COVER

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Cover: " Entwine"
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Introduction

In February of this year, Korean scientists reported in Nature[1] the first steps to engage in human therapeutic cloning. They took an unfertilized egg from a woman and utilized nuclear transfer technology to generate a pre-implanted embryo. The scientists then used this pre-implanted embryo as the tissue source to produce an embryonic human stem cell line that was genetically identical to that of the woman volunteer. As with the continual mapping of the human genome, these discoveries serve as "road signs" on a route to human beings controlling their own biological destiny. With each new advance and discovery, there arises a plethora of ethical questions and dilemmas. For example, bioethical debates regarding the beginnings of human life or when a human embryo attains the moral status of a human being continue both in the Congress, among scientists, and among various religious organizations.

Topics in Biology: Frontiers in Bioethics is a course that addresses these bioethical dilemmas to Columbia University students interested in pursuing careers in science-based fields. These students are at the front line of scientific discovery. Their future innovative research and ability to communicate science to the public will elicit, or inspire bioethical debate. Furthermore, they will become essential players in helping society resolve bioethical dilemmas.

The main objectives of this course were: to analyze bioethical dilemmas from a scientific perspective, to increase the sensitivity to and appreciation of bioethical concerns surrounding scientific breakthroughs, and to develop guidelines that either resolve or manage the ethical challenges of scientific discoveries. The authors of these essays are all students at Columbia University, many of which were enrolled in this course. However, all the authors represent aspiring scientists, physicians, lawyers and philosophers whose thoughts and opinions are the heartbeat of this Journal.

I would like to thank the various groups that provided financial assistance to publish this Journal including; The Department of Biological Sciences of Columbia University, The Center For the Study of Science and Religion of Columbia University, The Center for Bioethics of Columbia University, and the Department of External Relations of Columbia University. As the Instructor for Frontiers in Bioethics, I appreciate the efforts and energies of all those involved to create this Journal. I am especially indebted to the contributing authors and student editors who put in countless hours to ensure the journal's success.

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[1] Woo Suk Hwang , et al. 2004 Mar 12;303(5664):1669-74

Introductory letter from President Bollinger

Biomedical research in the twenty-first century promises discoveries that are nothing short of revolutionary. Stem cell research, gene therapy, and new technologies in fertility and vaccines are only some of the routes that may lead to dramatic improvements in human health. Columbia University is at the forefront of biomedical research, and it is incumbent upon us to analyze the extraordinary number of related ethical issues.

It is important to understand that these ethical issues are not merely abstract questions. They are, by definition, issues that arise from the application - or the potential application -- of research to human medical care. Those ethical dilemmas must be analyzed in ways that can usefully guide public policy as well as private action.

The Columbia University Journal of Bioethics seeks to expand our appreciation and knowledge of the ethical implications of biomedical research by addressing a broad range of topics, including issues of genetically modified organisms, therapeutic cloning, stem cells and pharmacogenomics. The journal also provides a forum for sharing the diversity of opinions at Columbia. I am especially proud of the inclusion of undergraduate and graduate students in the Journal. Student editors, under the guidance of John Loike, Ph.D., Course Instructor, and Ruth Fischbach, Ph.D., M.P.E., Director of the Columbia University Center of Bioethics, review and edit articles and design and produce the journal consistent with the high standards of the University.

It is with great pleasure that Columbia University supports this innovative project.

Dr. Lee Bollinger, President Columbia University

Preface

Columbia has an abundance of bright students. Nowhere is this valuable resource more evident than in this first Columbia College Journal of Bioethics. For it is here, inspired by their professor, Dr. John Loike, that the students in the Topics in Biology: Frontiers in Bioethics course set off to investigate the most novel and perplexing issues generated by biotechnology. These breakthroughs are often awesome, and it takes time for the ethical, legal, and social implications to be clarified. Composing the op-ed pieces in this journal provided the students singular opportunities to explore the many facets of profound, often wrenching issues and to provide their assessments, concerns, and recommendations for future action.

The interface between science and ethics is a notoriously gray area where intended and unintended consequences surface, where unique and unexpected outcomes are revealed. Germ-line engineering and designer eugenics, cloned organs, selective conception, patented genes, and transcranial magnetic stimulation are just a few of the sensational yet troubling innovations lurking nearby to confront us. Reading the pieces in this journal gives me confidence that there now is a cadre of students sensitized to identify and grapple with the exquisite ethical aspects of our scientific advances. They will consider the ethical imperative – it is not what can be done, rather it is what should be done. Their sharp minds and talented pens will guide us well.

The Center for Bioethics is proud to assist in the creation of this journal and privileged to promote these students. Sensitized, they will be our discerning and constructive critics who will guide us as a society as, inevitably, we must face the ever-new frontiers in science and bioethics.

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Genetics

Risky or Remediable? Issues with Genetic Screening

By Tanaz Sharifnia and Vera Trofimenko

The increased availability of genetic screening techniques in recent years has no doubt propelled a fierce wave of debate surrounding issues of regulation and proprietorship of genetic information. At the forefront of this debate is the question of whether knowledge of genetic information would give rise to a new brand of discrimination: discriminatory hiring practices and allocation of benefits such as insurance, differential treatment in the workplace, a eugenic approach to childbearing decisions, and the use of genetic determinism to justify and perpetuate racial and ethnic inequalities.

Common to these outcomes, is a danger associated not with the technology of genetic screening per se, but rather the abuse of the knowledge that genetic screening confers. This distinction becomes critical when assessing the risks associated with the practice of genetic screening; ethical dilemmas produced by the abuse of genetic knowledge may be ameliorated with legislation and appropriate regulatory practices, whereas this simply may not be feasible for problems associated with the technology itself. Further, it is clear that the advantages of genetic screening far outweigh the difficulties involved in constructing such a system of regulation.

Genetic screening provides knowledge that can be applied toward the prevention and treatment of various chronic diseases. Following a genetic screen, a patient can be informed about the risk of an occurrence of a particular genetic disorder, its diagnosis, the probable course of the disorder, and ways of managing the disease. This information offers an individual the power to proceed in making educated decisions regarding his or her health. Following a genetic screen showing a predisposition to a given disease, an individual has the ability to take preventative measures, such as engaging in a healthier lifestyle that could potentially prevent or delay the onset of the inherited disease. Also, genetic screening allows couples at risk for conceiving a chronically ill child to make informed reproductive decisions.

It is clear that the advantages of genetic screening far outweigh the difficulties involved in constructing such a system of regulation.

The value of the information provided by genetic screens, and the preventative

treatments for which this allows, cannot be underestimated. However, genetic screening technology must be used under the control of tight legislation in order to avoid practices that could lead to discrimination, such as involuntary testing and loss of patient confidentiality. Legislation calling for federal oversight of testing laboratories could help to regulate quality, ensure that screening is voluntary, and limit and control the use and interpretation of pre-symptomatic or predictive tests. Moreover, legislation could address dilemmas facing physicians with respect to disclosure of results. disease (HD), there must be specific codes of conduct dictating how the physician must first clarify his or her responsibilities to both patients and their families.

By taking the appropriate measures to control the ownership and dissemination of genetic information, we may soon be able to benefit from genetic screening while, at the same time addressing some of the ethical concerns surrounding its practice.

Good Crop, Bad Crop:
The Truth Behind GeneticallyModified Organisms

By Ryan Cordell and Diana Nguyen

For some, food biotechnology appears to be an evil plot to wreak havoc on the wellbeing of the world's inhabitants as well as to upset nature's delicate balance with its cunning release of rampant pathogens into the environment. Together with "Big Business," small-time farmers have managed to drive the United States to file a lawsuit against the European Union for its call to halt the production of genetically modified crops (GMCs) and biotech food products. Americans have even accused the EU of perpetuating starvation among the continental African masses due to the EU's current stance against crop biotechnology. The EU, on the other hand, will not idly stand by while the U.S. tries to stuff all of this down its throat. As we speak, Europe is oiling up its propaganda machines for yet another round of GMC-bashing and fear-spreading; it is also looking to make the labeling and tracking of GMCs mandatory.

There seems to be no middle ground to stand on (maybe it's choked with super weeds.) On the left side of the Atlantic, people sing the praises of GM foods and see a tomorrow without hunger, famine, or hay fever; they see crops with more vitamins, farmers with more money, and starving people with more food. Europeans, however, see a future overgrown with imperishable super weeds and air full of mutant pollen grains the size of ping-pong balls. They envision a world where eating a carrot gives you a mouthful of antibiotics, and where around each corner, a super-virus waits menacingly to take your lunch money.

Can this be? Let us leave the conjecture and guesswork behind and instead illuminate ourselves, and the subject at hand, by focusing on the pure science of the matter.

Farmers have been incorporating helpful traits into their crops for millennia. Developing the new trait in the lab under careful selection as opposed to in the field does not change matters. If a trait like herbicide resistance happened to find its way into a weed, the world still would not come to an end. Long before man created herbicides, farmers were clearing their fields of weeds that were better suited to grow in artificial environments.

There seems to be no middle ground to stand on (maybe it's choked with super weeds.)

Herbicide abuse is a concern that is a bit more realistic. For agriculturalists trying to kill off infectious weeds, it only becomes problematic when they get a bit overzealous with their herbicides after planting crops that are immune to them (though there is already an abundance of "conventional crops" that are immune to various herbicides.) Ironically, studies show that traditional foodstuffs are usu-

ally only immune to the more harmful herbicides, which can and do pollute soil and ground water. Biotech crops, however, are specifically designed for resistance to more mild herbicides that decompose quickly after they have carried out their purpose.

The third major concern for opponents of GM technology is the possible creation of super-viruses. While there are myriad plant viruses out in the wild and often they do take up and recombine new pieces of DNA, this is almost always a fruitless process. Hundreds to thousands of different plant viruses already exist, and possible genetic combinations are infinite throughout the whole plant kingdom. The probability that a manmade plant will have the key gene and that the prime circumstances are present to lead to a viral apocalypse is negligibly small.

The "Greens" assert that hazardous gene material is used to genetically modify biotech crops. The fact of the matter is, both organic and non-organic farmers have been incorporating the same Bacillus thuringiensis (Bt) genes- genes from naturally-occurring bacteria that contain insect-killing toxins- into their crops for ages. These genes have had an outstanding record of successful produce yield with a decreased necessity for pesticides. Moreover, most farmers consider organic crops to be more time-consuming and resourcefully wasteful, and to have a higher risk of failure.

Citing a negligent lack of research exploring the potentially harmful effects of genetically modified crops, anti-GMO activists claim that these farm products are not safe for human consumption for a plethora of reasons. A large number of these individuals claim that any transgenic DNA from these biotech crops that manages to survive long enough to reach the gut may be able to find its way into cells of the mammalian genome and, once in place, potentially trigger the growth of cancerous cells. Others contend that bacteria in the soil in which genetically modified produce has been planted may absorb transgenic DNA from the food and find their way into the human digestive tract. Here they may spread their antibiotic marker genes to dangerous bacteria and render resultant diseases extra-resistant to treatment.

GMOs actually bear a number of medical benefits; primarily, statistics have shown indications of healthier human populations in countries where genetically modified foods have been consumed for extended periods of time. According to the Institute of Cell and Molecular Biology at the University of Edinburgh, because genetically modified food is cheaper and its increased consumption has vastly enriched the health of the UK population (evidenced by the sharp decline in the population's stomach cancer rates since GMCs became widely distributed), it might actually be better for your health and your wallet.

To date, no concrete evidence of a correlation between cancer and transgenes has been found. Although the means by which the transfer may occur does exist, not one case of animal or human illness has ever been linked to the ingestion of genetically modified food products; this is because scientists have used alternative selection markers to accomplish the task of yielding enhanced produce while steering clear of any potentially harmful effects.

Furthermore, there has been no compelling evidence indicating why consuming these particular strands of DNA should be considered any more dangerous than the large quantities of DNA from numerous other sources that is ingested daily by humans.

So before writing off food biotechnology as a defiance of Mother Nature and a tool of mankind's self-destruction, consider the possibility that perhaps the initial objectives set by GMOs might have actually helped to make the world a better place.

