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**JOURNALS IN  
SCIENCE AND MEDICINE**

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**Development**

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**Volume 128, Number 19  
October 1, 2001**

**Blastomeres arising from the first  
cleavage division have distinguishable  
fates in normal mouse development**

*K. Piotrowska et al.*

Two independent studies have recently suggested similar models in which the embryonic and abembryonic parts of the mouse blastocyst become separated already by the first cleavage division. However, no lineage tracing studies carried out so far on early embryos provide the support for such a hypothesis. Thus, to reexamine the fate of blastomeres of the two-cell mouse embryo, we have undertaken lineage tracing studies using a non-perturbing method. We show that two-cell stage blastomeres have a strong tendency to develop into cells that comprise either the embryonic or the abembryonic parts of the blastocyst. Moreover, the two-cell stage blastomere that is first to divide will preferentially contribute its progeny to the embryonic part. Nevertheless, we find that the blastocyst embryonic-abembryonic axis is not perfectly orthogonal to the first cleavage plane, but often shows some angular displacement from it. Consequently, there is a boundary zone adjacent to the interior margin of the blastocoel that is populated by cells derived from both earlier and later dividing blastomeres. The majority of cells that inhabit this boundary region are, however, derived from the later dividing two-

cell stage blastomere that contributes predominantly to the abembryonic part of the blastocyst. Thus, at the two-cell stage it is already possible to predict which cell will contribute a greater proportion of its progeny to the abembryonic part of the blastocyst (region including the blastocyst cavity) and which to the embryonic part (region containing the inner cell mass) that will give rise to the embryo proper.

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**Journal of the American  
Medical Association**

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**Volume 286, Number 18  
November 14, 2001**

**Tamoxifen and Breast Cancer: Inci-  
dence among Women with Inherited  
Mutations in BRCA1 and BRCA2**

*Mary-Claire King et al.*

Tamoxifen reduced breast cancer incidence among healthy BRCA2 carriers by 62%, similar to the reduction in incidence of ER-positive breast cancer among all women in the Breast Cancer Prevention Trial. In contrast, tamoxifen use beginning at age 35 years or older did not reduce breast cancer incidence among healthy women with inherited BRCA1 mutations. Whether tamoxifen use at a younger age would reduce breast cancer incidence among healthy women with BRCA1 mutations remains unknown.

**Volume 286, Number 17  
November 7, 2001**

**Relationship between Interleukin 6  
and Mortality in Patients with Un-  
stable Coronary Artery Disease**

*Eva Lindmark et al.*

Circulating IL-6 is a strong independent marker of increased mortality in unstable CAD and identifies patients who benefit

most from a strategy of early invasive management.

**Association Between Myeloperoxidase Levels and Risk of Coronary Artery Disease**

*Renliang Zhang, M.D., et al.*

Elevated levels of leukocyte- and blood-MPO are associated with the presence of CAD. These findings support a potential role for MPO as an inflammatory marker in CAD and may have implications for atherosclerosis diagnosis and risk assessment.

**Positron Emission Tomography in Evaluation of Dementia**

*Daniel H. S. Silverman, M.D., et al.*

In patients presenting with cognitive symptoms of dementia, regional brain metabolism was a sensitive indicator of AD and of neurodegenerative disease in general. A negative PET scan indicated that pathologic progression of cognitive impairment during the mean three-year follow-up was unlikely to occur.

**Alcohol and Breast Cancer**

*Keith W. Singletary and Susan M. Gapstur*

The association of alcohol consumption with increased risk for breast cancer has been a consistent finding in a majority of epidemiologic studies during the past two decades. Herein, we summarize information on this association from human and animal investigations, with particular reference to epidemiologic data published since 1995. Increased estrogen and androgen levels in women consuming alcohol appear to be important mechanisms underlying the association. Other plausible mechanisms include enhanced mammary gland susceptibility to carcinogenesis, increased mammary carcinogen DNA damage, and greater metastatic potential of breast cancer cells, pro-

cesses for which the magnitude likely depends on the amount of alcohol consumed. Susceptibility to the breast-cancer-enhancing effect of alcohol may also be affected by other dietary factors (such as low folate intake), lifestyle habits (such as use of hormone replacement therapy), or biological characteristics (such as tumor hormone receptor status). Additional progress in understanding alcohol's enhancing effect on breast cancer will depend on a better understanding of the interactions between alcohol and other risk factors and on additional insights into the multiple biological mechanisms involved.

