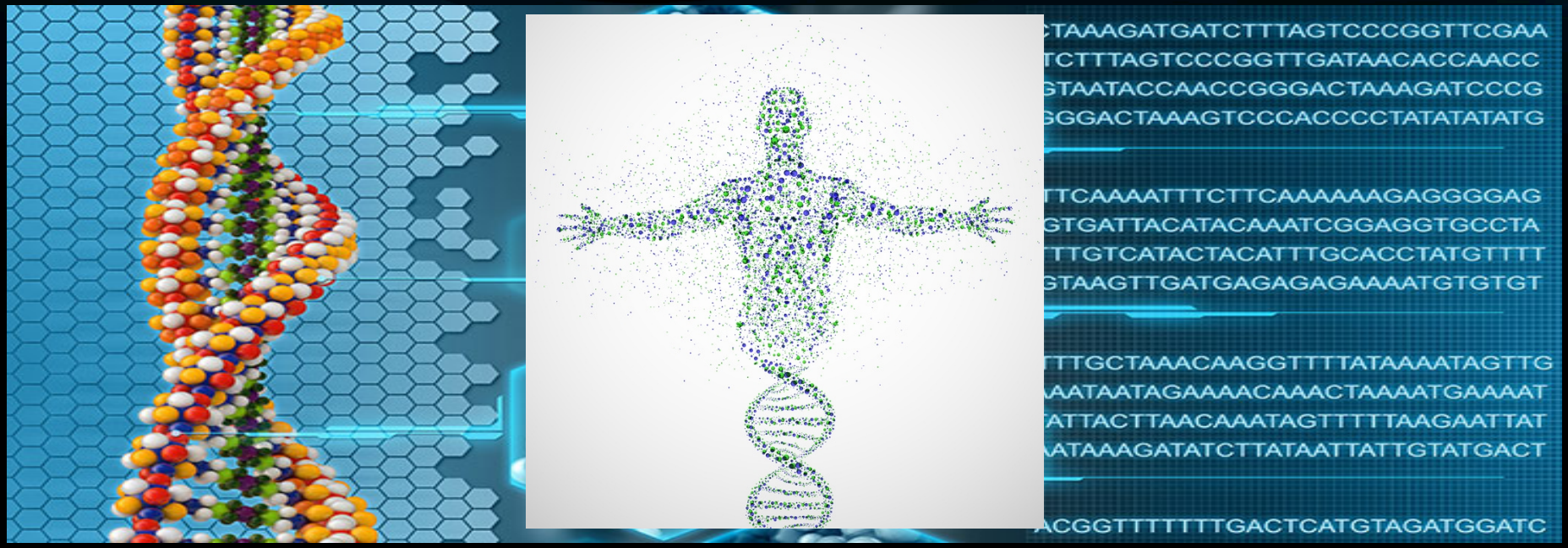
Issues in Modern Genomics

Ms. Sarah O'Leary-Driscoll



Andrew Adams
Arun Arjunakani
Mara Cardona
Grace Carlberg
Esther Chung

In collaboration with:

Sarah Dovgin
Joseph Jagusah
Michael Qian
Max Shramuk
Andy Xu

Breaking News or Science Fiction?

- CRISPR technology, a way to use bacterial proteins to make precise, targeted changes to the DNA of living cells, is under development by multiple scientists.

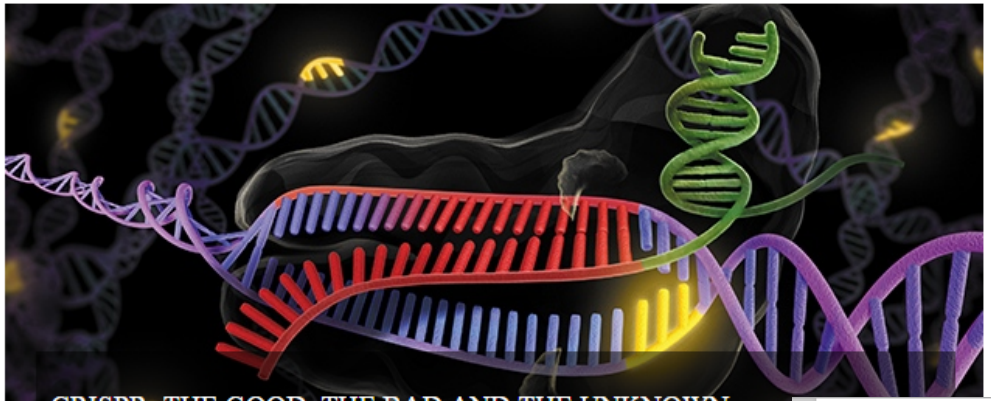
- The subsequent release of the process and data surrounding it has scientists around the world proclaim that a “new era” of in Molecular Biology has begun.

Breaking News or Science Fiction?

- Mid September, 2015, British scientists request permission to use newly developed procedure/technology to edit the DNA of viable human embryos.

- Sept 25, 2015 science news explodes with the findings that another set of proteins have been discovered that may rival or beat CRISPR when it comes to editing the DNA in humans.

Feelings among scientists, let alone society at large, are mixed, to say the least...



CRISPR: THE GOOD, THE BAD AND THE UNKNOWN

A DNA-editing technology called CRISPR has rapidly become one of the most pop
alter genomes. Concerns about its risks temper excitement about its usefulness. I
been used to modify human embryos, and the technology could alter wild animal p
works in everything from wheat to mice. *Nature* brings together research, reporting
opinion on gene-editing and its implications.