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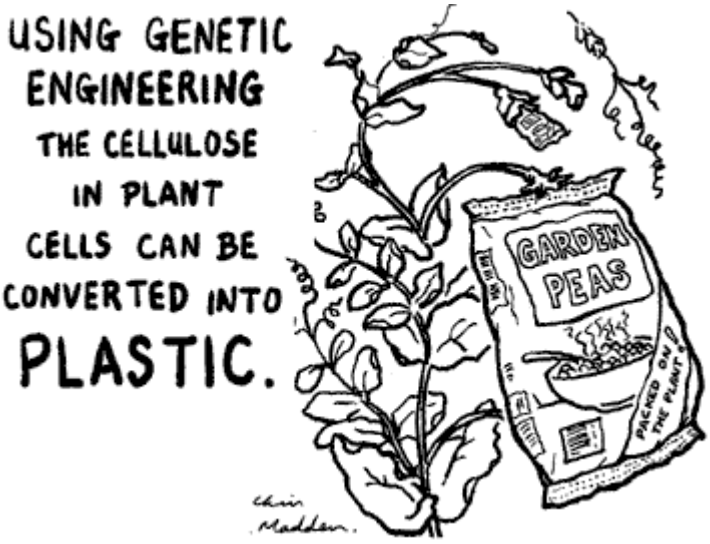


Coming to a Clonal Compromise

By Maya Sequeira and Nilo Couret

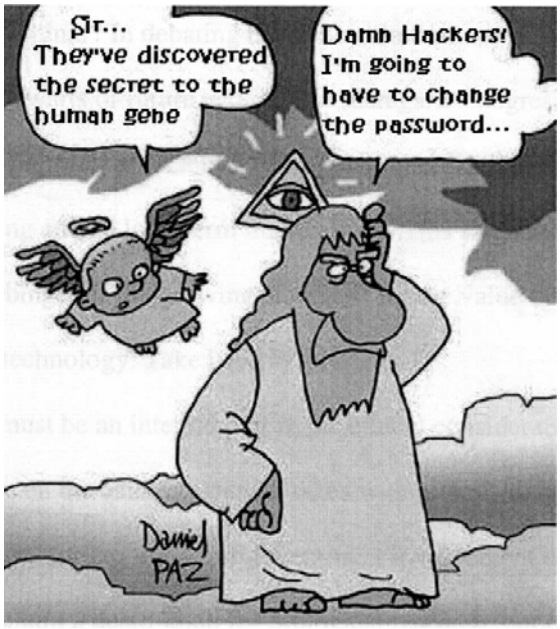
"Why have a bunch of clueless politicos legislating research technology?"

"You can't stop progress!"

Are these the crass opinions invoked by able-minded students in Columbia University's undergraduate bioethics seminar? In debating the policy alternatives regarding reproductive and research cloning, these stalwarts of future generations disregard Congress' supervisory role and extol an unquestioned supremacy of 'science.' The government and the public domain must take an active interest in cloning and its long-term implications. This sanctimonious group of Ivy League pre-meds is a harbinger of the growing disregard for the value of human life brought about by advances in biotechnology. Take heed Washington!

The government must be an integral part in the ethical considerations of cloning. It must strive to inform the public on the cautious steps it takes with regards to questionable bioethical research. Reckless disregard for the importance of government involvement is short-sighted: Bans and moratoria do not proclaim a death-knell for biological research, but rather they provide a means of proceeding cautiously and responsibly into a brave new future of unknown clonal possibilities.

It was no earlier than 1997 (when these students were hitting puberty) when the reported cloning of a sheep caused a hullabaloo in the international community. Dolly was produced through a process of 'nuclear transfer': a donor cell is found, its original DNA is extracted and discarded and then the nucleus from the organism to be cloned is implanted into this donor cell. Dolly's creation led to fears of human cloning, which were halfheartedly regarded because the nuclear transfer cloning procedure was unavailable to humans. However, recent news from South Korea and its premature success at nuclear transfer to create



human embryos has brought the reality of human cloning to the fore. The protection of embryos and stem cell research aside – both important issues but ethically different from the question of reproducing

The Scientific community cannot remain in the laboratory when the effects of its research extend far beyond the Petri dish.

human beings through cloning – cloning and the government's place in this dialogue are our specific focus.

Cloning gives birth to questions that go unanswered in the scientific "classroom": (1) Will the distribution of resources make cloning a privileged indulgence? (2) Will human beings be manufactured-to-order, lacking autonomy and individuality? (3) Will cloning promote eugenics? (4) What are the rights of cloned beings in an experimental situation? Are clones the new 'guinea pigs'? (5) Are clones second-class citizens subject to the control of their creator? These questions are of enough significance that they warrant the attention of the political and moral community. The scientific community cannot remain in the laboratory when the effects of its research extend far beyond the Petri dish.

Though we concede that governmental interference can be frustrating in its incessant red tape, the flippant attitudes taken by our undergraduate peers, a corps of future researchers, and their irascible disdain of the public domain are symptomatic of an unduly smug and complacent youth. Oh, it's not all their fault. It is the government's duty to clarify its role vis-à-vis research instead of effectively closing itself to a constituency it considers apathetic. Its unwillingness to tackle these issues will only further alienate up-and-coming researchers into the oppositional camp of those 'scientists' unwilling to dialogue and discuss, unwilling to consider the 'trifling,' 'unfounded,' and 'uninformed' concerns of the public.

We advocate a joint approach to fielding emerging clonal concerns. A permanent ban and an unwillingness to reconsider bioethical issues are irresponsible on the part of the government. A petulant disregard for the legislature's representative role is negligent. Legislators should be willing to tackle these issues and scientists should be willing to give credence to public concerns. And so in an effort to convert our disillusioned generation, we propose a compromise. A regulative body should be assembled in the vein of the United Kingdom's Human Fertilization and Embryology Authority (HFEA) – a twenty-one member committee appointed by health ministers, in which the Chairman, Deputy Chairman and at least half of the HFEA's membership are neither doctors nor scientists involved in research or providing infertility treatment. This committee would monitor clinics offering storage of eggs, sperm or embryos; would regulate research using cloned organisms; would codify a set of

guidelines on the proper conduct of clonal activities; and would work with the NIH in the disbursement of federal funding for this type of research. Through such a body the goal of pluralistic dialogue is realized. This inclusive debate will quell the skepticism of those like our classmates and will encourage this generation of future scientists to participate in a process that will render them prone to responsibly clone.

Reference: www.hfea.gov.uk

Trick or Treat?

By Kimerly Gardner and Anna Romagnoli

Every child has been told at least once in his or her life to be wary of strangers bearing candy, because "you never know what could be in it." In spite of this nearly universal desire to prevent children from consuming the unknown, we do so everyday: from the cereals we eat at breakfast to the mashed potatoes we have at Thanksgiving dinner. Many of the foods we eat on a daily basis have been genetically modified (GM) in some way. In spite of the fact that these GM foods have been on the market for more than five years, it is still not mandatory to label them in this country. The lack of government regulations requiring labeling of GM goods is an infringement upon our right to make informed decisions about the food we consume.

Consumption of genetically modified foods potentially presents a variety of associated potential health risks. Due to the lack of post-market research on these GM foods, the frequency with which these adverse effects occur cannot be determined. An allergen transferred from one organism to another could cause a potentially fatal allergic reaction, as in the case of soybeans containing genetic material from Brazil nuts, which caused severe allergies in individuals allergic to nuts. If all GM products required labels, physically traumatic experiences such as this could easily be avoided. Candy manufacturers are required to label products processed in the same factory as nuts with precautionary labels notifying the public that "This product may contain traces of nuts;" why should GM manufacturers be exempt from this regulation? By not requiring companies using genetically modified food products to adhere to labeling regulations, the health of individuals is jeopardized.

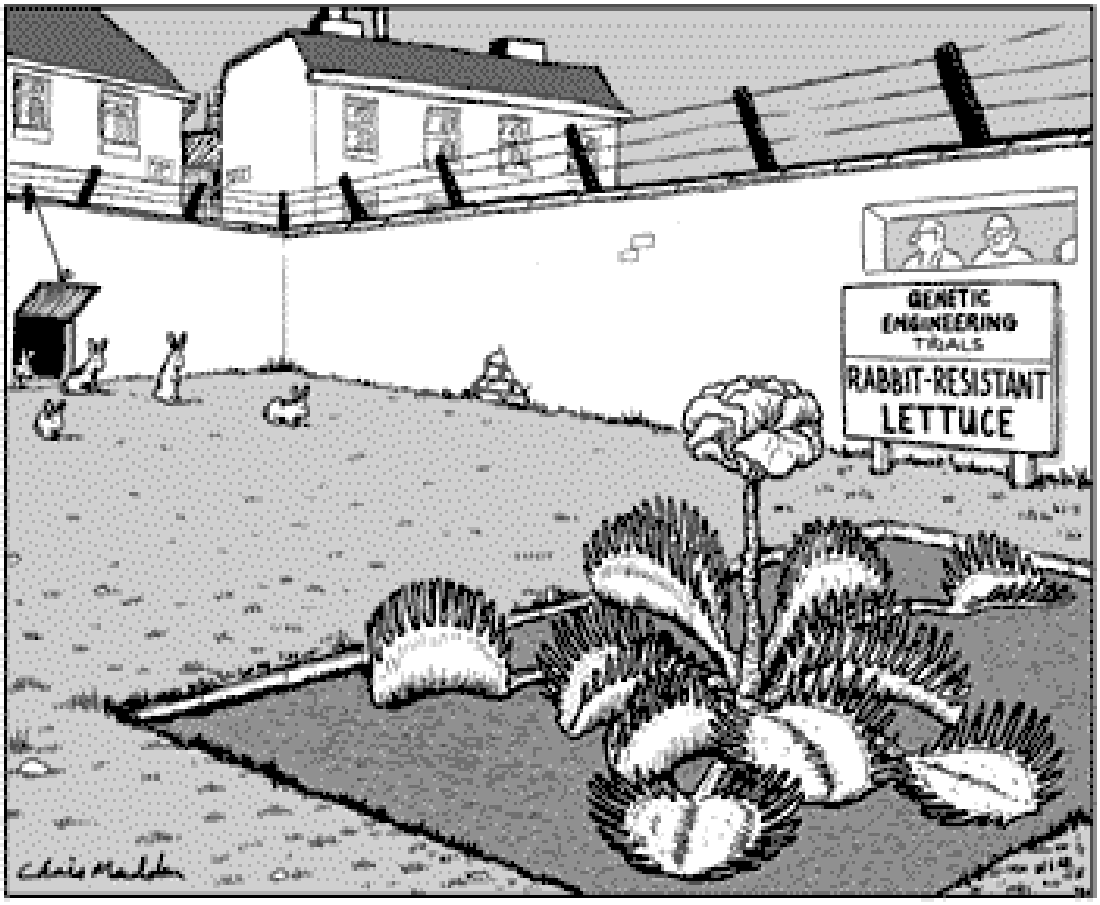
Not only is the health of individuals at risk, the overall well being of entire communities is placed in a precarious situation by the lack of labeling regulations. This larger health risk is due to the transfer of antibiotic resistance markers. In fear that the consumption of these markers will lead to increased antibiotic resistance in the population, some countries have banned the import of GM foods. Increased antibiotic resistance in the population could lead to the development of strains of antibiotic-resistant bacteria, creating a potential public-health crisis. Because of the current inability to discern GM foods from non-GM foods as a result of the absence of labeling regulations, communities are unable to protect themselves from this threat.

The lack of government regulations requiring labeling of GM goods is an infringement upon our right to make informed decisions.

In addition to these health risks, there are a variety of ethical considerations that arise from the unknown consumption of genetically modified food. Ethical and religious beliefs often restrict the dietary habits of certain individuals. The lack of labeling on GM food infringes on an individual's right to live according to his or her own beliefs. For example, staunch vegans who actively choose to not consume any animal products may unknowingly be subverting their beliefs by eating vegetables that contain animal-derived genes.

