fields will become, and even whether science spending is headed up or down, won't be clear until the budget is finalized around the end of the year. **–DENNIS NORMILE**

CREDITS: (TOP TO BOTTOM) JAMSTEC; A. TSIARAS/ANATOMICAL TRAVELOGUE INC.

EMBRYOLOGY

Embryo Development At the Click of a Mouse

After a 5-year gestation, the Visible Embryo is close to term. A Web site with hundreds of thousands of images capturing in mind-boggling detail the earliest stages of human development, the Visible Embryo is expected to debut later this month. "It's incredibly cool to look at how an embryo develops," says medical illustrator Elizabeth Lockett, who oversees the project for the U.S. National Museum of Health and Medicine (NMHM).

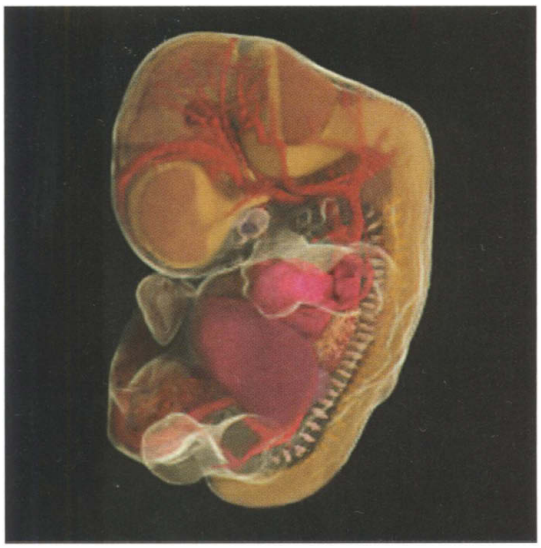
The Visible Embryo is based on the 115-year-old Carnegie Embryological Collection, a remarkable set of 7000 human embryos now housed at the national museum, a branch of the Armed Forces Institute of Pathology at the Walter Reed Army Medical Center in Washington, D.C. Initially, the project will post multiple high-resolution digital images of slices of 25 normal embryos at various stages of development. These are a subset of 700 embryos that researchers at the Carnegie Institution of Washington had carefully sliced into serial sections, all of which will eventually be included in the Visible Embryo. In all, the database will take about 9 terabytes of space at the San Diego Supercomputer Center, making it one of the largest medical image resources in the world.

An array of collaborators joined forces to make the Visible Embryo much more than a trove of pretty pictures. Coordinated by George Mason University in Fairfax, Virginia, the project will have educational tools, developed by a team at the University of Illinois, Chicago, that will include animation of organ systems as they develop. Researchers at Johns Hopkins University in Baltimore, Maryland, are designing ways for clinicians in separate locations to discuss and manipulate images that apply to specific cases. Technicians performing ultrasounds on pregnant women, for example, will be able to compare stored images of normal embryos with those in utero. Oregon Health & Science University in Portland has the task of modeling and annotating images of the heart. The whole enterprise, which has cost about $3 million so far, was funded by the National Library of Medicine (NLM) as part of its Next Generation Internet Initiative. NLM also backed the Visible Human Project, a database that posted digital cross sections of a complete male in 1994 and a female the following year.

Until now, researchers interested in using NMHM's collection had to travel to Washington; they came from all over the world, often staying for several weeks. "It's an absolute treasure," says Shirley A. Bayer, a professor emeritus at Indiana University–Purdue University Indianapolis who, with her husband Joseph Altman, used the collection for their extensive publications about the development of the brain. Making the images more accessible by putting them online will have tremendous benefits, Bayer predicts.

Two years ago, Lutz Breitsprecher, a maxillofacial surgeon at the University of Greifswald in Germany, spent nearly a month studying the Carnegie embryos to learn better surgical techniques. "Understanding facial development is important for better understanding how to do cleft surgery in the right way," says Breitsprecher. "There are different opinions about how to select the skin incision points. I found my answer there, and I never would have found it in the literature." Other surgeons, physical anthropologists, and the dying breed known as anatomists also have used the collection extensively.

The museum—which is famous for such macabre displays as a leg in a jar and an arthritic skeleton in a rocking chair—is planning two offerings in late October to tie into the birth of the Visible Embryo. One is a new exhibit titled "From Conception to Birth" featuring photographs by Alexander Tsiaras of embryos in the collection (see above), and the other is an overhaul of its long-standing exhibit on human development, which will include more embryos and fetuses at various stages. For those who can only visit the museum in cyberspace, log on to www.natmedmuse.afip.org for a tour of the museum and a link to the Visible Embryo Project. **–JON COHEN**



Digital embryo. Colored photograph by Alexander Tsiaris of 7-week-old embryo in collection at the National Museum of Health and Medicine.