Image credit: K.C. Roeyer

▼ Latest news & commentary ▼ News ▼ Commentary

▼ Research from Nature journals

LATEST NEWS & COMMENTARY

Biohackers gear up for genome editing
Amateurs are ready and able to try the CRISPR technique for rewriting genes.
Nature (26 August 2015)

Super-muscly pigs created by small genetic tweak
Researchers hope the genetically engineered animals will speed past regulators.
Nature (30 June 2015)

CRISPR: Move beyond differences
Researchers and ethicists need to see past what can seem to be gendered debates when it comes to the governance of biotechnology, says Charis Thompson.
Nature (24 June 2015)

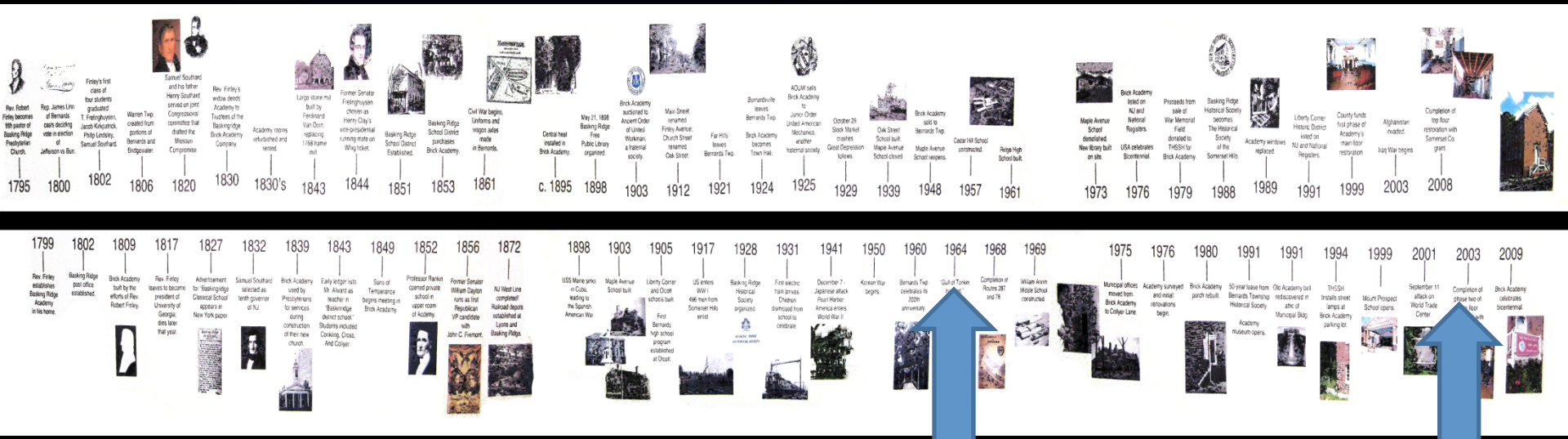
CRISPR: Science can't solve it
Democratically weighing up the benefits and risks of gene editing and artificial intelligence is a political endeavour, not an academic one, says Daniel Sarewitz.
Nature (23 June 2015)

CRISPR, the disruptor
A powerful gene-editing technology is the biggest game changer to hit biology since PCR. But with its huge potential come pressing concerns.
Nature (03 June 2015)

US science academies take on human-genome editing
National Academy of Sciences and National Academy of Medicine to develop guidelines for rapidly advancing technology to modify human embryos and germ cells.
Nature (18 May 2015)

CRISPR germline engineering — the community speaks
Nature Biotechnology talks to 26 influential researchers about the ethics of genetically editing human reproductive cells.

- The structure of DNA was published in 1953.
- The Human Genome project was completed in 2001.
- CRISPR was patented in 2014.



- *Essentially, the ability to change our genomes has arisen before we've fully come to terms as a society with how to handle personal genetic information, or personal genomics, in the first place.*

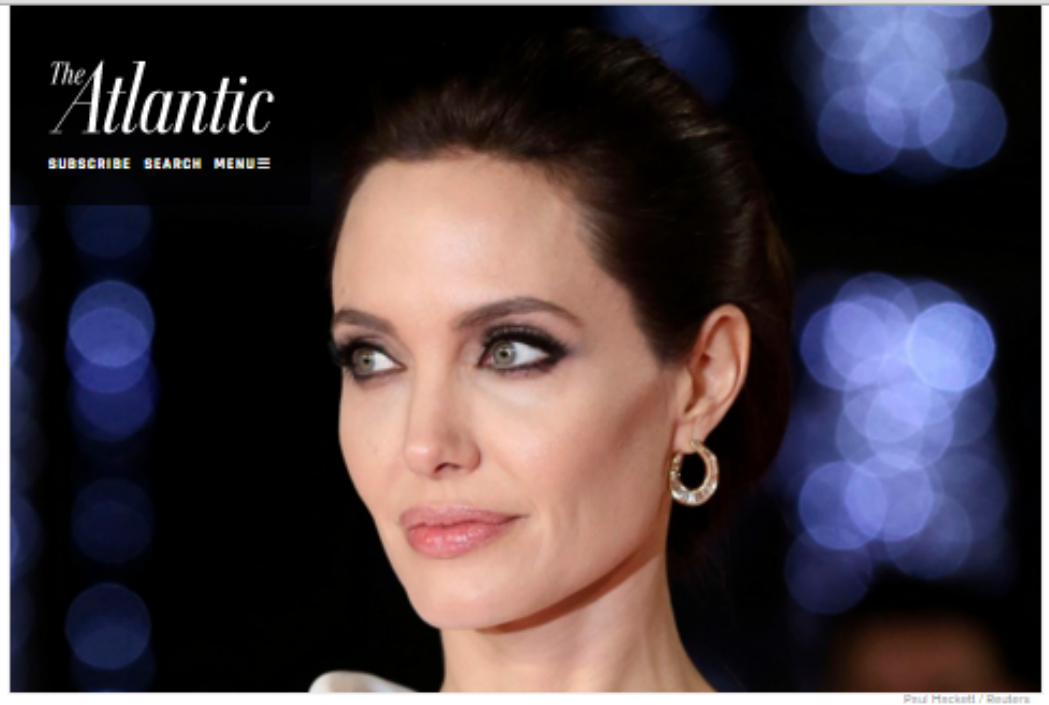
- *Where do we go from here? What are the issues? What questions do we ask to inform our opinions, and decisions as individuals and as a field?*

.....we're still trying to figure it out.