Not only does the lack of government-required labeling of genetically modified foods remove the right of a freethinking populace to make an informed decision, it also poses very real health risks and ethical implications.

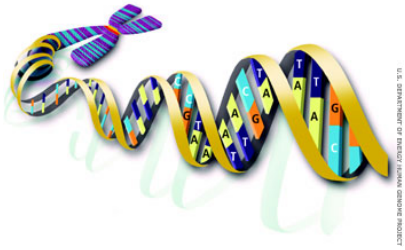
If we do not allow our children to consume unknown substances in their candy, why would we allow them to consume foods containing unknown transgenic substances?



It wasn't me, it was my genes

By Tova Ganz and Simi Hinden

As forensic science technology advances by leaps and bounds, the U.S. government is constantly faced with new possibilities to aid them in law enforcement. For example, in 1990 the FBI began a national DNA database called CODIS (Combined DNA Index System) of all sex offenders and other violent felons in order to correctly identify criminals and cross reference them with other crimes (http://www.fbi.gov/hq/lab/codis/program.htm). In continued study of criminal behavior, scientists are now searching for a genetic factor predisposing humans to aggressive behavior. As evidence that violence is indeed biologically based, an article printed in Science (Science, 297:851-4, 2002) links violent tendencies with a genetic deficiency in the neurotransmitter-metabolizing enzyme monoamine oxidase A (MAOA). In response to such data, it has been suggested that the United States analyze DNA samples of criminals to search for genetic markers predisposing them to violent behavior. With further research of MAOA deficiency and DNA sequencing of criminals, medications could be developed to treat individuals with a genetic predisposition to aggressive behavior at an early age, which could drastically reduce the nation's crime rate.



However, the article in Science does not conclusively determine that MAOA by itself is a direct cause of violent behavior. The study links violence only to those subjects with MAOA deficiency and a history of child abuse, but not to those with MAOA deficiency alone. Thus, the article suggests that violence is a result of both biological and environmental factors and there is no single gene that positively causes violence. Rather than allocate funds towards research in finding a genetic factor for aggression, which does not hold promising results, the money should be used to combat child abuse, a known contributor to violence in adults. Why spend money on developing a drug which would not even be necessary if proper counseling was given in the first place?

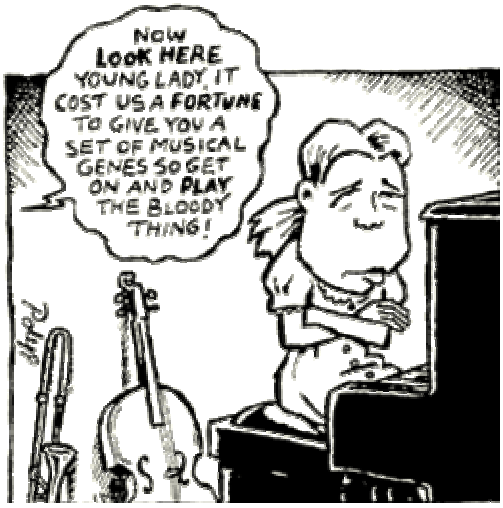
Assuming, however, that there is such a 'violent gene' yet to be discovered, it is unconstitutional to analyze a criminal's DNA without their permission. The Fourth Amendment prohibits unreasonable searches and seizures without a warrant issued "upon probable cause." Since there is currently no indication that a warrant can be given to sequence DNA for reasons beyond identifying an individual as the perpetrator of a crime, it is unconstitutional to do research on DNA without explicit permission of the individual to be studied. Moreover, prisoners are unlikely to agree to donate their DNA to a research project that seeks to brand themselves and their relatives as

biologically determined criminals. The nature of DNA research is itself an invasion of privacy as the individual's entire genome can theoretically be sequenced and analyzed. There is hardly 'probable cause' to violate a citizen's right to privacy in the hope that one might find a gene controlling violence.

How would the identification of a genetic marker for violence affect defense proceedings? While biological factors are not currently accepted as an excuse for criminal behavior, a recent article in Nature (Nature, 419:422, 2002) suggests that "criminal courts should take genetics into account" when determining punishments. In doing so, alleged criminals would be considered guilty or innocent based on the presence or absence of MAOA (or any other genetic marker predisposing them toward violence) rather than the evidence presented. Defendants will blame their DNA for their crimes, denying responsibility for their actions and absolving free will in the face of genetics. In a similar vein, judges will mitigate their sentences, rationalizing that the defendant is less guilty for his crime. The end result will be the condoning of criminal behavior by individuals predisposed to violence, which will have drastic affects on the U.S. justice system.

Criminal courts should take genetics into account when determining punishments.

One must also consider social ramifications in discovering a gene that may label someone as a biologically determined criminal. Children known to have a 'violence gene' would almost certainly suffer discrimination. In the 1960s, researchers mistakenly claimed that a disproportionate number of males in prison had an extra Y chromosome. After supposedly linking violence with a single biological factor, it was proposed that all boys be tested for the extra Y chromosome. Just as parents in the 1960s opposed the law because they feared their children would suffer discrimination, testing children for MAOA deficiency (or any other genetic marker to violence) in today's society would receive the same vehement opposition because it would create a social class of 'genetically inferior' citizens.



In short, research for a theoretical "violence gene" has far more drawbacks than benefits. With lack of evidence pointing to a single gene as cause for violence, as well as the violation of rights that would accompany the search for such a gene, there are far more effective ways

allocate our time and resources in preventing crime.

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Pre-Implantation Genetic Diagnosis

By Siddharth Srivastava

In 1989, scientists created a major breakthrough in the world of prenatal diagnosis when they announced the first successful application of preimplantation genetic diagnosis (PGD). PGD allows doctors to detect deadly mutations in human embryos before they are implanted in the womb. This technique is especially relevant to women considering in-vitro fertilization, because it lets them screen their embryos for genetic defects before they decide to become pregnant. At the same time, though, PGD raises the possibility of ethical abuses, like unfairly selecting and eliminating embryos based on genetic factors. Despite its potential for misuse, PGD offers the promise of alleviating some of the concerns surrounding the care of a genetically disabled child.

Every year in the United States, more than 70,000 babies – or approximately 2% of all newborns – are diagnosed with at least one of the many life-threatening genetic disorders, which are usually incurable and untreatable. Furthermore, genetic disorders are hard to detect with non-intrusive medical procedures like obstetric ultrasound. For years, women had no way of telling whether their fetuses would be born with a genetic mutation. With the advent of PGD, though, doctors provided women with a diagnosis tool capable of determining the possibility of an individual having a child afflicted with a genetic condition. The application to in vitro fertilization was enormous. For the first time ever, women could determine which in vitro fertilized pre implanted embryo would lead to healthy children.

In 1999, researchers at the Weill Medical College of Cornell University reported the first successful pregnancy using PGD for a family with a history of sickle cell anemia. The subject of the study was a 34-year-old female patient who had previously undergone two abortions after discovering that her fetuses were afflicted with sickle cell anemia. For the study, doctors carried out PGD on the patient and isolated three embryos that were unaffected and two that were carriers of the disease. After implanting the normal embryos, the patient delivered healthy twins. The results of this study suggest that PGT is a successful and effective way of preventing the inheritance of genetic diseases in children. For families with a history of genetic defects, PGT offers a way of breaking the chain of inherited disorders.

Not only can PGD prevent the inheritance of genetic diseases, it can also provide new ways of treatment for certain genetic defects. Many patients with non-genetic conditions (such as leukemia) require bone marrow transplants, blood transfusions, or other treatments derived from people with certain characteristics (like matching blood type or the correct plasma protein). If these characteristics are too rare to find in the general populace, treatment for the patient cannot proceed, and death often results. PGD can restore hope to parents of children with

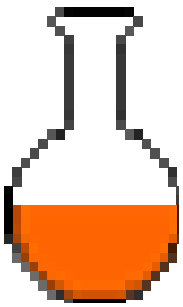
disorders requiring specific human interventions. With the aid of PGD, these parents can give birth to a child with a specific immunoglobin, a matching blood type, or some other life-saving property needed by that child's sibling.

However, when PGD is used for this purpose, though, controversy arises over the ethics of giving birth to one child solely to save another. Should newly born infants be used for this purpose? Do parents have the right to authorize the use of his baby for treatments of other human beings? The answers to these questions are unclear.

Furthermore, many people are concerned with the ethical implications of using PGD for purposes other than targeting specific fatal genetic disorders. Some doctors, for example, are using PGD to diagnose illnesses that remain dormant at birth but emerge much later in life. A group of researchers at the Reproductive Genetics Institute investigated this scenario in a 30-year-old woman genetically predisposed to early-onset Alzheimer's disease. After performing PGD, doctors identified the healthy embryos and transferred them back into the patient. She eventually delivered a healthy child, free of the predisposing genes for Alzheimer's disease. In some cases, genetic disorders cannot be diagnosed prenatally. However, an undetected genetic defect develops anyways only 2-3% of the time, a rate which is low enough for PGT to be used as an effective screening tool.

These studies demonstrate the potential for using PGD to detect non-congenital defects, but they also raise an important ethical question: should individuals be allowed to determine whether their children have predisposing genes, ones that are responsible for diseases later on in their lives? Some critics argue that the discarded embryos could have been the precursors to individuals who might have lived tolerably in spite of their condition. Although Abraham Lincoln had Marfan syndrome (a disorder of connective tissue usually characterized by excessive bone growth), he served as president of the United States and accomplished much in his lifetime. It is believed that Mozart had Tourette syndrome, an inherited movement disorder that is undetectable by prenatal diagnostic techniques. In spite of having Tourette syndrome, Mozart produced many brilliant works of classical music. Had the embryos of Mozart and Lincoln been culled out via PGD, the world would never have known these great men.

On the other hand, it is unlikely that an individual born with a serious genetic disorder will be cured sometime in his lifetime, given the substantial amount of scientific work that needs to be done to cure severe genetic diseases. For a person diagnosed with a genetic defect, the probability that he will lead a regular lifestyle is significantly smaller than the probability that he will have to endure pain and suffering throughout his life. The issue is complicated by the fact that there are various degrees of severity for inherited diseases. Some genetic disorders, such as phenylketonuria (an enzyme deficiency disorder) can be treated with special diet. Others, such as branched-chain ketoaciduria, which affects an infant's ability to metabolize three amino acids, are



very severe and often fatal. The ethical question, then, becomes whether or not it is justified to allow several hundreds of children to suffer so that one child can lead a productive life. Like many of the other questions raised by this debate, this one is difficult to answer.

Another ethical consideration is the concern that PGD allows individuals to choose an embryo based on circumstances that are likely to happen, but which are not guaranteed to happen. Opponents of PGD contend that if an individual is allowed to select an embryo on the basis of what may happen to him (e.g. Alzheimer's disease), then soon people will start using PGD for purposes other than preventive medicine. According to Dr. Robert Boyle and Dr. Julian Savulescu, scientists at the Murdoch Children's Research Institute, "There is opposition to the practice of seeking 'designer babies,' fuelled by concerns about eugenics at an individual family and societal level." In such a situation, parents could use PGD to design superficial characteristics, like sex or skin color, in their children.

The eugenics movement in Nazi Germany is a daunting reminder of why a "selection" process based on genotypes is such a bad idea. During that time, the purpose of the eugenics program was to manipulate heredity to produce "better people" and eliminate those considered "biologically inferior", according to Dr. Linda Hasadsri at the University of California at Berkeley. Unsurprisingly, people have already started raising questions about the potential to use PGD for eugenics purposes. For example, 80% of children with achondroplasty (a skeletal disorder resulting in dwarfism) are born to average size adults. Fearing that their children may be born as dwarfs, some people may undergo PGD to avoid having children with this unfavorable (in their eyes) characteristic.