**Volume 286, Number 16  
October 24/31, 2001**

**Process of Care and Outcomes for Elderly Patients Hospitalized with Peptic Ulcer Disease**

*Jane Brock, M.D., et al.*

This quality improvement program for elderly patients with PUD resulted in increased screening for *H. pylori* and increased treatment of *H. pylori* infection but no change in counseling about NSAID use. However, with the low prevalence of *H. pylori* detected, treatment of *H. pylori* infection was not associated with a reduction in repeat hospitalization for PUD or subsequent mortality, whereas counseling about the risks of using NSAIDs was associated with a reduction in the risk of both outcomes.

**Volume 286, Number 13  
October 3, 2001**

**Single vs. Weekly Courses of Antenatal Corticosteroids for Women at Risk of Preterm Delivery**

*Debra A. Guinn, M.D., et al.*

Weekly courses of antenatal corticosteroids did not reduce composite neonatal morbidity compared with a single course of treatment. Weekly courses of antenatal corticoids

teroids should not be routinely prescribed for women at risk of preterm delivery

**Volume 286, Number 12**  
**September 26, 2001**

**Endocrine Function and Oocyte Retrieval after Autologous Transplantation of Ovarian Cortical Strips to the Forearm**

*Kutluk Oktay, M.D., et al.*

Subcutaneous ovarian transplantation appears to be a relatively simple, novel technique to preserve endocrine function in women undergoing sterilizing cancer therapy or surgery.

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**The Journal of Regenerative Medicine**

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**Volume 2**  
**November 26, 2001**

**Somatic Cell Nuclear Transfer in Humans: Pronuclear and Early Embryonic Development**

*J.B. Cibelli et al.*

Human therapeutic cloning requires the reprogramming of a somatic cell by nuclear transfer to generate autologous totipotent stem cells. We have parthenogenetically activated 22 human eggs and also performed nuclear transfer in 17 metaphase II eggs. Cleavage beyond the eight-cell stage was obtained in the parthenogenetic-activated eggs, and blastocoele cavities were observed in six. Three somatic cell-derived embryos developed beyond the pronuclear stage up to the six-cell stage. The ability to create autologous embryos represents the first step towards generating immune-compatible stem cells that could be used to overcome the problem of immune rejection in regenerative medicine.

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**Nature**

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**Volume 414, Number 6863**  
**November 29, 2001**

**Transgenic DNA introgressed into traditional maize landraces in Oaxaca, Mexico**

*David Quist and Ignacio H. Chapela*

Concerns have been raised about the potential effects of transgenic introductions on the genetic diversity of crop landraces and wild relatives in areas of crop origin and diversification, as this diversity is considered essential for global food security. Direct effects on nontarget species, and the possibility of unintentionally transferring traits of ecological relevance onto landraces and wild relatives have also been sources of concern. The degree of genetic connectivity between industrial crops and their progenitors in landraces and wild relatives is a principal determinant of the evolutionary history of crops and agroecosystems throughout the world. Recent introductions of transgenic DNA constructs into agricultural fields provide unique markers to measure such connectivity. For these reasons, the detection of transgenic DNA in crop landraces is of critical importance. Here we report the presence of introgressed transgenic DNA constructs in native maize landraces grown in remote mountains in Oaxaca, Mexico, part of the Mesoamerican center of origin and diversification of this crop.

**Volume 413, Number 6856**  
**October 11, 2001**

**A sperm ion channel required for sperm motility and male fertility**

*D. Ren, et al.*

Calcium and cyclic nucleotides have crucial roles in mammalian fertilization, but the

molecules comprising the Ca<sup>2+</sup>-permeation pathway in sperm motility are poorly understood. Here we describe a putative sperm cation channel, CatSper, whose amino-acid sequence most closely resembles a single, six-transmembrane-spanning repeat of the voltage-dependent Ca<sup>2+</sup>-channel four-repeat structure. CatSper is located specifically in the principal piece of the sperm tail. Targeted disruption of the gene results in male sterility in otherwise normal mice. Sperm motility is decreased markedly in CatSper<sup>-/-</sup> mice, and CatSper<sup>-/-</sup> sperm are unable to fertilize intact eggs. In addition, the cyclic-AMP-induced Ca<sup>2+</sup> influx is abolished in the sperm of mutant mice. CatSper is thus vital to cAMP-mediated Ca<sup>2+</sup> influx in sperm, sperm motility, and fertilization. CatSper represents an excellent target for nonhormonal contraceptives for both men and women.