Uses of Genetic information:

- **as a predictor for disease and use in medicine.**
- **as a predictor for behavioral or psychological issues**
- **to genetically modify organisms for research or medicine (disease treatment)**
- **to genetically modify organisms for preference (particularly humans or other species that have a direct impact on humans)**

Predictions for disease and medicine



Paul Hackett / Reuters

SCIENCE

Taking the Uncertainty Out of Genetic Screening for Cancer Risk

A new technique will help genetic-test users make more informed decisions about their health.

ED YONG | OCT 12, 2015

In 2013, the U.S. actress Angelina Jolie learned that she had mutations in a gene called BRCA1, which conferred very high risks of breast and ovarian cancer. To obviate that risk, she opted to have a double mastectomy; in 2015, she had her ovaries removed, too.

Many women face similar choices on the basis of BRCA1 tests, which search the gene for mutations that are known to increase the risk of breast cancer.

Jen Ren/Fl

Scientists discover new gene that increases Alzheimer's disease risk

And it could be the key to slowing down or stopping progression of the disease.

BEC CREW 7 OCT 2015

An immune system gene that's associated with a higher risk of Alzheimer's disease has been identified by researchers in the US. Older adults and Alzheimer's patients who are carrying a specific variant of the IL1RAP gene were found to have higher rates of amyloid plaque accumulation in the brain, which is one of the key drivers of the disease.

Alicia Semaka Become a fan
Certified Genetic Counselor

Predictive Genetic Testing for Huntington's Disease: A Journey With a Genetic Counselor as Your Guide

Posted: 06/18/2015 10:17 am EDT | Updated: 06/18/2015 10:59 am EDT

In 1993, a remarkable scientific discovery was made -- the genetic mutation that causes Huntington's disease (HD) was identified. This breakthrough allowed for predictive genetic testing of individuals at-risk of the disease, like Marianna Palka in the film *The Lion's Mouth Opens*. Predictive testing involves a simple blood test to detect whether or not a person has the genetic mutation associated with HD. It is available to adults 18 years or older who have an affected family member but do not yet have symptoms of the disease. All individuals considering predictive testing should meet with a genetic counselor.

The role of genetic counseling

As a genetic counselor specializing in predictive genetic testing for HD, it is important

UPFRONT 28 October 2015

23andMe relaunches direct-to-consumer tests for genetic disease

WHAT are the odds of that? 23andMe is relaunching its direct-to-consumer genetic tests – now with official approval.

In 2013, the company was banned from selling a genetic test kit that provided customers with information about their risk of developing 254 conditions, including breast cancer and heart disease. The US Food and Drug Administration (FDA) said the company hadn't proved that it had clinically validated its tests for their intended uses.

Last week, 23andMe announced that it will resume selling a genetic health testing kit, for a smaller number of diseases. Each test has been FDA approved.

The kit, which costs $199, will provide customers with data based on "carrier information" about genetic mutations that could lead to diseases – such as cystic fibrosis – in offspring.

One concern about the previous kit was that the results didn't reflect the effect of environmental influences on many of the diseases. Such effects don't tend to matter for the conditions included in the new test package.

Potential Advantages

- Connecting genetic causes and outcomes in terms of physiological expression of disease can:
  - Improved research effectiveness in terms of cell biology, physiology, inheritance , and population genetics.
  - Improve drug design
  - Early detection of symptoms
  - Understanding of risk

Limitations

- Many diseases have a genetic basis but are not inherited
  - Can be connected to environmental influence
  - Genetic changes can occur during a lifetime
  - Insurances usually use family history to approve screening

- Predisposition does not necessarily lead to actual expression of disease or characteristic.

Limitations

- Genetic sequences may not have as big of an impact as the regulation of the genes. This is not as easily testable.
- Unknown cause and effect relationships between genes and traits
- Action based on risk can have associated negative outcomes, and the cost/benefit to the individual is inconsistent (risky surgery) from individual to individual

Questions/Issues to consider:

- Who owns or have access to information from genetic tests? What are your rights in terms of privacy?

- Can genetic testing be mandated? By insurance carriers? Who else?

Questions/Issues to consider:

- Genetic testing is expensive. What does this mean about who has access to the benefits of this type of testing?

- What do we do with information from genetic tests? As individuals? As a society? As business or governmental leaders?

- What kinds of psychological or emotional impact might the information provided have on individuals and their families?

Predictions for behavior

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NEWS PSYCHOLOGY, GENETICS

Gene variant may foretell success in program for at-risk kids

Disruptive children with DNA twist respond best to 10-year intervention, study finds

BY BRUCE BOWER 8:00AM, FEBRUARY 20, 2015

SCIENCE

MAY 25, 2015

WOMEN WITH A PARTICULAR GENE ARE SUSCEPTIBLE TO CHEATING – BLAME INFIDELITY ON GENETICS, SUGGESTS NEW RESEARCH

ALAP NAIK DESAI

The act of cheating may be explained scientifically, with the presence of a single gene determining if the woman is predisposed to infidelity.

While men may justify their unacceptable behavior by blaming it on the "biological urge to spread their seed," women had nothing to say to defend their act of betraying the trust of her partner, until now. Recent research suggests women may also genetically inherit the impulse to cheat.