One way of regulating genetic practices would be to rigorously examine a

person's motives for undergoing PGD. The problem with this approach, though, is that it requires outside regulation. Unfortunately, there is no reasonable or practical way of determining whether an individual or couple has less-than-admirable motives in their decision to use PGD. Should citizens, then, be concerned about issues like genetic diversity and the abuses by a select few? Some abuses are unavoidable. There will always be people who try to "breed" children with certain characteristics, and whether or not such a practice reflects discrimination, there is no way to determine their intentions. However, the fact that some abuses do occur is not sufficient cause for worry. Those who insist that PGD prevents genetic diversity fail to realize that several prenatal tests are already in place. Selection of children takes places in techniques like amniocentesis and chorionic villus sampling, both of which are designed to detect chromosomal abnormalities, albeit several weeks after implantation. The use of PGD therefore will not have a significant impact on the gene pool.

Although there will always be people who abuse PGT, scientists may have to proceed with what is best for society as a whole. Explaining the concept of utilitarianism, the philosopher John Stuart Mill wrote, "I regard utility as the ultimate appeal on all ethical questions; but it must be utility in the largest sense, grounded on the permanent interests of a man as a progressive being." Mill argued that moral policies or actions are those which achieve the best results, or the greatest good for the greatest number. PGD provides a countless number of individuals with the ability to make an informed decision about their pregnancy. These individuals no longer have to make guesses about the genetic conditions of their children, nor do they face the possibility of having to abort a fetus midway through pregnancy after discovering the presence of a genetic mutation. PGD causes no physical harm to the tested individual or to the implanted embryo. From one religious perspective, the church believes that a conceived pre implanted embryo has human status and destroying even IVF embryos is considered as murder).

There are other far-reaching benefits of PGD. For families with a history of genetic diseases, PGD offers the potential of preventing the occurrence of diseases in the lives of their would-be children, who otherwise might be severely disabled. Children born with genetic mutations often suffer from pain and discomfort resulting from their illness. Their disability forces them to struggle endlessly to achieve some of the goals they set for themselves. Trisomy 18, for example, is a genetic syndrome affecting less than one percent of all live births. Despite its low occurrence rate, trisomy 18 is a devastating condition that leads to hand abnormalities, mental retardation, congenital heart disease, and other serious medical problems. Most infants with the disease never survive past their first birthday.

In spite of the controversy surrounding PGD, one thing is clear: PGT holds promise as a beneficial new tool in the field of genetic testing. In 2000, the European Society of Human Reproduction and Embryology (ESHRE) Special Interest Group on Reproductive Genetics released the results of an extensive, 7-year-long

study evaluating the effectiveness of PGD, "In all, these data are encouraging: they show...that the practice of PGD is becoming more and more established, and an increasing number of different applications is emerging." Granted, discrimination and other misuses of PGD can be present. PGD's potential for good, however, far offsets these other consequences. PGD gives the next generation of children the possibility of leading healthy, genetic abnormality-free lives.

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Looking for Designated Runner: Only West Africans Apply

By Maya Sequeira and Sung-Min Park

Historically, or at the very least since the age of Enlightenment, there has been an effort to bring the certainty of the physical sciences to the society. The end goal of this practice is, through such fields as sociology, cultural anthropology, and especially political science, to engineer more efficient, more perfect communities. A fundamental problem exists, however, in the effort to study and manipulate human society: when dealing with people there are numerous variables, so many, in fact, as to preclude population study from achieving the status of exact science.

This uncertainty, this inevitable error, is an important fact to bear in mind as one considers the consequences of scientific positivism in social architecture. Science has been used as further justification for established prejudices; it has birthed unspeakable movements such as eugenics. Now, after world war and genocide, intellectuals, facilitated by both old and new critical thought, are attempting to repair what their forefathers have so distorted.

Arising from its founding and initial obscurity in the 1920's, the Chicago School of Sociology, led by Robert Park, directed itself against racial biologism—the notion that race is a fixed scientific category that determines both appearances and behavior. Their key rebuttal asserted that biologists mistook race for culture or ethnicity. They viewed that race, or one's physical appearance, did not entail one's ethnicity, i.e. culture and behavior. Further deconstruction of race and ethnicity yielded the idea of racial formation: that race is simply a social construct. The emergence of high-throughput DNA sequencing has not answered but seems to corroborate such sociological theories about race. Biology, still atoning for past sins, uses the rather neutral term of "population," and largely concludes that the common determinants of race such as skin color are a result of adaptation. For example, "Individuals from sub-Saharan Africa and Australian Aborigines might have similar skin pigmentation (because of adapting to strong sun), but genetically they are quite dissimilar" (Bamshad, et al.). This new genetic data adds a solid basis for our re-conceptions of race.

But whether one calls it a population or sub-race or ethnic group it is still an effort at categorization. This is an issue for some who believe that any categorical distinction between people recommits past crimes. Although as much as 95% of genetic differences occur within populations (Rosenberg, et. al), there are still genetic differences that set populations apart, and these distinctions could have significant consequences. Both scientists and physicians justify classification into genetic populations by pointing to its aiding both academia and medicine: through population study we can track both past dispersions and a group's potential susceptibility to diseases. These are real benefits. In addition,

genetic differences have the potential to aid many fields by providing possible answers as to what makes individuals with certain characteristics better suited for a particular task.

We turn here to the oft-debated topic of the seeming genetic advantages of certain groups in athletic competition. Of the most compelling evidence that these advantages exist is the dominance of Kenyan runners in long distance events. "This country of only 30 million (0.5 percent of the Earth's population) wins about half of all the Olympic and World Championship medals for men's distance running" (Sailer). Some believe it is a matter of training. Kenyan runners have greater endurance than most because they train at high altitudes, conditioning their bodies to pull a greater percentage of oxygen out of the air. But this does not seem reason enough for the overwhelming domination of this population. Many athletes train at high altitude, in fact, hypoxia training has become somewhat of a fad. Why don't all athletes who train likewise show similar results? It is a matter of nature as well as nurture.

Genetic advantages can be unique to an individual or unique to a population. While many Kenyans seem to share some characteristic that makes them superior runners, some athletes have variations that set them apart from their population. This trait is something of a superpower. An example: "One Olympic cross country skier had a medal winning mutation - his blood was naturally loaded with up to 50% more red blood cells which boosted his stamina" (BBC, 11/30/01).

A major problem arises, however, when these individual distinctions, or distinctions unique to a population, are generalized. We have discussed the success of Kenyans in long distance running, but it is important to note that the same group does not have any advantage when it comes to sprinting. Here, it is West Africans who show a penchant for the sport. Again, we look to physiology for an explanation: "Scientists believe there are three reasons West African athletes have an advantage in the sprint events. Firstly, they have more muscle and less fat. Secondly, they have higher levels of testosterone. Finally, they have more fast twitch fibers in their muscles than their white counterparts" (BBC, 9/7/01). The success of this population is attributed, at least in part, to biological advantage, an advantage distinct from the biological advantage of their Kenyan counterparts.

Noting the distinction is crucial. "Roger Bannister, an Olympic gold medallist and the first man to break the four-minute mile barrier, was a respected neurosurgeon. But even he was still pilloried as a racist when he said: 'Black sprinters and black athletes in general all seem to have certain natural anatomical advantages.'" (BBC, 9/7/01). As explained above, labeling a group based on such a relatively recent adaptation as skin color means nothing. The populations could be as different as Sub-Saharan Africans and Australian Aborigines. Bannister, in his generalization about black athletes, was rightly labeled a racist. It is likely that his racism was not out of malice, but despite his M.D., like most who find themselves uttering similar statements, out of pure ignorance.

There are notable genetic differences between populations, however, we ask how

much of this data should be acquired and subsequently published. The benefits of collecting this data have been mentioned, but the costs have the potential to outweigh the benefits. Despite abolishing old notions of race, new conceptions may emerge, further grounded in "physical" evidence and even more demanding than before. If one population is genetically better fit to perform a certain task than any other, well, it seems proper to reserve that task for that group—a matter of increased efficiency at the loss of liberty. While possible, we question whether this line of thinking is really not just a jazzed up version of racial biologism. This is evident the minute one's genetic makeup begins to determine the positions open to that person. Imagine a world in which marathons are run exclusively among East Africans of the Great Rift Valley, elite rowing is reserved for all Yugoslavian crews, and we leave the thinking to the South and East Asians. Children would grow up with the notion that they can be whatever they want to be… but if they're not genetically engineered for it, try as they might, they'll never be any good at it.

What must be clearly understood is that this sort of genetic study deals exclusively with probabilities and distributions, and despite an individual having a better chance at acquiring a particular set of genes due to her membership to certain population, that membership by no means determines acquisition. In the future, genomics will speak volumes to an individual's own genetic data, but as to how much it will speak to an individual based on population membership alone seems very limited. Consequently, we propose no censorship of future population studies; however, as responsible citizens, we ask that all published population data undergo extensive review by social scientists to weed out any words or phrases that might generalize or in any other way simplify what is really a complex, probabilistic, and decidedly imprecise study.

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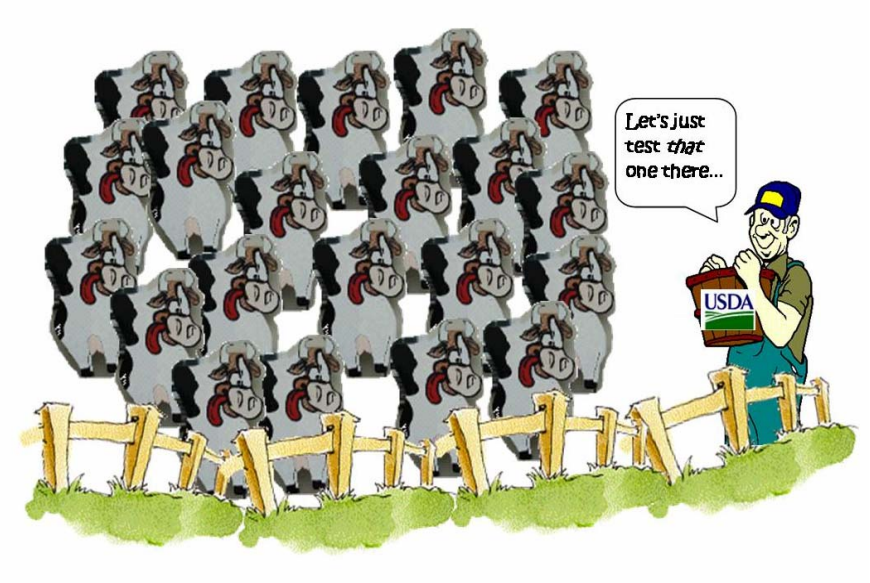
Fast food Hamburger: 99¢;Your Health: Priceless

by Jason Moss and Andrea Wershof

The average customer enjoying a hamburger in an American fast food joint probably doesn't spend too much time worrying about the risk that she will contract variant Creutzfeld-Jakob Disease (vCJD), the terrifying fatal neurodegenerative disease known as the human version of "Mad Cow Disease" or Bovine Spongiform Encephelopathy (BSE). Even though meat from the first cow in the US diagnosed with BSE made it to the shelves only to be recalled in December 2003, and allegations of falsified reports haunt the identification and recall process, she'll probably still enjoy her meal without a second thought. Her indifference may be due not to any great faith she places in the US Department of Agriculture's standards for testing beef before it gets to her restaurant, but rather stem from her blissful ignorance about the abominably irresponsible testing regulations now in force. This customer may not be quite as eager to chow down on her burger if she knew that the USDA tests for BSE in only 20,227 of the 35 million cattle slaughtered annually in the US, a measly 0.05 percent, or less than 1 in 2,000 cows.



Why isn't this consumer wary of the contents of her lunch? Probably because the USDA has succeeded in lulling her, along with millions of other American beef consumers, into a false sense of security. If she does think about vCJD, she most likely thinks the USDA has protected her by banning the feeding of MBM (Meat and

Bone Meal – that's ground up cow brains and bones) to ruminants, which it established in its 1997 Animal Feed Ban. She might think that she is safe since importing cattle from countries with identified cases of BSE has been banned since 1989. She might even think that the current testing procedures are adequate, as the January 2004 USDA standards banned the use of the meat of "downer" cows – those that are too sick to walk by the time they get to slaughter - for human consumption.

