

OFF THE BEAT

The Cleanest Pigs in Town



Researcher Yoon Berm Kim and one of the "mini pigs" reared in a sterile environment at Sloan-Kettering Institute for Cancer Research in order to study the development of the immune system.



Photos: J. Kenneth Boehm/Uniphoto

Immediately after entering the unimposing building through its locked door, we move into a locker room to strip down, leaving even our glasses behind. Entering the shower room, one at a time, through an airlock, we wash carefully and dry. We then proceed into the "clean" side of the building by passing into the dressing room. Once there, we step carefully onto the first of two floor mats, waiting for our still-damp feet to dry.

A purposeful ritual now begins. First, I pull on sterile gloves, a surgeon's mask and head covering. I'm still naked, and a bit chilly, but never mind — the attendant is helping me without seeming to notice my awkwardness. With head and hands covered, I'm ready to put on socks. I slip one on my left foot, which can then be set onto the second mat, leaving the right foot behind and leaving me quietly worrying about doing a split. But, no, the next foot gets its sock, with me still upright on the second mat. I'm now ready to climb into sterile, blue-green overalls (overnights, they could be renamed), replete with hood to go over my already covered head. Finally, a second pair of rubber gloves is snapped on over the first (they nearly reach my elbows), and after I step into mid-calf rubberized firefighters' boots I am ready to go through the next door.

Stepping into the hallway, I first must slosh my boots in a stainless steel pan full of a sterilizing solution (the boots already

had been treated to kill germs — this is just an added precaution) before tromping further. All of us do this, making the tiled floor glisten with the trickle of liquid that we leave everywhere we step.

And now we are clean enough to visit the pigs.

This elaborate hygienic ritual is vital to the survival of a special herd of miniature pigs being nurtured at the animal laboratories of the Sloan-Kettering Institute for Cancer Research in Rye, N.Y. The mini pigs are under the care of Yoon Berm Kim and his colleagues, who are studying the early developmental stages of the immune system. Ultimately, the scientists would like to know how that system sometimes combats — and at other times miserably capitulates to — cancer.

The mini pigs provide the Sloan-Kettering immunologists with an unusual opportunity for probing the fundamentals of the immune system. Mini pigs, which are about half the size of the typical farm variety, were developed in a special breeding program 30 years ago at the Hormel Institute of the University of Minnesota. Though their forebears were feral pigs, the mini pigs were selected in part for their docile temperaments. That, their size, and the organization of their main organ systems has made them a model system for surgeons.

Those conveniences helped to attract Kim to their charm and utility for experi-

mentation. But an important aspect of the mini pig's anatomy is what persuaded him that such animals might be unique for immunologic research. The placenta, the barrier between a developing fetus and its mother, is unusually thick in mini pigs, consisting of six layers of tissue compared with three in humans and only one in mice. The pig placenta thus silences immunologic crosstalk between a fetal piglet and its mother, preventing the mother's antibodies (proteins of her immune system) and antigens (immune-system-stimulating molecules and cells) from impinging on the fetus's immature immune system cells. Then, because the piglets are delivered by Caesarian section into sterile confines, they come into Sloan-Kettering's special laboratories as true "immunologic virgins," Kim says.

These newborn mini pigs, when subsequently deprived of the sow's immunologically rich colostrum (the first flow of milk), have no antibodies, Kim continues. There is nothing organically wrong with the immune systems of these newborn animals. Instead, they are truly blank slates. But that simple fact makes their immune systems unlike those of any other animal. For most animals, fetal life is a period of gradual immunologic indoctrination by maternal antigens and antibodies that cross the placenta. It is a gentle preparation for the intense barrage of unfriendly microbes and chemicals in the outside world.

Indeed, when the germ-free piglets are challenged, when the germ-free piglets are challenged with an antigen for the first time, they respond with ample antibodies after a bit of a lag. To Kim, this signifies that the whole apparatus for making antibodies — mainly cells known as B-lymphocytes — is set to go in animals, even before birth. Yet the system doesn't begin operation until it is needed. The jolt of an outside stimulus, such as protein acting as antigen, gets it going.

This behavior is proving helpful in discerning how the immune system copes with cancer cells. For example, scientists studying mice whose immune systems are impaired genetically were puzzled at the animals' low susceptibility to cancer. Because the mice have defective thymus glands (the site of much of the important activity of the immune system, such as readying antibody-producing cells for action), the mice were expected to be unable to ward off tumor cells. Such mice, however, have natural killer cells that do just that to tumor cells, and so protect the animals from cancer.