Scientists claim to have found one gene in particular that seems to be linked to a woman's likelihood of being unfaithful. A study published late last year observed 7,400 sets of twins in Finland aged between 18 and 49 in long-term relationships. From the volunteers, 9.8 percent of men and 6.4 percent of women had secretly admitted that they had at least one affair within the last year.

Is post-traumatic stress disorder in your genes?

By Sandee LaMotte, Special to CNN
Updated 4:28 PM ET, Thu March 12, 2015

What are causes and effects of PTSD? 01:00

Story highlights

- More than 13 million Americans have PTSD
- Genes account for about 30% of risk
- Immune system plays a role in risk and resilience

(CNN)—Could a simple blood test someday tell if you're genetically predisposed to post-traumatic stress disorder? That's what a team of international researchers is hoping after finding a genetic marker linked to PTSD in the blood samples of Marines stationed in conflict zones.

"We'll draw the blood and have a way to do this very rapidly and start to tease apart who is a little more at risk and who is a little more resilient for PTSD," says principal investigator Dr. Dewleen Baker of the University of California-San Diego. "It's exciting."

Focus on Health


Mom with ALS: My disease will make my daughter stronger


Inside students' heavy backpacks, why it's too much and how to help

Potential Advantages

- Earlier interventions for potential problems
- More informed or specific treatment options and therapies
- More informed choices

Limitations

- The connections between genes, brain physiology and function, and our thoughts, emotions, decisions, and behavior is sometimes unclear.

- We are influenced by our genes, but the extent to which they determine our behavior is not well established.

  - Environmental factors and experiences play a role

  - We can make a conscious effort to go against those influences, which may impact outcome and consequences

Questions/Issues to consider:

- Similar to those related to medical predictions, such as who has rights to the information, Can these sorts of tests be required, Etc.

Genetic modification of organisms for research or medicine

Fluorescent Cats Aid Research

Tiny, adorable and...green? Glowing kittens may answer questions about neurobiology and disease.

By Rachel Nuwer | September 13, 2011

This glow-in-the-dark kitten has a unique set of genes.
MAYO CLINIC

Cats come in all sorts of colors—tabby, orange, and calico—but scientists are most interested in the fluorescent variety. Eric Poeschla, a molecular virologist at the Mayo Clinic, used a technique called transgenesis to bestow kittens with a heightened immune system as well as an unearthly green glow, which allows researchers to track the expression of genes of interest.

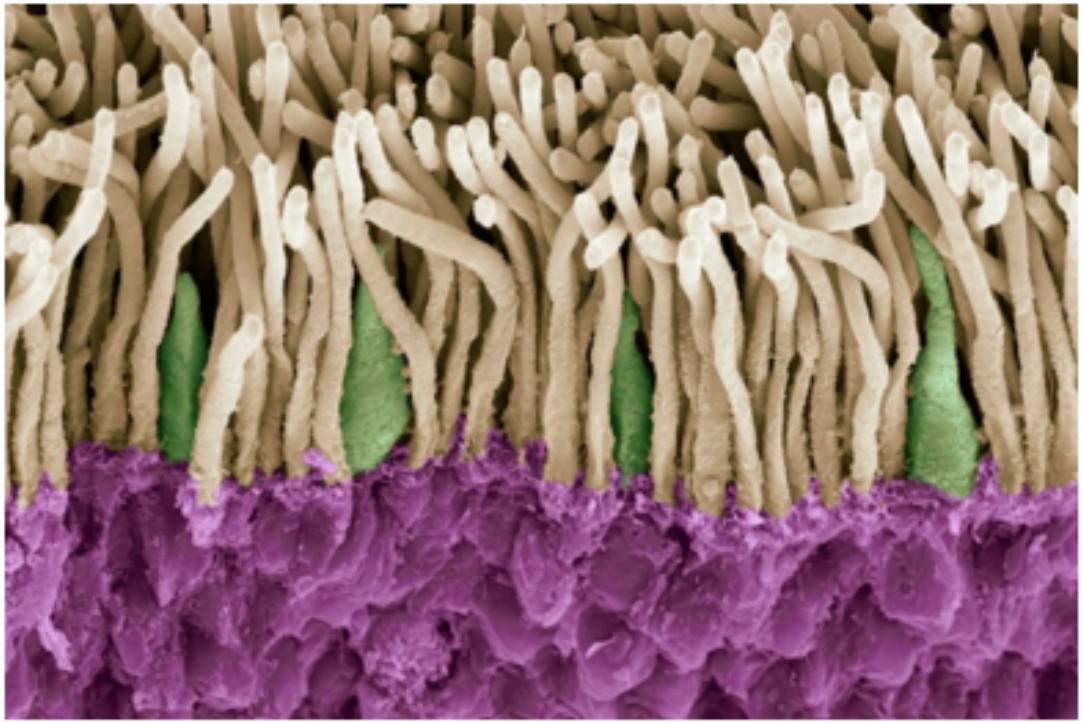
Poeschla and colleagues used a modified virus to transfer the green fluorescent protein gene into cat egg cells. The green marker allowed them to visualize their real target: a monkey-derived protein called TRIMCyp. This protective protein, found in some primates but not in cats, prevents organisms from becoming infected with an HIV-like disease called feline immunodeficiency virus (FIV).

The transduced cat eggs were then fertilized and injected into adult female cats. Of the 11 successfully-implanted embryos, 10 contained the TRIMCyp and GFP genes. "Almost all the offspring [carried the new genes], so you're not screening hundreds of animals to find the transgenic ones," Poeschla told told *Science*NOW. After about two months, five kittens were born, three of which survived.