But this unsuspecting indulger may not be aware that these "firewalls," however imperfect they may be, only protect consumers from consuming meat from cows already displaying symptoms of BSE. BSE is caused by misfolded proteins known as prions, and consumption of contaminated meat has been linked to the development of vCJD in humans. Scientific research has been inconclusive as to the incubation period of these prions prior to the surfacing of symptoms, but some research has indicated that it may lay dormant for as long as 21 years in humans. This fact means that both humans and cattle that appear healthy may harbor the infectious prions. One consequence of this prolonged incubation period is that humans who carry the misfolded protein may inadvertently pass it on through blood transfusions, as a February 2004 British study suggested. It also means that cows that meet USDA criteria for slaughter could easily be in the pre-symptomatic stages for BSE, and thus pose a risk for humans who consume their meat.

The USDA has a moral obligation to safeguard the health of people in this country no matter what the cost

Why doesn't the USDA follow the lead of countries like Britain, that has banned MSM feed altogether? Feeding animals MSM is remarkably efficient economically: it turns waste that would otherwise need to burned or disposed of in a costly manner, into sellable protein to fatten up sellable meat. Setting aside the enormous ethical questions associated with feeding herbivores remnants of their own species (who would want to be fed their mother's brain?), this method makes a great deal of economic sense. The advent of vCJD and its link to MSM-fed cattle led the USDA to ban the feeding of most mammalian protein to ruminants, but until last month it could still be fed to poultry whose waste, in turn, was fed back to cattle. Given the long incubation period of the disease, one would expect that the USDA would follow up its improved (although not sufficient) feeding bans by testing all cattle who were previously not subject to these rules. Japan followed this model, and currently tests all cattle slaughtered for human consumption.

Unfortunately, the USDA has made no such decision, announcing instead that it will boost the number of mad cow tests in 2004 to about 40,000, still an

testing more animals? Economics again. A recent study estimates the cost of testing all US cattle slaughtered for human consumption at more than 360 million dollars annually. Even though this may be a small price to pay in the US. cattle industry of 50 billion dollars, even though some cattle companies losing over $80,000 a day in lost exports to Asian markets who won't accept the likely untested US meat, and even though th current standards pose a questionable level of risk to consumers, the USDA has yet to approve any of the new rapid diagnostic tests for BSE developed both domestically and abroad that would lower the cost of the testing.

If the potential meat-buying customer was aware of this abysmal failure of the USDA to enforce testing that would catch pre-symptomatic cases of BSE before the meat hit the market, perhaps she would think twice before ordering a burger. A 1997 study raised the possibility that BSE can cross species, infecting other animals consumed by humans (besides cattle) that are fed MSM, and may even be contagious through occupational exposure to infected animals. A 2003 study suggested the BSE may even

be passed through milk of infected animals, and a 2004 study explored the likelihood that it could be transferred through the blood of infected animals that is fed to cattle as a source of protein. Another 2004 study revealed a new variant strain of BSE appears in a different region of the brain than the typical mad cow strain, and could thus escape current testing measures altogether.

Given that Japan has detected 9 cases of BSE since 2001, testing all of its 1.2 million cattle slaughtered annually, the fact that only one case has been detected in the US provides little comfort. Finding one case is likely indicative of a larger number of cases gone undetected, and testing less than one cow in 1500 is not sufficient to protect consumers. Given how much is unknown about the incubation and transmission of both BSE and vCJD, extreme caution and concern for the health of consumers, and not economics, should govern the USDA's approach. The USDA has a moral obligation to safeguard the health of people in this country no matter what the cost: whatever the dollar total of testing all cattle slaughtered for human consumption may be, it is a small price to pay to minimize the risk to humans of contracting this fatal disease. Until the USDA rises to its responsibility to increase testing standards, consumers should opt for the fish filet.

Research Bioethics

Apocalypse Now: Scientific Education

By Brian Lee and Sung-Min Park

In our humdrum lives, not even our downfalls reach anywhere near a melodrama—never a Greek tragedy and at best a WB sitcom—and so, what else could we expect from the nation's most boring policy topic: math and science. Citing studies at the turn of the century, pundits foresaw an academic doomsday in which a new generation of bumbling Americans would collapse under the lack of technical leadership. This, however, is far from the truth: mathematical and scientific expertise abounds—enough to carry us through the era. A more realistic and immediate concern—although not terribly sensational—is the way our substandard education undercuts science-related government policy. Any misunderstanding between the people and the government leads to both major and minor policy changes that could stifle the national authorization and funding that constitute science's lifeblood. Meaning, instead of a distant apocalypse, the dominance of American science ends now in a slow and prolonged chokehold; the recent South Korean advance in cloning technologies is perhaps a beginning to that end.

The wages have never been higher than with the related field of stem cell research. This research stands to cure that which we can presently only treat or sadly, only observe. Despite such promises, devoid of public funding, stem cell research has sputtered under current policy and is stuck in a virtual catch-22, where it needs results to tip the people and government in its favor, but first, government funds for those results. While we love to blame the administration, the system of government, and even the gods, what we always seem to overlook is ourselves and our education. America's failure to provide the bitter medicine of education is matched by our repulsion in accepting it, especially the geek-ridden math and sciences. Undereducated, we misinterpret and skew, unable to take a critical perspective on what might be empty rhetoric. Moreover, uninformed, we tend to see science as a magic black box of eventual advances—much like our computers—and fail to see the enormous intellectual and economic investments required for it. In a day when polls more than shape politicians, we owe it to ourselves to make informed decisions that can attenuate or even break the government hold on science and stem cell research.

To say education is the only solution to scientific policy is downright naïve; America has a unique historical and religious background that must be respected. Nonetheless, strong educational systems in Europe and Asia seem to advance stem cell research under remotely comparable political ideologies, namely Judeo-Christian beliefs operating under democratic capitalism. Thus, despite the time and complexities needed

to change the educational system, perhaps in the meantime we can do ourselves a favor and get our children, our peers, and especially ourselves interested in science.

"I'm here to emphasize values. Remember . . . work hard, aim high and always use your parents' connections."

*Publish **or** Perish Vs Publish **and** Perish*

The perils of open publication

By Deepa Sarkar and Laura Baur

The anthrax and ricin attacks that followed 9/11 transformed the abstract threat of bioterrorism into an ugly reality and heightened public awareness of the potential misuses of biological research. Although research on toxins and deadly pathogens goes on for the public's benefit, some discoveries, such as novel means of augmenting virulence or toxicity, can be abused. Scientists are faced with a dilemma: are they to publish research and risk its deadly misuse, or not to publish possibly sensitive research and hinder the free flow of ideas on which scientific progress is based? It is our belief that neither scientific integrity nor public safety need be compromised if certain precautions are taken by authors and editors. The government should organize a committee of scientists and defense experts to establish guidelines for the proper dissemination of sensitive information.

The threat posed by the misue of scientific research is too great to be left unregulated.

Resistance to the regulation of scientific publications is rooted in the nature of the research process. The open exchange of information is essential to progress, since research builds upon the preceding work of others. Many claim that restricting publication would impede valid therapeutic research and prevent valuable advances; some even fear that restrictions would threaten national security if the products of defense research were restricted. There is also the sense that such measures only delay the inevitable, since scientists working outside of regulatory bounds could independently make the same discoveries. However, such views fail to recognize that restrictions on publication are not tantamount to completely blocking the open exchange of ideas.

Modifying a paper frequently involves editing the "methods" portion so that sensitive details are not explicit and do not write out an easy-to-follow bioterrorist "cookbook." Some claim that even modified publication is not acceptable, since it is essential to the scientific process that an experiment's results can be verified. These individuals fail to recognize that restricting the publication of sensitive material does not preclude sharing such information with others conducting research; it simply prevents the methods from being accessed indiscriminately. If a scientist wishes to repeat an experiment, the research group can provide such information at their own professional discretion. If an illegitimate company or unaffiliated individual requests sensitive information, the scientist can decline to release it. It could be argued that this step provides an

additional level of security: should something go wrong, the point of contact provides a starting point for investigation.

The therapeutic potential of research now attracts the attention of private investors, and biological research is no longer tethered to federal funding and its attendant red tape. The danger of this new freedom is that private companies' need to attract funding and produce profitable research creates a new pressure to publish and publicize promising work that could override security concerns.

As it stands, research journals are self-regulating and can screen for articles they feel could pose a threat to the public, and journals have exercised their prerogative to edit or decline to publish submissions that they deem dangerous. The peer reviewers and editors who review the articles are knowledgeable in their fields and are well positioned to assess the potential for abuse of research. Still, the lack of standardized screening guidelines and the lack of consequences for indiscriminating journals or unscrupulous companies make this system precarious – it only takes one poor judgment call to cause problems. What is needed is centralized oversight, a committee of scientists and defense experts appointed by the Department of Homeland Security, to establish guidelines dictating what information is a risk. Once guidelines are in place, penalties can be laid out for those who publish sensitive information. This policy would simultaneously allow journals to continue efficient self-regulation and provide a consistent standard, ensuring that journals have a personal interest in not publishing anything dangerous to the public.

The government has always been able to regulate federally- funded research through national security classifications, but it's time to extend these concerns to private research. Although we find ourselves neither in an open war nor in a cold war against a rival state, we are in a war on terrorism and must take the threat of biological or chemical terrorist attacks seriously. The threat posed by the misuse of scientific research is too great to be left unregulated, but the potential of research is too great to make it a government monopoly or to drown it in a sea of red tape. These measures show a third option through the apparent dichotomy of private and governmental research that creates an enforceable standard for self-regulation by journals without smothering research in inefficient bureaucracy. Regulation will not mean the end of productive research; it is simply a means of preventing people from using the wrong edge of the double-edged sword.

Bioethical Pharmacology

Pop that Pill: Getting Ahead at any Cost

By Jason Moss and Cedrick Mendoza-Tolentino

An Ivy League Institution, let alone one in the middle of New York City, can be a competitive environment. Having gotten this far, students attending Columbia University have a strong academic background and have come here to excel. As a college athlete, a member of the Varsity Crew Team, and a pre-medical student, competition has a way of seeping into many facets of my life. Coffee and cans of Red Bull only constitute two of the wide array of stimulants that students are willing to pump into their bodies to get ahead. In the midst of midterms, someone can walk into Butler Library or any of the other libraries on campus to find students with some form of stimulant by their side in the hopes that they'll be able to one-up the competition. Whenever I go to the Dodge Fitness Center and begin with my daily reps, I can't help but look with envy at some of the other guys lifting two to three times my weight. The question of whether or not they obtained their physique through natural means or through the use of supplements almost always crosses my mind.

Rather than learning from the past, the FDA has recently opened the floodgates on the sale of potentially hazardous suppplements.

In an age in which self-prescription is almost second nature, the temptation to seek out some sort of edge or enhancement is overwhelming. The underlying problem with all of this is the fact that perfectly healthy individuals are willing to expose themselves to just about anything if the label promises them fast and easy results. In the past few months, ephedra, a substance that has been used extensively for weight control and enhanced athletic performance, has been a hot topic. On February, 6, 2004, the FDA released its final statement concerning the ban of all dietary supplements containing ephedra alkaloid (ephedra). What is most notable about this recent decision is that in 1994, a full 10 years ago, the FDA published a statement saying that they had received increasing reports of people having adverse reactions to products containing ephedra and that further research would be going into the supplement. Being on the market since 1970 ephedra has been associated with health risks including hypertension, increased risk of ischemic and hemorrhagic strokes, development of psychoses, and even death.

What is most startling about the case surrounding ephedra is how it echoes what took place with tobacco and cigarettes just a few decades ago. In the 1950's, studies began to show a direct link between cancer and tobacco smoking, but it was not until 1964 that the FDA released a Surgeon General's Warning. For those of you who do smoke and feel as if this warning would

have had no effect, you'd most likely be surprised to discover after peaking in 1963, per capita cigarette sales began to decline, the same year the FDA released its warning. Coincidence? I'll let you decide. Now, as a college student I can understand the temptations surrounding smoking – I can't tell you how many times I've hung my head in shame whenever someone came up to me to ask for a light and all I could do was mumble a simple, "Sorry, don't smoke." It just does not change the fact that I am aware of the health risks involved as well.

