'Petri dish' mouse embryos go halfway through normal gestation

Embryos transferred from mother mouse to laboratory dish have set a new record. They can survive to the 10-day stage, or halfway through the normal mouse gestation period, report Yu-Chih Hsu and Li-Tsun Chen in the Oct. 1 SCIENCE. The laboratory-grown embryos appear identical to those that develop naturally in a mouse uterus, except the laboratory embryos grow a bit more slowly and are slightly larger. The 10-day, 4-millimeter mouse embryos have the beginnings of limbs, lungs, liver, pancreas and circulating blood. This stage is comparable to a human embryo after 29 days of gestation, according to the scientists.

The laboratory life of mouse embryos in some ways mimics that of a premature, but of course much further developed, baby. The embryos are kept in a warm incubator and are even rocked, or rather agitated, at the later stages. But the embryo, removed from the mother after just 3.5 days, is kept in a fluid environment. A liquid culture medium (containing blood serum) surrounds the embryo and provides the nutrients that would normally come from the mother's blood. "Petri dish mice," fertilized in the mother and then transferred into laboratory culture, must not be confused with "test-tube babies," which are fertilized in the laboratory then transferred to the womb.

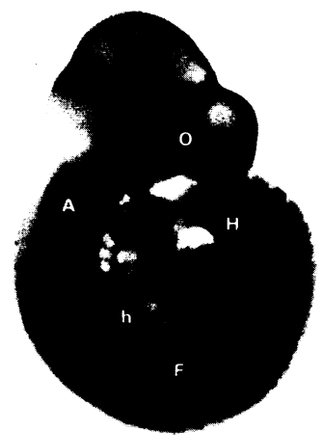
Several technical changes allowed Hsu of Johns Hopkins University and Chen of the University of Southern California to extend the mouse embryonic development in the laboratory two days beyond Hsu's previous record. "We attribute the successful growth of mouse embryos *in vitro* from the blastocyst stage to the limb bud stage to certain improvements in the culture conditions from days 7 to 9," Chen and Hsu say. They provided the embryos with blood serum from rats, increased the oxygen in the gas mixture in the incubator at the time the embryos began circulating blood and agitated the laboratory dishes, 60 oscillations per minute, to facilitate exchange of nutrients, waste products and gases.

For more than a decade Hsu has explored the conditions for embryonic survival in the laboratory. Mice have been the only mammalian embryos successfully grown. In the most recent experiments, Hsu provided the mouse embryos sequentially with serum from fetal calves, from human umbilical cords and finally from rats. Hsu says it would be preferable to use mouse serum, but that it is too difficult to harvest serum from so small an animal. The successful use of human cord serum suggests similarities in mouse and human embryonic development.

Even with the recent technical improvements, the yield of 10-day mouse embryos is low. Of 86 blastocysts moved to laboratory culture, only 9 embryos grew successfully to establish blood circulation. Hsu says that about half the embryos live for 7 days in the laboratory, but a big drop in survival occurs during the eighth day. But Hsu says there is no funding for research aimed at improving this yield.

Hsu's immediate goal is not to further extend laboratory growth of embryos to later developmental stages. He says such work would not be as useful as the earlier stages, because the embryo becomes opaque after day 10. Instead he plans to analyze the blood sera used in the culture to determine what components are essential at different stages of development, a task he says may take 10 years. Eventually laboratory-grown mouse embryos could serve as a model for the study of spontaneous abortions and birth defects.

—J.A. Miller



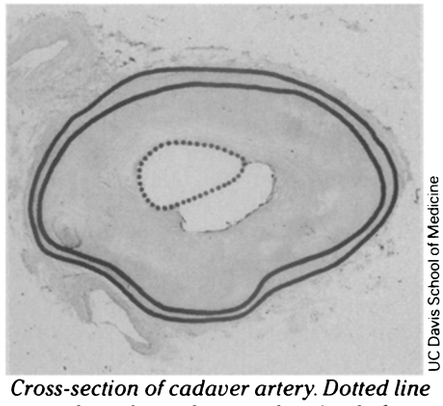
Chen and Hsu, x30

Mouse embryo after 10 days' growth in a laboratory dish is identical in organ development to 10-day-old embryos growing in the womb. With the yolk sac and amniotic sac removed, the heart (h), hind limb bud (H), forelimb bud (F) and the beginnings of ear (A) and eye (O) development are visible.

Vaporizing cholesterol with lasers

The underlying cause of most heart attacks and strokes is a buildup of plaque — fatty deposits including cholesterol — inside the body's blood vessels. A cardiologist at the University of California at Davis has successfully vaporized plaque with a miniature laser catheter. Within 10 years, Garrett Lee believes, a refined version of his technique could be on its way to replacing bypass surgery as treatment for individuals with serious arterial blockages in the heart and legs.

Once a plaque buildup has been identified (using techniques such as contrast angiography) the one-eighth-inch diameter catheter is inserted into the affected vessel and threaded along to the obstruction. Nested inside the catheter is a bundle of optical fibers that act as a gunsight for the laser. Light projected down the bundle illuminates the region adjacent to the catheter's head so that other fibers within the bundle can transmit back a view of the scene. If the optical bundle is attached to an eyepiece, one can view directly any plaque lining the vessel's interior. Alternatively, a video camera can be hooked up to project the scene onto a video monitor. On-scene viewing is necessary, Lee points out, because "it's so easy to hit the blood-vessel wall" and puncture it with the laser.



UC Davis School of Medicine

Cross-section of cadaver artery. Dotted line notes the only unobstructed region before laser burned open adjacent white area.

Adjacent to the gunsight bundle is another thread-like optical fiber. Coupled to an argon or YAG laser, this fiber transmits the laser-generated beam of coherent light used to burn away plaque. A suction tube is packed alongside it to vacuum away any residue crumbs once the lasing is complete. To date, Lee's work has been carried out on animals and plaque-ridden arteries extracted from cadavers. Human trials could occur "in about two years, maybe earlier," Lee says, pending refinement of the laser catheter. In the meantime, he has begun feeding rabbits a diet high in cholesterol to model plaque formation in living animals. Monkeys will be recruited for similar experiments soon.

Lee's goal is to do away with a need for arterial-bypass surgery. Bypass surgery, while effective, he says, "is costly, about $20,000 per case." It also requires an average 10-day hospital stay. "Hopefully we can do [laser catheterization] as a nonsurgical technique," he told SCIENCE NEWS. Without requiring anesthesia or hospitalization beyond a day or two, he believes it could dramatically cut the cost and trauma now associated with bypass surgery.

What's next? Laser vaporization of blood clots. Lee says he expects to begin presenting experimental results early next spring.

—J. Raloff