More importantly, Poeschla and colleagues report in *Nature Methods*, when the scientists exposed blood samples from the transgenic kittens to FIV, the virus didn't replicate well, suggesting the TRIMCyp protein

DAILY NEWS 14 August 2015

Gene therapy cures blindness by replacing vision cells in eyes



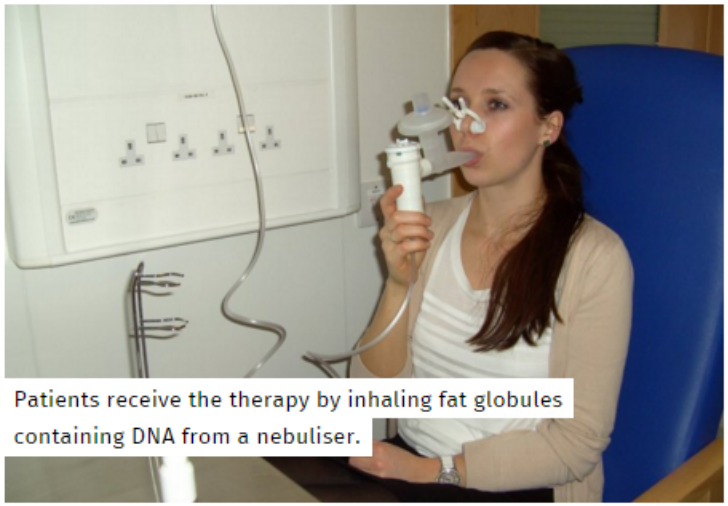
The rods (yellow) and cones (green) in the retina of a human eye (Image: Steve Gschmeissner/SPL)

When the owl swooped, the "blind" mice ran away. This was thanks to a new type of gene therapy to reprogramme cells deep in the eye to sense light.

After treatment, the mice ran for cover when played a video of an approaching owl, just like mice with normal vision. "You could say they were trying to escape, but we don't know for sure," says Rob Lucas of the University of Manchester, UK, co-leader of the team that developed and tested the treatment. "What we can say is that they react to the owl in the same way as sighted mice, whereas the untreated mice didn't do anything."

Gene therapy for cystic fibrosis shows encouraging trial results

by Sam Wong, Maxine Myers
03 July 2015



Patients receive the therapy by inhaling fat globules containing DNA from a nebuliser.

A therapy that replaces the faulty gene responsible for cystic fibrosis in patients' lungs has produced encouraging results in a major UK trial.

One hundred and thirty six patients aged 12 and over received monthly doses of either the therapy or the placebo for one year.

The clinical trial reached its primary endpoint with patients who received therapy having a significant, if modest benefit in lung function

CASE STUDY

Mary Bondonno, 16

GEN News Highlights

More »

Oct 14, 2015

CRISPR-Clean Pig Genome Could Mean Safer Pig-to-Human Transplants

Click Image To Enlarge +

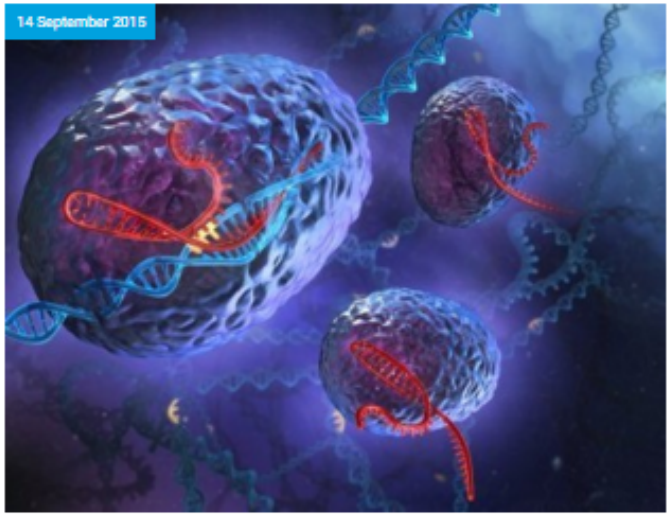
In a gene-editing tour de force, CRISPR-Cas9 achieves genome-wide inactivation of all 62 endogenous retroviruses identified in a porcine kidney cell line. [© byrdyak/Fotolia]

Before pig organs can be made safe for transplantation into human patients, two problems need to be solved. Both problems, ultimately, come down to features of the pig genome. First, the pig genome contains genes that give rise to proteins that the human immune system will not tolerate. Second, it contains retroviruses that could be transmissible to humans. The retrovirus problem, at least, may soon be tractable, thanks to the CRISPR gene-editing technique.

According to a newly published report, the CRISPR technique has been used to inactivate all 62 copies of a retrovirus in a pig cell line. CRISPR, then, has succeeded where other techniques—vaccines, RNA interference, and genetic editing by means of zinc finger nucleases and TAL effector nucleases—have failed. The feat is impressive even from a CRISPR-centric point of view. Never before have so many gene genes been modified in a single round of CRISPR editing. (Previously, the maximum number of genome sites to be edited

Genome editing in embryos is "essential"

14 September 2015



An artist's depiction of the CRISPR system in action. Illustration by Stephen Dixon