While dietary supplement health risks may be a far reach from tobacco's place among America's most prevalent killers, the trend of the FDA's failure to inform consumers about health risks of products until they have been available for decades remains. Rather than learning from the past, the FDA has recently opened the floodgates on the sale of potentially hazardous supplements. In 1994, the FDA passed the Dietary Supplements Health Education Act, which paved the way for herbals, botanicals, and other food ingredients to reach consumers before undergoing safety testing. If the FDA is unwilling to require companies to demonstrate the safety of their products, what incentive do they have to research the short and long term effects of these substances? Why is it that rather than having in place a series of measures requiring a company to show that their product is safe, do we instead have a system that can only react to problems rather than stopping them before they start? As the FDA begins to examine some of the other non-therapeutic drugs on the market, it should re-evaluate how resources are allocated towards the testing of products.

This week is yet another week of midterms in my short tenure here at Columbia. I still have practice every morning and I know that every night when I go to Butler Library and sit down to try and get some studying done, I'll be wondering whether or not I should be taking something and whether or not the label is telling me the truth. I just can't help but feel sometimes that I'm just another human guinea pig.

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Bio Imperialism: Issues of Overseas Drug Testing

By Nithya Nagella and Ashley Davidson

Human rights activists are at it once again—championing human rights and of course, hindering scientific advancement in the process. But this time if their efforts succeed, everyone involved will end up at a loss.

In America today, the government's extensive involvement in healthcare often allows us to forget what it would be like to for example, not have our prescription drugs paid for. We would never need to participate in new drug trials as our only means of receiving some relief for our ailments. However, this is not the case for many countries in Eastern and Central Europe—the very areas where such American drug companies happened to have found their most willing participants.

CV Therapeutics of Palo Alto, California is one such company currently testing three drugs and studies relating to the heart. One drug, Ranexa, could even be the first new treatment for angina in 25 years. However, studies are only enrolling nearly half as many US participants as they were just five years ago. Also, less than half of study participants live in the US and nearly 600 of the 1,014 patients in the study live in Eastern Europe in Russia. In such countries, subjects are willing due to a lack of other options and there are increasingly more qualified doctors who are eager to enroll patients. So why wouldn't a small, relatively low-budgeted firm look abroad in order to get the chains moving?

But the actual issue has nothing to do with where the subjects are coming from, but rather with what is happening to them. Such small companies as CV Therapeutics do not have the resources to continue treatment for the subject patients in these countries that lack their own healthcare infrastructure. Many physicians themselves feel unsettled with the idea of introducing a helpful drug to a patient but not being able to continue with them once the trial ends. And so, many ethicists are calling for reforms to "stop the use of human beings in poor countries as guinea pigs". Now, while these concerns are warranted, issues of participant rights have been addressed before resulting in the formation of strict guidelines for the very purpose of not treating subjects like "guinea pigs". In 1976, from the highly unethical abuse of the African American male participants in the research at the Tuskegee Institute

emerged the current widely accepted and practiced Belmont Report. This report established the necessary steps and procedures to be followed in order to promote its three goals of respect, beneficence, and justice. The Belmont Report is the only reason we now need informed written consent by every participant in a study. Even now due to the increasing concern for foreign subjects, the pending Export Administration Act will, amongst other rules, require a detailed list of planned human experiments to be approved before any drugs can be shipped abroad. Contrary to the popular ethical opinion, this is not about an infringement on human rights, because the government has already taken the steps needed to ensure that no bounds are crossed in America or anywhere else in the world.

Granted the bigger companies such as Merck with many drugs on the market can easily set up a method to freely or cheaply distribute drugs to impoverished areas in need. The construction of such distributive systems is not only quite expensive, but also a highly imposing act of American healthcare policy into a foreign government. But as Dr. Louis Lange, the chief executive of CV Therapeutics, aptly puts it, "We're not Merck". What is a company supposed to do that has a drug that could possibly dramatically increase the human standard of living when the people who can afford the drug don't care about it, but the people who do care can't really benefit from it in the long run. Their financial limitations leave the company with two options: continue with the same foreign research plan, or withdraw all together. Well folks, it is better to have loved and lost than to have never loved at all. And surely if we are just willing to allow a man who would never in his lifetime feel any sort of relief for his chronic angina experience relief even for a few weeks or months or years, he would agree as well.

Because of the backlash created by the ethical demands of some, even less research may be attempted, and fewer drugs created to help humanity. Thus the most sensible solution at this point in time would be the current one, an already rigorous, carefully monitored process. We now stand at the border between an extensive intrusion into the affairs of third-world countries or a detrimental retraction of possible therapeutic aid for all. So stand firm drug companies, stand firm America.

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Nanotechnology

By Brian Lee and Diana Nguyen

The mere mention of its name generates more buzz than a hive of honeybees upon their queen's return to the nest. Investors have seen it cause their stock prices to skyrocket. Modern science is convinced that it will transform the face of the world as we know it, revolutionizing everything from medical engineering to military apparel to motor technology. The future of humanity appears to rest in the hands of those who can claim possession or control of this one magic word: nanotechnology.

What is nanotechnology? Nanotechnology is the process of building working devices, systems and materials molecule by molecule by controlling matter at the scale of a nanometer and exploiting the unique powerful electrical, physical, and chemical properties found at this small scale. An example of this process in action is presented in the article "Controlled Atomic Doping of a Single C60 Molecule."Nanotechnology has been made possible by recent major advances in microscopy, material science, molecular level manipulation, and the knowledge of classical and quantum physics. Scientists have been able to create single-molecule transistors, enzyme-powered biomolecular motors, and tiny carriers of tumor-fighting chemicals that deliver their payload directly to the tumor cells. Nanotechnology has begun to appear in our daily lives in the form of stain-resistant nanopants, sunscreens and cosmetics using nanosized titanium dioxide particles. Other applications include improvements in solar panels using nanocrystals, abrasion resistant coatings using nanoscale polymer matrices, and alarms that signal to scientists when apoptosis is occurring.

Nanotechnology doesn't come without its drawbacks, however. There are some that have reservations about nanotech research, having seen the fallout from other areas of cutting edge scientific research such as biotechnology and genomics, and recent field evidence shows that nanotechnology can pose dangers for the environment as well as to the humans living in it. American researcher Eva Oberdorster's recent study, "Manufactured Nanoparticles Induce Oxidative Stress in Brain of Juvenile Largemouth Bass," showed that brain damage occurred in fish that were exposed to fullerenes and brought to light the fact that in the process of hyping the promises of nanotechnology, we have overlooked the potential dangers of it. Other individuals such as Prince Charles, author Michael Crichton, and Sun Microsystems co-founder Bill Joy have also raised concerns over the possibility of nanosized machines, or "grey goo," self-replicating and running over the

> Manufactured nanomaterials and the myriad possibilities they hold for the future

earth, while others have raised similar concerns about nanosized biologically based machines, or "green goo". These concerns raise bioethical issues related to nanotech and nanotech research that will be discussed in this paper: funding (who and what), equity (who will benefit or reap the gains), privacy and security (regulation), environmental concerns, and the question whether or not these manmade nanosized entities can be considered living organisms. Discussion of these bioethical issues at this time is crucial to prevent a disruption to the progress of nanotech research when ethics and science inevitably collide, as it did in the cases of genomics and biotechnology.

Nanotechnology's strongest proponents tout its potential to revolutionize modern medicine by eliminating the necessity of many presently existing invasive surgical procedures and methods of cancer treatment; if by injecting nanosized biological agents designed to treat cancerous growths into the body, doctors may be able to target and destroy specific cancer cells without harming healthy cells, thereby eradicating the need for chemotherapy and eliminating the many unpleasant side effects its patients currently endure. But like all other medical innovations still in their infancy, the potentially harmful effects of nanomedicine remain to be uncovered by scientific research for which the allocation of appropriate funding may be called into question. The question of how research should be funded, as well as which projects, is based upon criteria that have not yet been clearly defined.

The issue of the impact that nanotechnology will have on domestic and international socioeconomic equity must also be addressed. Ever since "nano" emerged as the next big thing in the twentieth century, today's nanotech research centers and endeavors command an astronomical amount of money; every major university in the U.S. has a nanotech research division, or has at least applied for the funding to establish one. But underdeveloped nations, without the resources for the practical applications of nanoscience, sufficient funding for research, and the means to educate their population in the benefits and/or dangers of nanotechnology, will not be able to keep up with countries that do. As the use of manufactured nanomaterials proliferates and humans become more and more dependent upon them, the disparity between the rich and educated (who control the means of nanotechnology production by monetary investment jurisdiction and/or the scientific knowledge required to reproduce it) and the poor and uneducated (who depend upon nanotechnology to maintain or advance their standard of living, yet do not possess the money and/or knowledge needed to generate it themselves) could find itself enlarged both within developed nations and beyond their borders, creating a neo-Marxist power struggle in which poorer, underdeveloped countries could become largely dependent upon richer, more developed countries for this technology that would be virtually impossible for them to independently recreate on their own turf.

In the near future, scientists predict that nanotechnology will provide the military with the ability to create light, flexible, and bulletproof armor that would be able to resist agents of biological and chemical warfare.[6] Nanotechnology may also allow armies to build nanosized surveillance and identification devices that could be positioned in strategic places or attached to the body and remain undetected by the naked eye. In this day and age, the ability to efficiently accumulate mass quantities of accurate information has become perhaps the most valuable resource known to man, lending power to those who are privileged enough to possess and control it. While increased surveillance and personal identification capabilities may enable greater security and military intelligence, it concomitantly entails the need for technology that would detect enemy nanocameras and tracking devices. Modern societies would then be provoked to reevaluate individual privileges of privacy and reconsider government policy with respect to public versus private information, and then be forced to reconcile these with what the government—in its newfound possession of these technological capabilities—came to believe to be within its power, right, and jurisdiction to keep track of. Moreover, ownership of the surveillance capabilities that nanotechnology would provide could give rise to factions of authority within modern societies whose limitations would be difficult to define and regulate.

The Internet offers information on many weapons that are much easier for terrorists to build than biological weapons.

Nanotech applications spark hot debate with respect to a wide range of environmental concerns, particularly with respect to the application of fullerenes, stable arrangements of carbon atoms that resemble soccer balls and are affectionately termed "buckyballs" after R. Buckminster Fuller, the man who designed them. At this point in time, it is impossible to know exactly where, and how far, fullerenes may travel when they enter the environment and become exposed to living organisms and ecosystems; likewise, it is difficult to ascertain the full extent of their positive and negative effects upon nature. Two recent studies documented lung damage in animals after they inhaled a manufactured carbon nanotube (a kind of buckyball), while another study showed that inhaled C60 molecules can find their way into the brain.

Scientists are aware that nanoparticles are small enough to cross cell walls, leak into their nuclei where the organisms' DNA is housed, and kill bacteria; while they may be able to exploit this application of nanotechnology to make advancements in medicine, fullerenes may pose a potentially serious threat to the environment, where bacteria regularly play an extremely important role (e.g., maintaining soil fertility). Thus, within nanotechnology's potential lies the dangerous possibility that fullerenes and other similar microstructures may disrupt nature's finely-tuned ecological processes.

If the products of nanotechnology are composed of living atoms, then by definition, could they themselves be considered living things? The proposed manufactured nanomaterials and the myriad possibilities they hold for the future smack of science fiction, but as history has shown us, that which is sci-fi today may very well be the reality of tomorrow. Currently, nanotechnology is nowhere near the point of being able to self-replicate; for nanotechnology to emulate the mutated airborne viruses of science fiction and produce swarming armies of nano-robots that threaten to take over the world would require far more flexibility and intelligence within its technology than scientists could possibly design into it. That does not, however, necessarily mean that the ability for nanomaterials to reproduce on their own is not within the realm of future possibility. If nanomaterials qualify as living organisms, then, would be it ethical for scientists to contain, manipulate, and exploit them for the purposes described above?