Just what are natural killer cells? Many immunologists had come to think that they are like other immune system cells called more simply "killer cells," but they don't need added antibody to show killing activity. The dogma was that natural killer cells are an antibody-armed version of killer cells. If so, where do they get their antibodies in antibody-deficient mice?

Here is where the mini pigs come to the

rescue. "We find there are true 'natural killer cells,'" says Kim. Such cells are distinct from killer cells, he adds, and function without need for or benefit of antibody molecules. The natural killer cells develop early during an animal's life and thus may represent a primitive feature of the immune system that functions before other more sophisticated components are put into action. Kim and his colleagues are confident of this explanation because their mini pigs have been so scrupulously prevented from developing antibodies.

Making such observations does not come easily, Kim admits. The mini pig facility took three years of punctilious planning and building before it was ready to house animals four years ago. The animals' bland food undergoes sterilization before entering their closed world. The pigs' drinking water and even the wash water is sterilized and air is carefully filtered, making the Sloan-Kettering pigs certainly the most pampered, cleanest pigs anywhere. And they appear to be content, albeit somewhat bored.

"This pig model is a lot of hard work," Kim says. But he adds that he is "hooked" on it as a means of solving some of immunology's most intricate puzzles.

—Jeffrey L. Fox

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COSMOS, EARTH, AND MAN: A Short History of the Universe—Preston Cloud. The author, a polymath, relates for the educated layman the story of the co-development of earth's air, water, crustal rocks, climate and life in cosmic perspective as a vantage point from which to view the present state and future prospects of human beings. Originally published in hardback in 1978. Yale U Pr, 1980, 372 p., illus., paper, \$7.95.

THE HEALTHY HYPOCHONDRIAC: Recognizing, Understanding, and Living with Anxieties about our Health—Richard Ehrlich. Divides hypochondriacs according to the way they express their worries about their health and explains how children learn the responses and attitudes that tend to make them hypochondriacal as adults. Also discusses hypochondria as to the role it plays in different people's lives and society, together with a brief word on self-help. Saunders Pr(HR&W), 1980, 211 p., \$11.95, paper, \$6.95.

LEARNING TO THINK—E. R. Emmet. The author feels that the study of the basic principles of reasoning helps one to think effectively and reason logically. Exercises to test your ability to reason are provided throughout the book. Emerson, 1980, 172 p., \$8.95.

THE PURPOSIVE BRAIN—Ragnar Granit. Explains and integrates two major brain systems—the physiology of vision and the control of motor activity. Visual perception is seen as an input system, motor control as an output system with the goal-oriented brain mediating between the two systems. Originally published in hardback in 1977. MIT Pr, 1980, 244 p., illus., paper, \$5.95.

RAPID VIZ: A New Method for the Rapid Visualization of Ideas—Kurt Hanks and Larry Belliston. A practical workbook to help individuals learn to visualize their thoughts. In this method of drawing, the eye, together with the brain and other muscles, makes a continuous cycle of expression and feedback that enables you to transfer thoughts from your head to expressions on paper, where they can be refined and recorded. W Kaufmann, 1980, 151 p., illus., paper, \$7.95.

THE WORLD OF LEARNING 1979-80, 30th ed. A two-volume directory of educational, cultural and scientific institutions around the world. Contains names, addresses and other details of over 24,000 academies, universities, colleges, libraries and archives, museums, art galleries, learned societies and research institutes and 150,000 people active in them. Europa Pub(Gale), 1979, 2061 p., \$105.

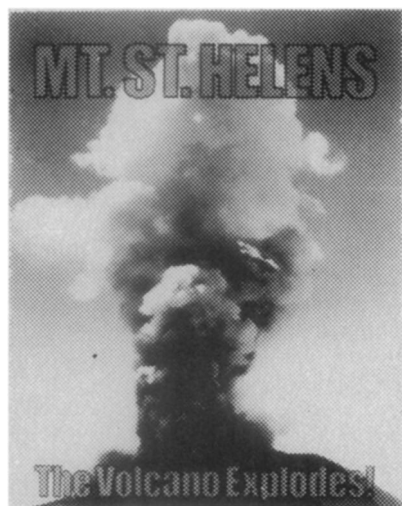
AN X-RAY ATLAS OF THE ROYAL MUMMIES—James E. Harris and Edward F. Wente. Includes photographs and microfiches of the plates made in a radiological survey of the New Kingdom pharaohs and queens to determine the states of health, types of diseases, ages at death and mummification techniques. The text covers such topics as pharaonic medicine and dentistry, the family relationship within dynasties and craniofacial variation. U of Chicago Pr, 1980, 402 p., illus., \$60.

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