Related topics

Genome editing

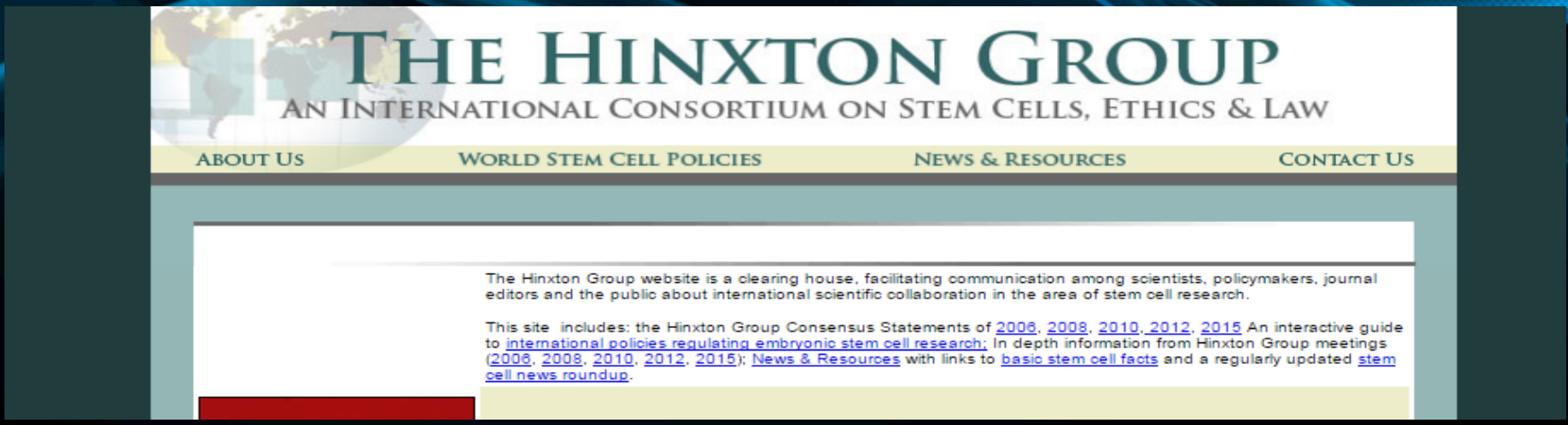
Policy

Liz Harley

Hinxton Group report states that human genome editing research using embryos is "essential".

An international coalition of scientists, ethicists, and policy experts has argued that genome editing in embryos is of "tremendous value" to research. The Hinxton Group, formed in 2004 to discuss ethical challenges around embryo research, firmly back the need for gene editing research while making a clear distinction between research and clinical application.

"We believe that while this technology has tremendous value to basic research and enormous potential for somatic clinical uses, it is not sufficiently developed to consider human genome editing for clinical reproductive purposes at this time," the consensus statement reads.



- Firmly back the need for gene editing research while making a clear distinction between research and clinical application.

"We believe that while this technology has tremendous value to basic research and enormous potential for somatic clinical uses, it is not sufficiently developed to consider human genome editing for clinical reproductive purposes at this time"

Potential Advantages

- Easier method to modify animals for disease and medical research
  - Superior to “knockout” animals, which take several generations of breeding and which can have varied success
  - Means fewer animals are needed for research purposes and medical testing

Potential Advantages

- Can be effective treatments to improve quality of life for individuals with genetic disease
- Genetic modifications to human embryos can give insight into disease, development, cell differentiation and other processes
- In the future, may be able to “fix” or cure genetic disease before it is even a problem, if done in embryonic or early developmental stages

Limitations

- In terms of modification of animals for research, the limitations so far have been in the efficiency of the procedures (which means more time, and use of live organisms). This is becoming less of an issue.

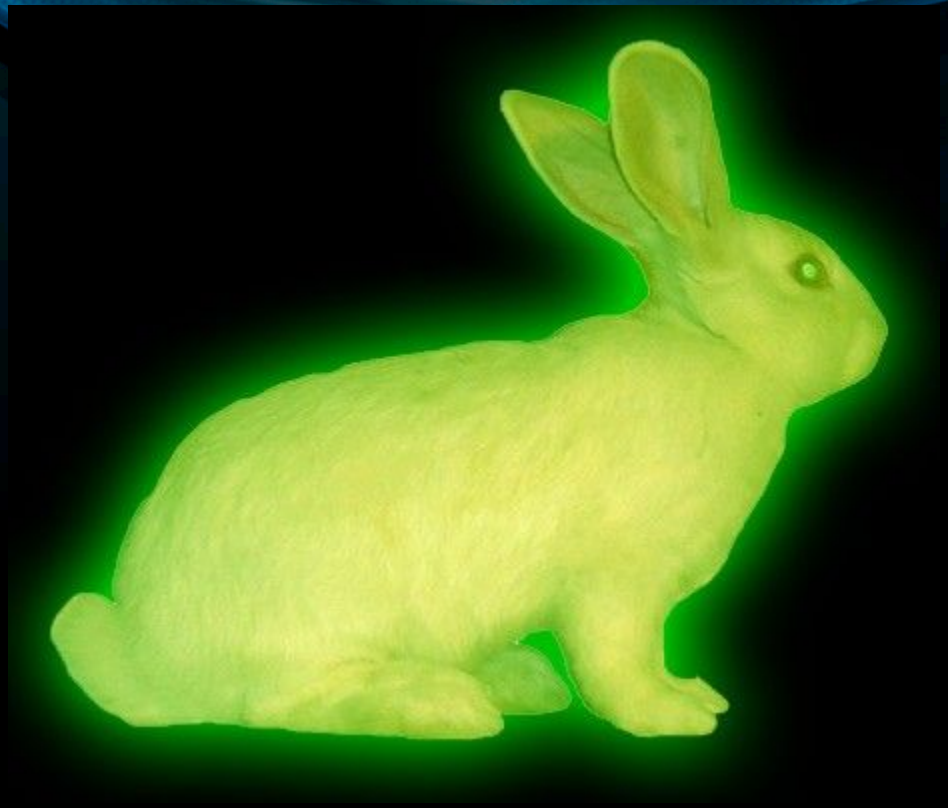
Limitations

- Many diseases, even with a genetic component, are affected by multiple genes as well as other physiological and environmental factors

- Effectiveness of genetic therapy can lessen over time.
  - Results in a need for continued therapy
  - This means increased costs for the patient

Limitations

- Questions that can be answered from genetically modified embryos is limited if research is limited to only early stages of development.