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**The New England  
Journal of Medicine**

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**Volume 345, Number 22  
November 29, 2001**

**Decreased Rate of Coronary Restenosis  
after Lowering of Plasma  
Homocysteine Levels**

*Guido Schnyder, M.D., et al.*

Treatment with a combination of folic acid, vitamin B12, and pyridoxine significantly reduces homocysteine levels and decreases the rate of restenosis and the need for revascularization of the target lesion after coronary angioplasty. This inexpensive treatment, which has minimal side effects, should be considered as adjunctive therapy for patients undergoing coronary angioplasty.

**Simvastatin and Niacin, Antioxidant  
Vitamins, or the Combination for the  
Prevention of Coronary Disease**

*B. Greg Brown, M.D., et al.*

Simvastatin plus niacin provides marked clinical and angiographically measurable benefits in patients with coronary disease and low HDL levels. The use of antioxidant vitamins in this setting must be questioned.

**Volume 345, Number 21  
November 22, 2001**

**Nonsteroidal Anti-inflammatory Drugs  
and the Risk of Alzheimer's Disease**

*Bas A. in 't Veld, M.D., et al.*

The long-term use of NSAIDs may protect against Alzheimer's disease but not against vascular dementia.

**The Safety of Inactivated Influenza  
Vaccine in Adults and Children  
with Asthma**

*The American Lung Association Asthma  
Clinical Research Centers*

The inactivated influenza vaccine is safe to administer to adults and children with asthma, including those with severe asthma. Given the morbidity of influenza, all those with asthma should receive the vaccine annually.

**Volume 345, Number 19  
November 8, 2001**

**Recurrence Rates after Treatment of  
Breast Cancer with Standard Radio-  
therapy with or without  
Additional Radiation**

*Harry Bartelink, M.D., et al.*

In patients with early breast cancer who undergo breast-conserving surgery and receive 50 Gy of radiation to the whole breast, an

additional dose of 16 Gy of radiation to the tumor bed reduces the risk of local recurrence, especially in patients younger than 50 years of age.

**Implantation and the Survival of Early Pregnancy**

*E. Norwitz, M.D. et al.*

**Volume 345, Number 18  
November 1, 2001**

**Impact of High-Normal Blood Pressure on the Risk of Cardiovascular Disease**

*Ramachandran S. Vasan, M.D., et al.*

High-normal blood pressure is associated with an increased risk of cardiovascular disease. Our findings emphasize the need to determine whether lowering high-normal blood pressure can reduce the risk of cardiovascular disease.

**Volume 345, Number 17  
October 25, 2001**

**Blood Transfusion in Elderly Patients with Acute Myocardial Infarction**

*Wen-Chih Wu, M.D., et al.*

Blood transfusion is associated with a lower short-term mortality rate among elderly patients with acute myocardial infarction if the hematocrit on admission is 30.0 percent or lower and may be effective in patients with a hematocrit as high as 33.0 percent on admission.

**Volume 345, Number 15  
October 11, 2001**

**A Pooled Analysis of Adjuvant Chemotherapy for Resected Colon Cancer in Elderly Patients**

*Daniel J. Sargent et al.*

Selected elderly patients with colon cancer can receive the same benefit from fluorouracil-based adjuvant therapy as their younger counterparts, without a significant increase in toxic effects.

**Volume 345, Number 14  
October 4, 2001**

**Pregnancy-Associated Plasma Protein A as a Marker of Acute Coronary Syndromes**

*Antoni Bayes-Genis, M.D. et al.*

PAPP-A is present in unstable plaques, and circulating levels are elevated in acute coronary syndromes; these increased levels may reflect the instability of atherosclerotic plaques. PAPP-A is a new candidate marker of unstable angina and acute myocardial infarction.