Because the promise and potential of nanotechnology is still in its early stages, it is of little use to begin blowing the possible dangers it poses to society and the environment completely out of proportion. Perhaps the most effective way of dealing with nanotechnology—as well as all new advancements in modern science—is to support all those who endeavor to explore uncharted scientific territory in search of greater understanding of the world we live in, as well as continue to sustain relevant dialogue that questions and challenges it.

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Academic-Industry Collaboration in Clinical Trials:A Necessary Evil

By Neiha Arora

The integrity of industry-sponsored clinical research has come under increasing scrutiny in recent years. With ever increasing momentum, the biotechnology and pharmaceutical industries are continually introducing new therapies, therapies which first be tested before being accepted into clinical practice. This bench-to-bedside transition is often facilitated by the pharmaceutical companies themselves, who finance clinical trials led by researchers at academic institutions. This financial intertwining of academia and industry had led to concern regarding researchers' conflicts of interest, and what the implications of such conflicts are for evidence based medicine and patient care. Can a researcher financed by a certain company to study its latest new drug truly be trusted to be impartial in his assessment? Can a pharmaceutical company realistically be expected to rigorously test its own product and to report both favorable and unfavorable discoveries equally? Most importantly, do these probable inherent biases stand to compromise the well-being of research participants? And given these treacherous possibilities, should an alliance between academia and industry be allowed?

The answer is yes. Clinical trials are a necessity; this is indisputable. Moreover, with increasing emphasis on prevention and treatment of chronic diseases, many clinical trials must span several years in attempts to prevent or treat undesired end points. The current standard in clinical research is that trials be large, long, and conducted at various centers to guarantee statistical validity of results. It costs roughly $300 million to $600 million to develop one new drug and bring it to market.1 Seventy percent of funding for drug trials in the United States comes from industry rather than the National Institutes of Health (NIH).1 Given these stark financial realities and the lack of an obvious alternative source of funding, denying or even decreasing industry support of clinical research is simply a nonoption. Medical progress would stagnate and patient care would ultimately suffer.

In assessing the relative peril of the academic-industry alliance, it is also crucial to consider the dangers of alternative research models. During the past decade, industry has shifted its focus from academic medical centers to more commercially oriented research networks.1 Specifically, pharmaceutical companies have taken to working with contract- research organizations (CRO) to design, implement, and interpret clinical trials. CROs employ physician-scientists, pharmacists, and biostaticians to provide these services and recruit patients at multiple sites through both academic and community physicians. At specific sites, CROs have the option to subcontract with site-management organizations (SMO) to organize local networks of community physicians and patients. Both CROs and SMOs are for-profit constructs that aim to conduct trials for industry more rapidly

and more cheaply than academic medical centers. The interaction between industry and clinical investigators, however, is less regulated here than in the academic sector. Pharmaceutical companies are able to have greater control over study design, data analysis, and publication rights. Companies have been shown to design studies in ways intended to favor their product. For example, they will test a drug in healthier subjects than it is intended to treat (so as to minimize adverse effects) or test it against a subtherapeutic dose of a competing agent so that the new drug appears more effective. It is thought that physicians in the commercial sector, often recruited from the community, are less concerned with authorship and publishing rights, more readily yielding to industry representatives to determine which research results should be reported and how. This shift of power has especially important implications when a trial delivers unfavorable or disappointing results. In the absence of an internal review board (IRB) and other such regulations mandated by academic medical centers, transgressions of pharmaceutical companies in these settings often go unhindered, if not unnoticed. These associated dangers of commercialized clinical research should prompt academia to renew its participation in industry-sponsored research, so as to slow or ideally reverse this disturbing trend.

In examining the problems stemming from the rise of the commercial research sector, it is not unreasonable to hope that an academic-industry alliance would have the potential to better achieve a balance between the commercial and scientific goals of research. However, it would be foolish to deny that similar financial conflicts of interest exist in the academic arena as well. In defending academic-industry partnerships, it is necessary to examine the regulatory measures that currently exist and ponder which may need to develop in order to maintain a high standard of clinical research. Most medical schools have guidelines regarding financial ties between faculty members and industry. Examples include requiring disclosure of financial interests by investigators and limiting stock owned in a company whose product they are researching. The problem is that such policies vary widely from one institution to the next. Moreover, institutions with strict guidelines find themselves becoming more lax so as not to lose star faculty members to more permissive institutions.3 Similarly, the Internal Committee of Medical Journal Editors (ICMJE), concerned about the integrity of clinical research in an increasingly privatized setting, revised in 2001 its guidelines for investigators' participation in study design, access to data, and control over publication. However, a 2002 survey of 108 medical schools revealed that many institutions fail to adhere to these guidelines when participating in industry-sponsored research. Institutions are supposed to ensure that their researchers have full participation in trial design, access to all trial data (not just data at their own site), and rights to publish the data as it appears, whether good or bad. Yet these clauses often go unfulfilled in sponsor-institution contracts. Again, it is thought that the current competitive, market-based research environment is in part

responsible for this loosening of standards. Several of the survey respondents reported feeling "powerless" in contract negotiations with sponsors;4 smaller medical schools, which typically have less clout but a greater need for funding than the bigger, more prestigious centers, are especially vulnerable to industry domination. It is thus evident that guidelines do exist to protect scholarly integrity but are not always followed.

It is these troublesome compromises that have led the research community to criticize academic-industry partnerships in the past. The answer, however, should not be to abandon such partnerships but rather to work towards better ones. While the interests of academia and industry are generally viewed as being at odds, the fact remains that each needs the other. Academia needs industry's financial support. Industry, though primarily driven by profit incentive, also stands to benefit greatly from the prestige and merit that academic endorsement can give a new product. Allowing commercialization of clinical research as an alternative to academic-industry collaboration has only served to magnify the conflicts of interest inherent in industry-sponsored trials, while lessening the quality of research produced. Academic-industry partnerships in comparison are a preferable model. Academic institutions, however, have an imperative challenge to uniformly standardize and uphold research practices, to support each other in maintaining strict regulations with industry rather than softening in response to market pressure. Even in the face of this challenge, this partnership is a difficult but necessary enterprise that should be allowed to proceed. The ultimate shared goal of academia and industry -improved disease treatment and prevention - is well worth the struggle.

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Back to the Future

Wonder Fertility Therapy

By Radha Ram and Elodi Dielubanza

Despite their many cultural differences, there seems one commonality among modern world citizens: they want families. The right to reproduce represents not only one of the most cherished human rights but children and family represent a universal ideal. This ideal, as many painfully know, is not always easily achieved because of infertility. This is why assisted fertility treatments enjoy a booming popularity. People sink life savings into therapies for the mere chance of conception. Science, fielding the demand and wanting to cash in on this lucrative avenue, continues to push the envelop with new therapies. Now, with new recommendations from the President's committee on bioethics, science can continue to press the limits further. The Committee's call for self-regulation by doctors and self-managed, post-treatment patient surveillance leaves room for dangerous oversights. With today's technologies becoming more sophisticated, it seems more important than ever to impose strict guidelines for use and post-treatment surveillance of fertility therapies. Not doing so is to run the risk of subjecting children born from assisted therapies to a plethora of defects and impediments. In essence, the committee is giving doctors and patients the right to privilege their desires over possible harm to a child. This allows emotion and financial gain rule over prudence.

With cytoplasmic transfer, a "promising", new fertility therapy, making progress towards FDA approval, the new recommendations from the committee on bioethics seem acutely alarming. In a common form of infertility, embryos begin to fragment early in development. The cause of this fragmentation is unknown but it is believed that certain women may lack mitochondria that can provide sufficient energy to fuel the rapid cell divisions that sustain development. Cytoplasmic transfer seems to offer a solution to this problem. The healthy cytoplasm from donor eggs is injected into recipient eggs, providing mitochondria and other vital organelles. In several human cases, this has prevented fragmentation and allowed for the development of viable fetuses resulting in live births. But with the transfer of mitochondria, this treatment amounts to a crude gene transfer. The resultant children have maternal and paternal nuclear DNA, and mitochondrial DNA from both mother and donor. There is no historic precedence for individuals with three genetic parents and interaction between the different types of DNA may result in significant defects. Mothers may pass on mutated mitochondria that could lead to mitochondrial disease pathologies. But only long-term strict surveillance, would give an accurate assessment of risks for such conditions. Further, one may be activating eggs carrying mutated nuclear DNA resulting in abnormal development.

In follow- up reports given by couples that have used the treatment to conceive in controlled studies, two of the seventeen respondents reported fetuses with abnormal 45, XO karyotype and one other infant was diagnosed with Pervasive Development Disorder, which is linked to several autism diagnoses.

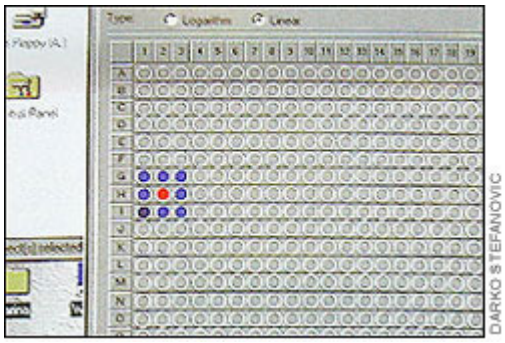
Though this technology offers infertile couples a new chance at biological parenthood, we should proceed with caution towards the wide use of this treatment - a treatment which as already begun growing in popularity. Little attention has been given to the long term effects that cytoplasmic transfer might have on the health and well-being of the resultant children. In all frankness, science is uninformed as to how the transfer works to facilitate development. It is in the realm of possibility that it could indiscriminately revive problem eggs and lead to mutated offspring. To know for sure would take many more years of research.

The successful use of cytoplasmic transfer in comparison to other treatments seems promising for infertile couples around the world, but the high incidence of mutation and defect demands healthy suspicion of wide use of this treatment. Continued surveillance of cytoplasmic transfer children and further investigation using primate models will help illuminate unknown risks and allow parents and doctors to make informed decisions about the use of this technology. It is important that science come to understand the specific mechanism of intervention before further practical application. There should be clear data for this and many other assisted fertility treatments that help patients and doctors understand risks so that they can determine who is and is not a candidate for successful treatment, thus increasing the chance of a healthy resultant child. The "let's try everything until something works" approach being carried out by many fertility specialists today, seems to be aimed at catering to the emotions of the patient and is at best irresponsible. Paramount in fertility treatment decisions should be the health of the child. After all, isn't that the least we owe to the precious children so many of us are longing to bring into the world?

Pharmacogenomics

By Fidalene Cepeda and Yvette Martinez

"I almost died from an adverse drug reaction and I can't help but wonder if I would have gone through so much physical pain and near death if my medicine were made just for me?" said a fellow Columbia College student. The sad reality is that this student was only one out of the millions of victims that suffer from adverse drug reactions. Yearly there are over 2 million Americans who have experienced the horror that this student did. Adverse drug reactions are one of the leading causes of hospitalization and death in this country. The fact is that adverse drug reactions will continue to exist because there is no simple way of determining which drug will do what to which person. Practitioners are cornered and are faced with having to prescribe "one size fits all" drugs. This "one size" system is based on an average, on how the "average" patient responds to medications but we all know that "average" is not reality. If it were, we wouldn't have millions of adverse drug reaction victims yearly. Each individual is unique and reacts differently to different medications. There is no "average" individual when it comes to drugs. The question we should all be asking ourselves is, what can be done to prevent adverse reactions? The answer is here and it is pharmacogenomics.



The way in which an individual's genetic material can affect the body's response to drugs is the principle behind pharmacogenomics. Pharmacogenomics has such promise that one day, we will achieve the possible reality of having tailor-made drugs for each individual. With pharmacogenomics, we could have medicine adapted to each person's genetic makeup. For instance, the Genentech drug which is approved to treat psoriasis, failed to show statistical significance in improvement by 20% in Phase II Trial. Despite the fact that 28% of the patients improved, 19% did not reach the primary endpoint. Genentech did work for certain patients and we should not ignore those results. This illustrates how medication should not be uniformed for everyone due to the individuality of each person.