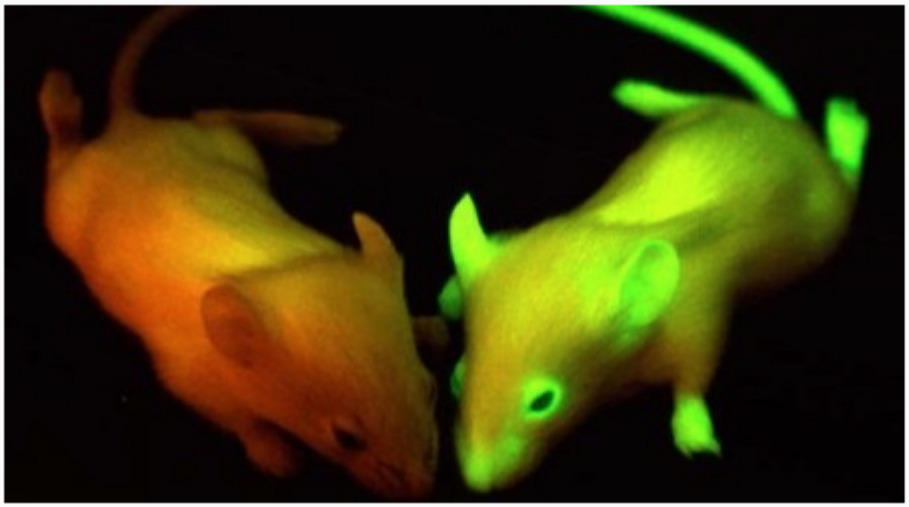
Genetic modification of organisms for preference

LATEST

Novel Artistic Expression Through Biotechnology

By Lucia Lu · November 26, 2013

FILED UNDER AESTHETICS, BIOART, BIOLOGY, BIOTECHNOLOGY, EDUARDO KAC, EMERGING TECHNOLOGIES, GREEN FLUORESCENT PROTEIN, NEW MEDIA ARTISTS, VISUAL ARTS



"Bio art" is a term coined in 1997 by Eduardo Kac, one of its earliest artists and pioneers. He used the term to describe *Time Capsule*, a performance piece where Kac surgically inserted a tracking microchip into his ankle in front of a live audience [1]. In the late 90s, this work was a timely interrogation of the growing relationship between humans and technology. Eduardo Kac and his peers have since used biotechnology to address futuristic technological developments and age old cultural concepts alike.

BIOMEDICINE NEWS

16 COMMENTS

First Gene-Edited Dogs Reported in China

An extra-muscular beagle has been created through genome engineering. Are we on our way to customizing the DNA of our pets?

By Antonio Regalado on October 19, 2015

Beagles named Hercules, at left, and Tiangou are the world's first gene-edited dogs.

Man's best friend is now his newest genetic engineering project.

Scientists in China say they are the first to use gene editing to produce customized dogs. They created a beagle with double the amount of muscle mass by deleting a gene called myostatin.

The dogs have "more muscles and are expected to have stronger running ability, which is good for hunting, police (military) applications," Liangxue Lai, a researcher with the Key Laboratory of Regenerative Biology at the Guangzhou Institutes of Biomedicine and Health, said in an e-mail.

Lai and 28 colleagues reported their results last week in the *Journal of Molecular Cell Biology*, saying they intend to create dogs with other DNA mutations,

WHY IT MATTERS

Genetic engineering of animals will open up remarkable possibilities in medicine and agriculture but also

PUBLIC RELEASE: 21-OCT-2015

Gene therapy could aid weight loss without affecting bone loss, new research finds

OREGON STATE UNIVERSITY

CORVALLIS, Ore. -- Delivering the hormone leptin directly to the brain through gene therapy aids weight loss without the significant side effect of bone loss, according to new collaborative research from Oregon State University and University of Florida.

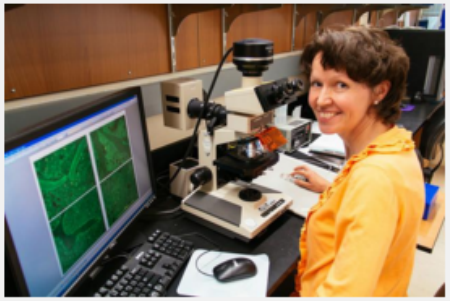


IMAGE: RESEARCHER URSZULA IWANIEC OF OREGON STATE UNIVERSITY. view more ›

CREDIT: OREGON STATE UNIVERSITY

Rapid or significant weight loss through dieting can trigger bone loss. Loss of bone density, in turn, can lead to increased susceptibility to bone fractures in older adults, which can have a debilitating effect on quality of life.

The bone loss is most concerning in people whose weight fluctuates due to "yo-yo" dieting, or repeated cycles of weight gain and loss, because bone lost during weight loss is not typically regained when the person gains weight again, said Urszula Iwaniec, an associate professor in the College of Public Health and Human Sciences at OSU.

Will genetic cyber-athletes come to dominate sports?

Jon Entine | June 23, 2015 | Genetic Literacy Project

It is sport's doomsday scenario: a new generation of bioengineered performance-enhancing agents that can transform also-rans into gold medalists. Imagine athletes injecting artificial genes right into their muscles—a virtually undetectable act that would give them the sinewy muscles of a cougar, or endurance like that of an antelope.

But this is not the science fiction of Hollywood, the movie "Gattaca" or a long-lost chapter of H.G. Well's 1904 pharmacological fantasy "The Food of the Gods," about a

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- Myth busting: Evaluating anti-GM activist claims of no long term safety studies
- Australian National Press Club: Sustainability benefits of industri agriculture
- Sustainable potato that resists blight given green light by USDA,

Potential Advantages (?)

