Biology

From Palo Alto, Calif., at the annual meeting of the Society for Developmental Biology

Understanding the Big Bang of life

Astronomers believe they can accurately describe the initial moments after the Big Bang, the cosmic explosion that gave rise to the universe. Paul Primakoff envisions doing the same for the beginning of a new life. "Sperm and egg fusion is the Big Bang of development. We want to understand the seconds before and after," says the biologist from the University of California Davis School of Medicine.

As part of that endeavor, Primakoff and his colleagues have recently created a strain of mice unable to make fertilin-beta, a protein normally present on the surface of sperm. The males of this genetically engineered strain are infertile. While that was expected, the full explanation for this infertility has proven to be full of surprises.

Primakoff thought he knew the importance of fertilin-beta. After a sperm penetrates the zona pellucida, the protective barrier around the egg, it travels to the egg's outer membrane. The tip of the sperm's head then binds to the egg. Following this initial contact, the sperm prepares to fuse with the egg by turning on its side and making even greater contact with the egg. Primakoff knew from previous work that the sperm's fertilin-beta mediates this so-called lateral binding.

His assumption proved right. When mice are unable to make the protein, their sperm bind poorly to eggs and therefore fuse with them at a much lower rate. Yet the animals' infertility may stem from unanticipated consequences of fertilin-beta's absence, reports Primakoff. The investigators find that sperm lacking the protein fail to penetrate an egg's zona pellucida efficiently. Even more important, sperm lacking fertilin-beta rarely even made it from the uterus to the oviducts where eggs reside. It's unclear, says Primakoff, whether fertilin-beta participates directly in zona pellucida binding and the journey to an oviduct or whether its absence leads to other changes in sperm that affect both phenomena. —*J.T.*

Building a pancreas from scratch

Doug Melton is upfront about his seemingly futuristic goals. He ultimately wants to take laboratory-grown embryonic cells and induce them to form a pancreas, the organ that secretes crucial enzymes and hormones, including insulin. Melton, a biologist at Harvard University, is equally frank about his progress. "We're practically nowhere on the problem," he says.

The path leading from the earliest embryonic cells to a pancreas has many important milestones. In one of the earliest stages, embryos differentiate into three layers: the endoderm, ectoderm, and mesoderm. From the endodermis, the lungs, thymus, liver, stomach, and pancreas eventually arise. Although investigators have identified chemical signals that trigger formation of ectodermal and mesodermal cells, they've remained largely ignorant of the molecules prompting endodermal development.

Melton believes he has found one of those molecules. He and his colleagues have been looking for genes that prompt embryonic stem cells to turn on known endodermal-specific genes but not genes associated with the mesoderm or ectoderm. They found one gene, named *mixer*, that fits the bill. The gene encodes a protein that regulates the activity of other genes. This so-called transcription factor "can induce cells of the embryo to become endoderm," says Melton.

Once an embryonic cell becomes endodermal, it must still decide whether to be part of the pancreas or of some other organ. The molecules guiding that decision are also under investigation by Melton and his colleagues. They've found that the notochord, another area in a developing embryo, instructs a portion of the endoderm to form a pancreas. The command may come in the form of secreted proteins such as activin or fibroblast growth factor. Each can induce endodermal cells to become pancreatic, says Melton. —*J.T.*

Science and Society

Informed consent—Not

A nurse hands a breast cancer patient a seven-page, single-spaced consent form describing the potential risks of an experimental treatment. The patient signs on the line, indicating she understands the possible dangers of unproven cancer therapy. But does she really?

Two new studies raise troubling questions about the way researchers and physicians gather informed consent for experimental and routine medical procedures. In the first study, Terry C. Davis of the Louisiana State University Medical Center in Shreveport and her colleagues recruited 183 people, including 53 who had cancer or another medical condition.

The researchers gave the participants an adult literacy test. They discovered that, on average, the recruits were reading at a 7th to 8th grade level. Next, the team gave 69 participants an informed consent form that had been used in a cancer treatment study. The form had been written at a 16th grade level.

The remaining 114 people got a consent form written at a 7th grade level. The researchers gave all the recruits time to read the forms and then interviewed them about the contents.

Most people preferred the simplified form, the researchers found. However, those who read the easier version didn't seem to gain any better understanding of the implications of the experimental treatment. "It really didn't improve comprehension," Davis told SCIENCE NEWS.

About 90 million adults in the United States have literacy skills ranking below 7th grade, the authors note. "Our findings raise ethical and legal questions about the ability of informed consent documents to aid all individuals in the decision-making process for study participation," the authors say in the May 6 JOURNAL OF THE NATIONAL CANCER INSTITUTE.

A second study suggests that forms used by hospitals to obtain consent for routine surgical procedures are needlessly complex.

Kenneth D. Hopper of the Pennsylvania State University College of Medicine in Hershey and his colleagues studied 616 hospital consent forms. They found that 25 percent of the forms assumed that patients have college-level skills and 9 percent required postgraduate education in order to fully understand the risks and benefits of a given procedure.

Even so, the team found that many forms didn't give patients enough information to make an informed decision about a procedure. The study appears in the May issue of SURGERY. —*K.F.*

Journals make family secrets public

Many researchers have studied detailed family trees to trace disease-causing genes as they are passed from generation to generation. The diagrams can reveal incest, mistaken paternity, and other skeletons in a family's past. A study in the June 10 JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION suggests that publication of such genealogies can violate patient confidentiality.

Ethicist Jeffrey R. Botkin of the University of Utah in Salt Lake City and his colleagues surveyed 177 investigators regarding the publication of genealogies. They found that 131 did not obtain written consent for such publication and 61 researchers said they did not tell participants that their family tree would be included in a scientific article.

Once the paper appears in a scientific journal, "there may be breaches of privacy," Botkin says. He recalls a family feud after a young Catholic woman found out about her aunt's abortions.

Some scientists, on the other hand, seem well aware of privacy problems caused by the publication of family trees. Thirty-two of the researchers reported that they had altered the published genealogies in order to protect families. Only 14, however, had reported the alterations to the journal's editor. —*K.F.*