**The Prognostic Value of B-Type Natriuretic Peptide in Patients with Acute Coronary Syndromes**

*James A. de Lemos, M.D., et al.*

A single measurement of B-type natriuretic peptide, obtained in the first few days after the onset of ischemic symptoms, provides predictive information for use in risk stratification across the spectrum of acute coronary syndromes. Cardiac neurohormonal activation may be a unifying feature among patients at high risk for death after acute coronary syndromes.

**Volume 345, Number 12  
September 20, 2001**

**The Effect of Irbesartan on the Development of Diabetic Nephropathy in Patients with Type 2 Diabetes**

*Hans-Henrik Parving, M.D., et al.*

Irbesartan is renoprotective, independently of its blood-pressure-lowering effect in patients with type 2 diabetes and micro-albuminuria.

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**Effects of Losartan on Renal and Cardiovascular Outcomes in Patients with Type 2 Diabetes and Nephropathy**

*Barry M. Brenner, M.D., et al*

Losartan conferred significant renal benefits in patients with type 2 diabetes and nephropathy, and it was generally well tolerated.

**Renoprotective Effect of the Angiotensin-Receptor Antagonist Irbesartan in Patients with Nephropathy Due to Type 2 Diabetes**

*Edmund J. Lewis, M.D., et al.*

The angiotensin-II-receptor blocker irbesartan is effective in protecting against the progression of nephropathy due to type 2 diabetes. This protection is independent of the reduction in blood pressure it causes.

**Volume 345, Number 11  
September 13, 2001**

**Severe Pulmonary Embolism Associated with Air Travel**

*F. Lapostolle et al.*

A greater distance traveled is a significant contributing risk factor for pulmonary embolism associated with air travel.

**Helicobacter pylori Infection and the Development of Gastric Cancer**

*N. Uemura*

Gastric cancer develops in persons infected with *H. pylori* but not in uninfected persons. Those with histologic findings of severe gastric atrophy, corpus-predominant gastritis, or intestinal metaplasia are at increased risk. Persons with *H. pylori* infection and nonulcer dyspepsia, gastric ulcers, or gastric hyperplastic polyps are also at risk, but those with duodenal ulcers are not.

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**Proceedings of the National Academy of the Sciences**

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**Volume 98, Issue 24  
November 20, 2001**

**Conservation of methylation reprogramming in mammalian development: Aberrant reprogramming in cloned embryos**

*W. Dean et al.*

Mouse embryos undergo genome-wide methylation reprogramming by demethylation in early preimplantation development, followed by remethylation thereafter. Here we show that genome-wide reprogramming is conserved in several mammalian species and ask whether it also occurs in embryos cloned with the use of highly methylated somatic donor nuclei. Normal bovine, rat, and pig zygotes showed a demethylated paternal genome, suggesting active demethylation. In bovine embryos methylation was further reduced during cleavage up to the eight-cell stage, and this reduction in methylation was followed by de novo methylation by the 16-cell stage. In cloned one-cell embryos there was a reduction in methylation consistent with active demethylation, but no further demethylation occurred subsequently. Instead, de novo methylation and nuclear reorganization of methylation patterns resembling those of differentiated cells occurred precociously in many cloned embryos. Cloned, but not normal, morulae had highly methylated nuclei in all blastomeres that resembled those of the fibroblast donor cells. Our study shows that epigenetic reprogramming occurs aberrantly in most cloned embryos; incomplete reprogramming may contribute to the low efficiency of cloning.



**Volume 98, Issue 23**  
**November 6, 2001**

**Transgenic mice produced by retroviral transduction of male germ-line stem cells**

*M. Nagano et al.*

Male germ-line stem cells are the only cell type in postnatal mammals that have the capability to self-renew and to contribute genes to the next generation. Genetic modification of these cells would provide an opportunity to study the biology of their complex self-renewal and differentiation processes, as well as enable the generation of transgenic animals in a wide range of species. Although retroviral vectors have been used as an efficient method to introduce genes into a variety of cell types, postnatal male germ-line stem cells have seemed refractory to direct infection by these viruses. In addition, expression of genes transduced into several types of stem cells, such as embryonic or hematopoietic, is often attenuated or silenced. We demonstrate here that *in vitro* retroviral-mediated gene delivery into spermatogonial stem cells of both adult and immature mice results in stable integration and expression of a transgene in 2-20% of stem cells. After transplantation of the transduced stem cells into the testes of infertile recipient mice, approximately 4.5% of progeny from these males are transgenic, and the transgene is transmitted to and expressed in subsequent generations. Therefore, there is no intrinsic barrier to retroviral transduction in this stem cell, and transgene expression is not extinguished after transmission to progeny.