The benefits of pharmacogenomics are far-reaching. We would replace the risk of running the traditional trial-and-error method of attempting to match the patients to the right medications with the precise drug therapy based on a patient's genetic profile. This safer technique not only takes out the guessing in prescribing drugs, but it will also ensure that patients will recover quicker. It is key to understand that with pharmacogenomics, maximizing a drug therapy is the goal. Doses of medications will also be more accurate. By using a patient's genetic profile, dosages are catered around the body's ability to process medications and how long it takes to metabolize them.

Therefore, the possibility of overdosing is virtually eliminated. Pharmaceutical companies will be able to produce safer drugs by basing them on proteins and enzymes. Drugs will be able to better locate their target points and decrease damage to nearby tissues.

Furthermore, there will also be better vaccines made from genetic material. Tailored vaccines will have the benefits of current ones but the risk of infections will be eliminated. Disease susceptibility can also be better managed. Knowing what diseases a person's genes code for will allow that particular person to make personal changes, whether it be lifestyle or environmental, to avoid or minimize the severity of genetic diseases. Advance screening will help patients have careful monitoring of the disease and the most appropriate drug therapy.

Although the cost of having tailored drugs would be expensive in the short term, in the long run, by manufacturing drugs in bulk, they will be more accessible for purchase. Nevertheless, if each individual had at least an option of having the benefits of pharmacogenomics, there would be a dramatic decline in the number of people dying from adverse drug reactions.

The benefits of pharmacogenomics are almost endless - lives would be saved, injuries would be avoided, and the cost of time, energy, and money would dramatically fall. Pharmacogenomics is still in its early development phases but its new technologies are embedded in old ones that are sure to revolutionize medicine.

Transgenic Animals: Silk from Milk

Simi Hinden and Yvette Martinez

"Got Silk?" The phrase, coined by Lawrence Osborne of *The New York Times Magazine* in June of 2002, depicts the follow-up research of Nexia Biotechnologies in their search for a method to mass-produce spider silk. In January of 2002, researchers from the Nexia Biotechnologies group in Canada published a paper in *Science* illustrating their initial experiments in transfecting mammalian cells with spider silk genes. Afterwards, as the *New York Times Magazine* article relates, entire organisms were grown from embryos which possessed the spider silk gene, and as of two years ago, Nexia was in the process of developing methods to mass produce the silk obtained from the mammary glands of transgenic goats.

Biological researchers, animal rights activists, environmentalists, and even government officials have been involved in the ongoing debate about the ethics of such research. Biologists argue that transgenic animals will greatly benefit human life by enabling production of pharmaceutical compounds as well as other compounds, like silk, which would advance technology. Environmentalists, however, contend that the research has not been fully tested to make sure it has no adverse effects in nature. They claim that transgenic organisms could grow out of control and affect evolution, as well as wild type organisms of the same species. In this paper, we plan to discuss these issues in depth, as well as propose potential solutions to the bioethical conflict so that both sides can agree on how to make research on transgenic organisms work without any negative side effects.

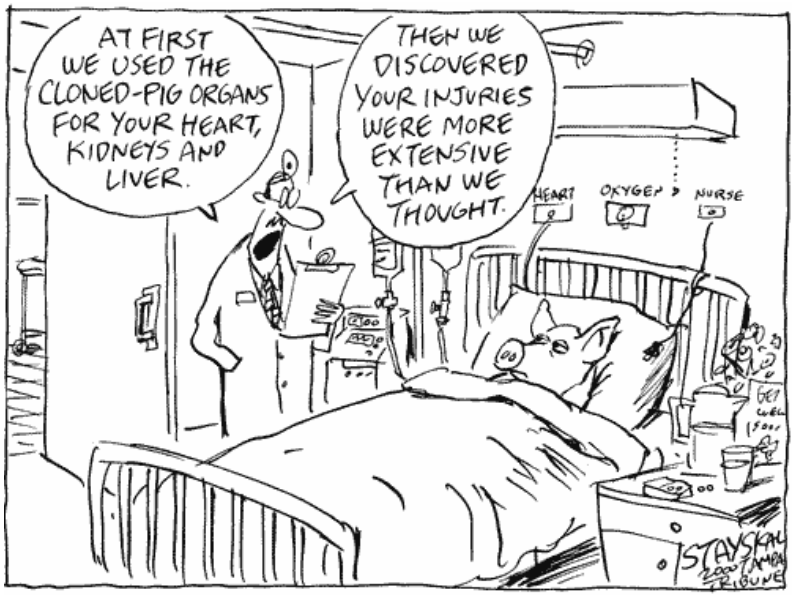
In the study performed by researchers at Nexia Biotechnologies, scientists transfected bovine mammary epithelial alveolar cells and baby hamster kidney cells with cDNA encoding silk-weaving genes from two spider species, *Araneus diadematus* (genes ADF-3 and ADF4) and *Nephila clavipes* (genes MaSpI and MaSpII). Silk proteins produced by these cells were purified and spun at various concentrations, and then stretched out to produce fibers. When their tensile strength was tested, fibers drawn four or more times had the most toughness, tenacity, and modulus. However, the biggest difficulties were encountered in the spinning process, because while a spider uses different kinds of silk and weaves multiple strands together, the man-made machines for drawing the silk were unable to achieve that level of complexity.

Later that year, *The New York Times Magazine* published an article by Lawrence Osborne about Nexia's continued research on spider silk. Osborne reported visiting Nexia's laboratories, and he viewed their next project – making transgenic goats that produce spider silk in their milk. Silk genes were attached to a promoter, which is only expressed in mammary glands, and then the genes were transfected into goat embryos. When the goats began to lactate, their milk

contained silk proteins which could be purified stretched using an extrusion machine, and woven to create silk fibers. These transgenic animals pass the spider silk gene to their offspring, thus ensuring new generations of silk-producing goats for Nexia to use in their research and new technologies. The main difficulties with the research are with the stretching and weaving aspect of making the silk, as it is difficult to replicate the spider's mechanism. In addition, the goats only have one silk gene, while spiders typically have several different genes which are all expressed to make silk protein. The article did not mention any data regarding the tensile strength of the silk produced from the goats.

As genetically modified organisms, or GMOs, these goats are part of a huge debate about the ethics of creating such animals and plants. The biggest argument in favor of the development of transgenic organisms is that they will benefit human life. For example, spider silk, which is extremely thin yet one of the strongest materials on earth could be used as biodegradable sutures in surgery or as hemostatic dressings. Even bulletproof vests could be manufactured from spider silk, and they would be considerably lighter than ones used today, thus lightening the load for law enforcement officers and the armed forces.

Transgenic animals are also used for "pharming," or production of pharmaceutical drugs ranging from hemoglobin to tPA, to CFTR, a treatment for people with cystic fibrosis. The easiest way of obtaining the drugs is to have mammals produce them in their milk, as with the goats that produce spider silk, because the animals do not have to be killed or subjected to invasive procedures. Even those who oppose genetically modified organisms cannot deny that pharming has clear benefits, in that it lowers drug costs and thereby makes them



available to more people in larger quantities.

However, those who are anti-transgenic organisms also have compelling arguments. One common point is that these organisms could affect other members of their species if they escaped, as with the goats, or if they grew out of control, as with genetically modified plants. What would happen if a silk-producing goat escaped and mated with a wild-type goat? Would the introduction of this new spider gene into the wild adversely affect the goat population? Because the technology is relatively new, few, if any, studies have been done on the effect of genetically modified organisms on other members of their species, and the results of crossbreeding would only be seen after several generations at any rate. Studies also need to be done on the effect of transgenic organisms on themselves, as in how the new gene or genes affect the organism into which they are transfected. For example, goats expressing the spider silk gene may be adversely affected, especially offspring which would feed from their mother's milk and ingest silk proteins as well. The silk proteins may have a minimal effect on the feeding offspring and may just be broken down in the digestive tract, but on the other hand, they may coagulate and cause problems. In addition, research needs to be done on the interactions between transgenic animals and different species, such as those which feed upon the transgenic organisms or that live in the same environment and share the same resources.

There is no doubt that little is known about the effects of transgenic animals on humans as well as on the world environment as a whole. However, due to the strong benefits of transgenic animals from pharming and production of materials useful to humans, such animals cannot be outlawed. Therefore, it is best that such research be managed, as it will go forward with or without any controls or public debate. One way of managing the transgenic organism debate is to limit the growth of the animals, either so that they cannot reproduce with wild-type members of their species or to keep them under close control so that they cannot escape into the wild. For example, silk-producing goats could be sterilized so even if they did escape, they would not affect normal goat populations. Alternatively, their genes could be further altered so that they could not naturally reproduce with members of their own species. These preventative measures would be taken in addition to keeping the animals physically separated from the natural environment.

As for determining whether transgenic animals are themselves adversely affected, more studies would have to be done. Research organizations should have to prove that the new genes do not harm their transgenic organisms. A standard of guidelines could be set for what constitutes harm or negative side effects in transgenic organisms, and animals could be measured against it to determine whether they are treated well and or are unfavorably affected by the additional genes.

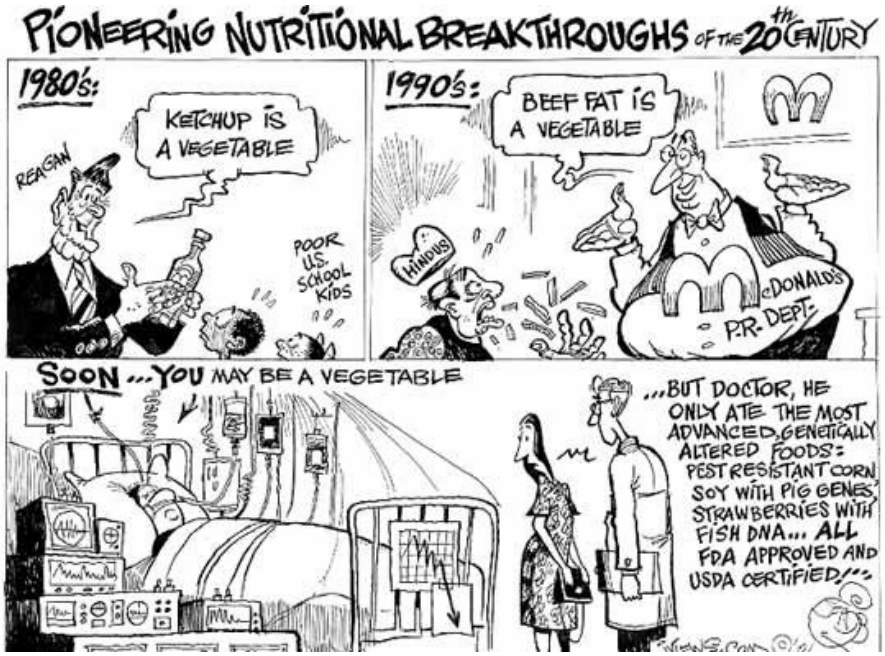
Clearly, transgenic organisms are going to continue to be developed, with or without regulation, and it is important that the entire scientific community agrees to uphold certain standards and practices to manage the issue. In this way, the benefits of transgenic organisms will

be harnessed while minimizing damage to humans, the transgenic organisms themselves, and the environment as a whole.

Lazaris, Anthoula; et al. "Spider silk Fibers Spun from Soluble Recombinant Silk Produced in Mammalian Cells." *Science*. 295: 472-476.

Osborne, Lawrence. "Got Silk?" *The New York Times Magazine*. 16 Jun, 2002.

"Animal Pharming: The Industrialization of Transgenic Animals."



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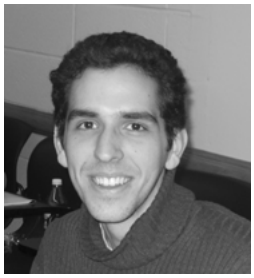
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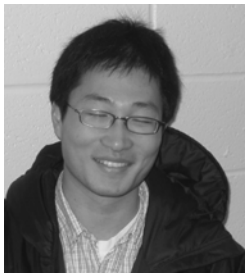
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