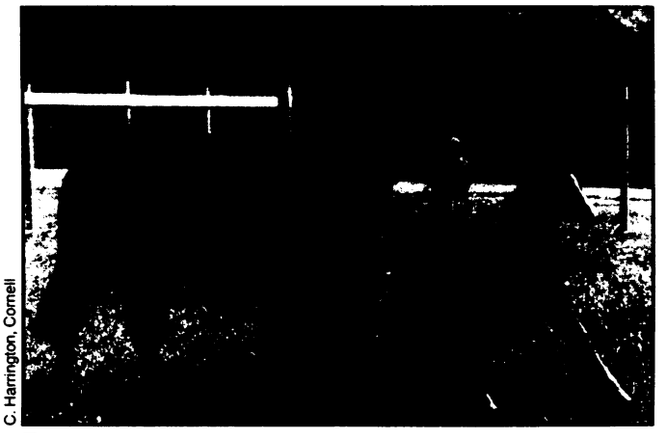
Zoology

Mules mother two species

Donkeys can serve as surrogate mothers to horses, but donkey embryos in horse mothers usually abort. Now scientists have shown that mules, the hybrids of horses and donkeys, can act as "neutral vehicles," successfully carrying to term both horse and donkey fetuses.

Two thoroughbred horses and a donkey born at Cornell University in Ithaca, N.Y., this summer are the first U.S. products of embryo transfer into mules. The transfers of eight-day-old embryos were performed by Douglas F. Antczak of Cornell and William R. Allen of the British Thoroughbred Breeders' Association in Cambridge, England. There has also been one report of a mule in Colombia serving as surrogate mother to a horse.



C. Harrington, Cornell

Thoroughbred colt frolics with its surrogate mother, a mule.

Mules in general are sterile, with one recent exception (SN: 8/18/84, p. 108). But the Cornell mules proved quite maternal. All three of the surrogate mothers were protective of their offspring and produced ample milk.

The embryo transfer research is not aimed at giving mules a regular role as surrogates in the horse breeding industry, says Antczak. The scientists rather are working to delineate the roles of mother and fetus in directing the hormonal and immunological characteristics of pregnancy.

Observations of the mule surrogate mothers have demonstrated, for example, that levels of a key pregnancy hormone are determined by the fetus. In natural horse pregnancies, levels of equine chorionic gonadotropin (ECG) are much higher than in natural donkey pregnancies. Antczak this year found that the ECG levels were also higher in mules pregnant with horse fetuses than in the mule pregnant with a donkey fetus.

The development of a specialized placental structure, unique to equines, is also being investigated with the mule mothers. In a natural pregnancy, the horse or donkey placenta forms 10 to 15 characteristic structures, each about the size of a fingertip, that secrete ECG. These structures, called endometrial cups, also appear in the surrogate mother mules. When a donkey embryo is implanted in a horse, however, no endometrial cups form. "The embryo is fine, the uterus is fine, but there is something inappropriate about the interaction," Antczak says.

Researchers also want to study the unusually strong natural response of the horse immune system to pregnancy. Antczak suggests that the failure of horses to successfully bear donkey fetuses has at least in part an immunological basis.

These studies may aid the horse breeding industry in a major problem, the high rate of spontaneous abortion. "Pregnancy loss could be caused by a failure to make an appropriate immune response," Antczak says. "The data gathered from these embryo transfer pregnancies may help us to understand the immunoregulatory mechanisms that operate during normal pregnancy."

Biology

From our reporter in Boston at the international NATURE conference on the molecular biology of cancer

Antibody linked to cancer survival

Cancer patients make antibodies against a protein called malignin, and a recent study shows that the more of this cell-killing antibody there is in a patient's blood, the longer the cancer victim is likely to live. This doesn't necessarily mean that anti-malignin antibody (AMA) fights cancer. "Whether it's simply an accidental association ... or whether it has something to do with actual survival, we don't know," cautions Samuel Bogoch of Boston University Medical School, who coauthored the report.

While it's been known for several years that patients with active cancers have much higher AMA levels than do healthy controls, clearly terminal patients or recovered patients, Bogoch believes the new data are the first to show a quantitative relationship between the blood serum concentration of a "general cancer antibody" and the patient's survival time.

Bogoch and his colleagues measured AMA levels in over 500 cancer patients and correlated these values with how long the patients lived following the measurement. Those with the lowest AMA levels, less than 25 micrograms per milliliter of serum, fared worst: 80 percent of those who survived eight months died within the next five. Survival times increased reliably with AMA levels. Those few patients at the other end of the concentration spectrum, who had 500 micrograms of AMA per milliliter or more, on average lived longest.

This tantalizing relationship between anti-malignin antibody and survival begs some obvious questions. If AMA does inhibit cancer (and it's been associated with over 30 types of cancer so far), how does it do so, and what role might malignin, the protein it attacks, play in malignancy? To approach these questions, Bogoch and colleagues are working to unravel the structure of malignin and its protein relatives. No complete structure has yet been determined, but some of AMA's known structural features suggest, Bogoch says, that malignin may be related to the protein produced by the known cancer gene called c-*myc*.

The Boston University group's second strategy is to study the action of the antibody directly. Three years ago they made a monoclonal antibody to mouse malignin, and now they report (and have submitted for publication) that they can make monoclonal antibody to the human protein as well. Bogoch hopes experiments to study the effects of the human antibody on cancer cells in culture and in animals will be under way within a year.

Recessive gene tied to cancer

Retinoblastoma is an inheritable eye tumor that strikes young children. Although scientists know roughly where the gene responsible for this cancer lies—on chromosome 13—it hasn't been isolated or characterized. Nonetheless, they believe "it's perhaps a new kind of gene," says Ray White of the Howard Hughes Medical Center at the University of Utah in Salt Lake City.

The gene appears to be a mutant recessive, and so heterozygous cells, which have one dominant and one recessive copy (allele) of the gene, are normal — they are not associated with retinoblastoma. But "this is not a normal oncogene," says White, who notes that all the known oncogenes (cancer genes) are dominant. In retinoblastoma cells, the dominant allele is missing — in some cases the entire chromosome carrying the gene is lost — and so the mutant recessive allele is left to run the show.

Two molecular models have been proposed, White says, to explain how the dominant allele loss might lead to cancer. One model supposes that the normal (dominant) allele makes a product that suppresses a true oncogene in the same cell. When this allele is lost, the remaining mutant gene fails to suppress the distant oncogene, and that oncogene activates, turning the cell cancerous. According to the second model, the dominant allele encodes a protein that regulates cell growth. When this allele is lost, the mutant allele fails as a backup, and cell growth goes awry, resulting in cancer.