- Change yourself or your offspring based on own ideals
- A new way to create or change your own identity from a biological standpoint
- Superhumans? The perfect pets? Utopia?

Limitations

- Again, connections between genes and traits/ behaviors are not always clear.

- Potential unintended side effects of modifications to humans relatively unknown due to lack of research currently

Questions to Consider about genetic modifications

- Where do we draw the line between medical use and preference?
- If treatment is not permanent, how does this impact the risk/benefit balance?
- Cost could be a limitation for many, how will this change the relationship between different socioeconomic groups?

- Is it ok for parents to make decisions for their offspring in terms of genetics?
- What are the impacts of genetic modifications that may cross generations, or be inherited?
- Can you be forced or coerced into changing your genes or those of your offspring if they put you/them at risk for disease?
- What about if they are risk for socially unacceptable behaviors? Violence? Criminal acts?
- Questions, currently, are endless...

Consensus

- Use of genetic information for research or medical purposes is generally accepted as a positive by the scientific community and society as a whole.

- Use of genetic information for evaluatory or discriminatory purposes is controversial.
  - Viewpoints depend on perspective
  - For example individual rights to privacy vs risk analysis for insurance purposes

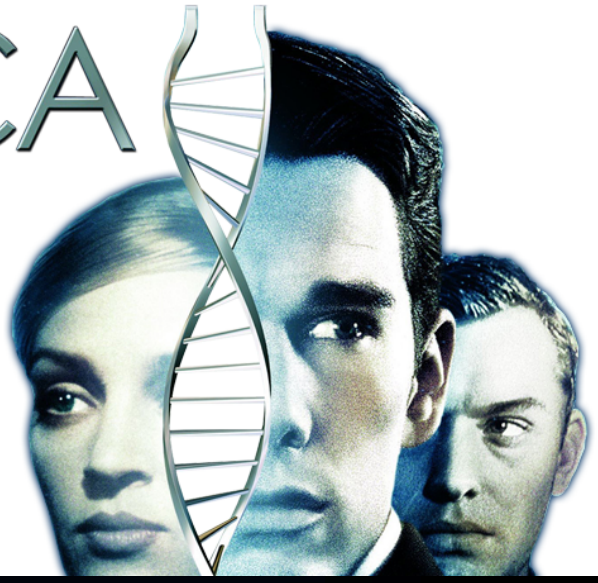
Consensus

- Use of genetically modified organisms for research or modifying medical purposes is generally supported by the scientific community:
  - Exceptions being with human embryos
  - Most support it in terms gene therapy for existing patients
  - Many varied viewpoints in society

- Modifying for preference, art, etc is frowned upon overall by the scientific community

- Why does access to genetic information and the possibility of genetic modification create so much controversy?
- what are our biggest fears about genetic information and modifications?
- Back to the land of science fiction for the answer...

GATTACA



Universal Declaration on the Human Genome and Human Rights (UN)

A Human Dignity and the Human Genome

Article 1

The human genome underlies the fundamental unity of all members of the human family, as well as the recognition of their inherent dignity and diversity. In a symbolic sense, it is the heritage of humanity.

Article 2

a) Everyone has a right to respect for their dignity and for their rights regardless of their genetic characteristics.

b) That dignity makes it imperative not to reduce individuals to their genetic characteristics and to respect their uniqueness and diversity.

Article 3

The human genome, which by its nature evolves, is subject to mutations. It contains potentialities that are expressed differently according to each individual's natural and social environment including the individual's state of health, living conditions, nutrition and education.

Article 4

The human genome in its natural state shall not give rise to financial gains.

Research on the Human Genome

Article 10

No research or research applications concerning the human genome, in particular in the fields of biology, genetics and medicine, should prevail over respect for the human rights, fundamental freedoms and human dignity of individuals or, where applicable, of groups of people.

Article 11

Practices which are contrary to human dignity, such as reproductive cloning of human beings, shall not be permitted. States and competent international organizations are invited to co-operate in identifying such practices and in taking, at national or international level, the measures necessary to ensure that the principles set out in this Declaration are respected.

Article 12

a) Benefits from advances in biology, genetics and medicine, concerning the human genome, shall be made available to all, with due regard for the dignity and human rights of each individual.

The Big Questions:

- How do our genes define who we are? As individuals? As a society?

- What decisions can we make about our own biology and behavior?

- Would we make the decision to change ourselves (or our children or family members), at the genetic level, given an opportunity?

The Big Questions:

- How will our genetic make up impact how we are treated? By other individuals? Insurance companies? Employers? Society?

- What decisions can other people make for or which affect us based on our genetic make up?

The Big Questions:

- Who gets to answer these questions and decide how we proceed into the future? Who draws the lines?

- How do we, as scientists and individuals decide what is right or wrong when it comes to genomics? What criteria do we use to make these decisions?
  - *Hopefully your experiences in this program will help!*

From today

We're on the cusp of a revolution that will change the world as much as computers did

Kevin Loria
21h 17

FACEBOOK LINKEDIN TWITTER EMAIL PRINT

Most people do not yet understand the potential impact of our newfound ability to edit and eventually rewrite genetic code, the blueprint for life itself.

At least, so say a number a number of experts in genetics and genomics. That idea was the major common thread in a series of interviews with some of the leading researchers in the field.

The latest gene-editing technology, known as CRISPR, can find and replace sections of DNA, turning genes on or off, removing harmful mutations,

Will we be ready?

See Also

What s found deep

Thank you!

Feel free to get in contact with me or one of my collaborators if you have questions or would like more information!

- - Ms. O, Andrew, Arun, Mara, Grace, Esther, Sarah, Joseph, Michael, Max, & Andy