**Lifetime correction of genetic deficiency in mice with a single injection of helper-dependent adenoviral vector**

*I.H. Kim et al.*

Ideally, somatic gene therapy should result in lifetime reversal of genetic deficiencies. However, to date, phenotypic correction of monogenic hyperlipidemia in mouse models by *in vivo* gene therapy has been short-lived and associated with substantial toxicity. We have developed a helper-dependent adenoviral vector (HD-Ad) containing the apolipoprotein (apo) E gene. A single I.V. injection of this vector completely and stably corrected the hypercholesterolemia in apoE-deficient mice, an effect that lasted the natural lifespan of the mice. At 2.5 years, control aorta was covered 100% by atherosclerotic lesion, whereas aorta of treated mice was essentially lesion-free. There was negligible toxicity associated with the treatment. We also developed a method for repeated HD-Ad vector administration that could be applied to organisms, e.g., humans, with life spans longer than 2-3 years. These studies indicate that HD-Ad is a promising system for liver-directed gene therapy of metabolic diseases.

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**Science**

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**Volume 294, Number 5548**  
**November 30, 2001**

**Cloned Cattle Can Be Healthy and Normal**

*R.P. Lanza et al.*

**Volume 294, Number 5540,**  
**October 5, 2001**

**Is a New Eugenics Afoot?**

*Garland E. Allen*

During the first three decades of the 20th century, eugenics became a popular concept in several countries throughout the world, especially the United States and, after World War I, in Germany. In his essay, Allen provides a historical account of this early eu-

genics movement and asks whether we are now moving toward a new era of eugenics, where reproductive decisions are made on the basis of social cost.

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**JOURNALS IN  
PHILOSOPHY, LAW,  
AND THEOLOGY**

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**Child and Family**

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**Volume 23, Number 1  
Summer, 2001**

**Fetal Memory: Does It Exist?  
What Does It Do?**

*P.G. Hepper*

Thus there are a number of possible reasons why the fetus should have a functioning memory, not perhaps of the complexity of the adult or even infant, but sufficient to ease its progress in its new world after birth. Further studies are required to examine whether these proposed functions, or indeed others, do actually exist. They may also serve to direct future research into fetal memory, the existence of which, in some form, is no longer in doubt.

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**Ethics**

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**Volume 112, Number 1  
October, 2001**

**A Virtue-Ethical Account  
of Right Action**

*Christine Swanton*

It is a common view of virtue ethics that it emphasizes the evaluation of agents and

downplays or ignores the evaluation of acts, especially their evaluation as right or wrong. Despite this view, some contemporary proponents of virtue ethics have explicitly offered a virtue-ethical criterion of the right, contrasting that criterion with Kantian and consequentialist criteria. I too believe that though the virtues themselves require excellence in affective and motivational states, they can also provide the basis of accounts of rightness of actions, where the criteria for rightness can deploy notions of success extending beyond such agent-centered excellences. They can do this, I shall claim, through the notion of the target or aim of a virtue. This notion can provide a distinctively virtue-ethical notion of rightness of actions.

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**Ethics and Medicine**

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**Volume 17, Number 3  
Fall, 2001**

**Prenatal DNR Orders and the Baby  
Doe Regulations:  
Case Review and Analysis**

*Robert E. Cranston, M.D.*

With this in mind, some hospitals have established policies for withholding or withdrawing life-sustaining treatment from infants. Carle Foundation Hospital, a not-for-profit facility in Urbana, Illinois, is such a hospital. Carle's policy, currently in draft form, emphasizes the importance of parental rights in making decisions for their newborns, while abiding by state and federal laws.

**A Thirty-Year Perspective on  
Personhood: How Has the Debate  
Changed?**

*Dennis M. Sullivan, M.D.*

This paper will review the concept of personhood and its relevance to bioethics. I