

Genomic Enhancement & the Myths of Merit

Lisa S. Parker, PhD

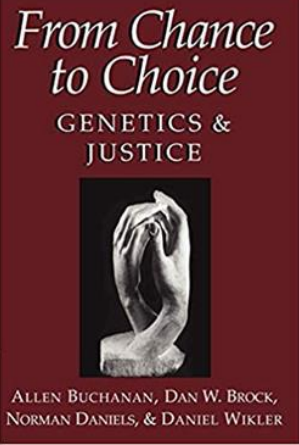
Dickie, McCamey & Chilcote Professor of Bioethics

lisap@pitt.edu



Themes for today

- Genomics is primarily a tool (not a revolution in medicine)
 - Genes mix with environments → body, traits, health, disease, (dis)ability
 - Genomics must mix with other bodies of knowledge and actions → value (treatment, prevention, “control”)
- Nature ~~vs.~~ & nurture
 - ~~Nature & nurture~~ → With knowledge it all becomes social
 - What was natural or “given” becomes a matter of choice (choosing to leave something alone is a choice)
 - The social realm of justice and responsibility overtakes the realm of the natural

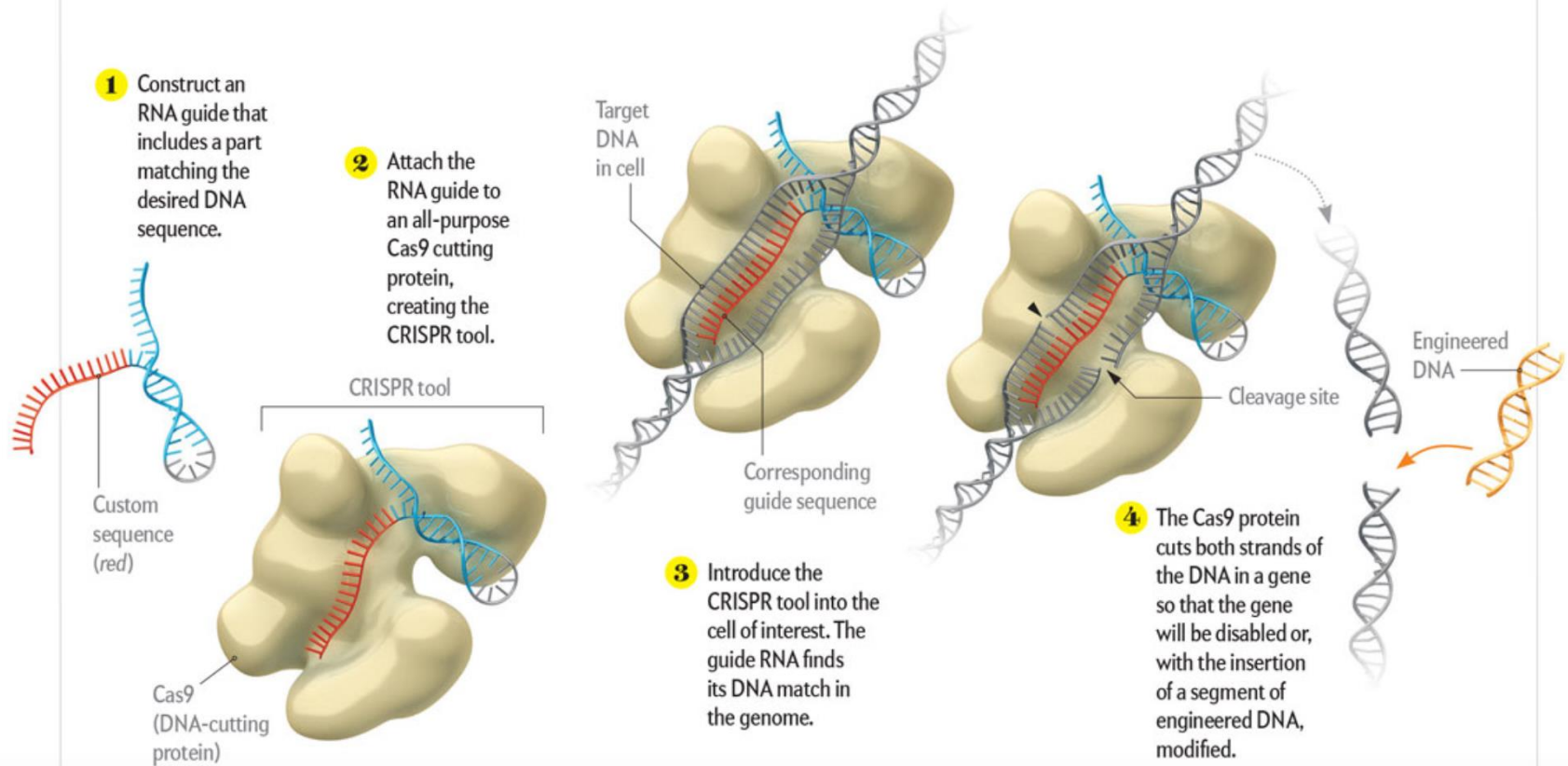


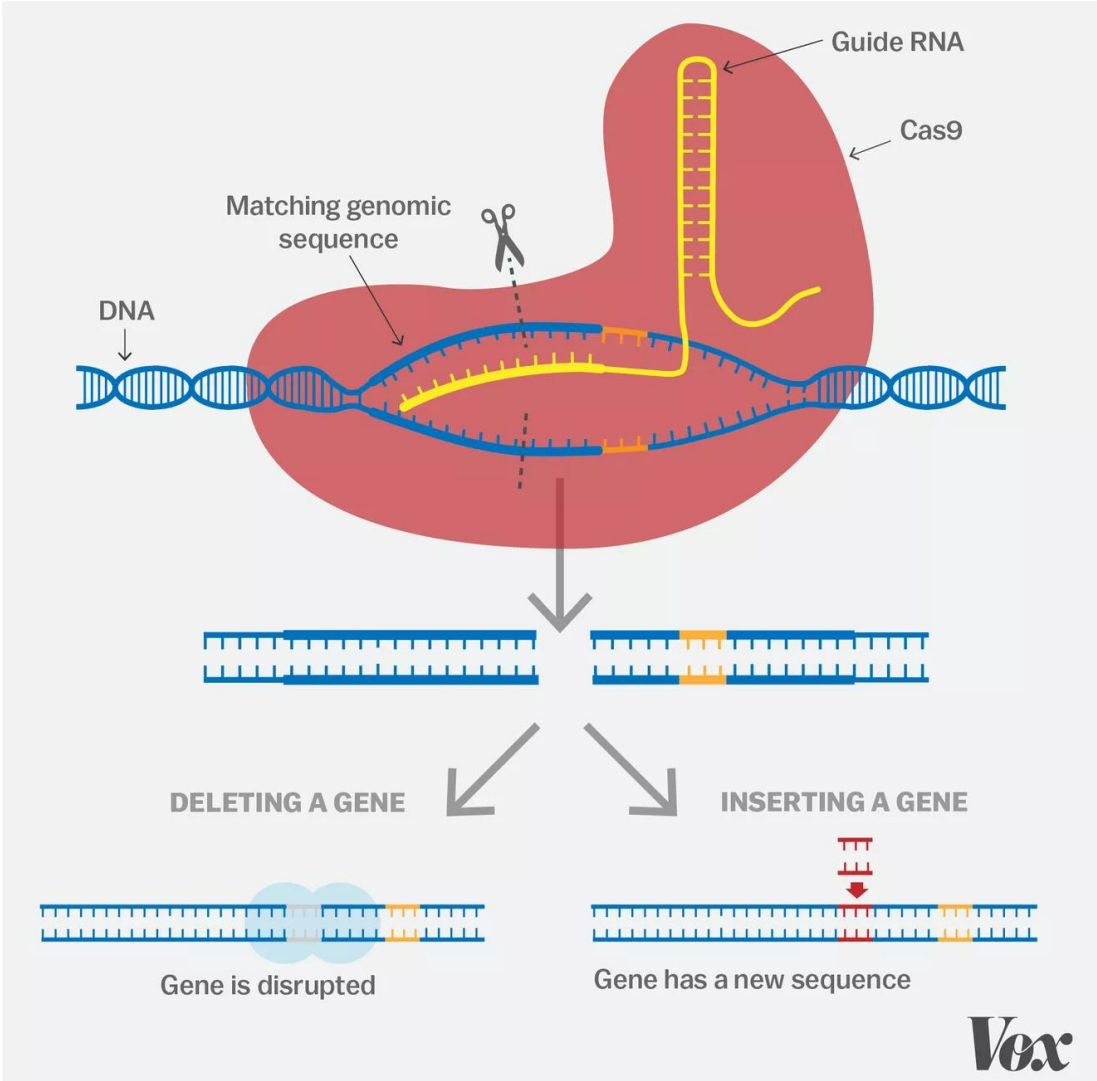
Genetic testing → alter behaviors → alter genes
Gene therapy
Gene editing
Genetic enhancement



How CRISPR Works

Bacteria use a weapon called CRISPR to julienne invading viruses. Scientists can hijack this process to chop up sequences of DNA they would like to modify instead. Unlike previous genome-editing methods, the CRISPR system uses a single, all-purpose enzyme, called Cas9, to do the slicing. All the researcher has to do is create an RNA “guide” to steer it there; RNA is vastly easier to synthesize than enzymes.

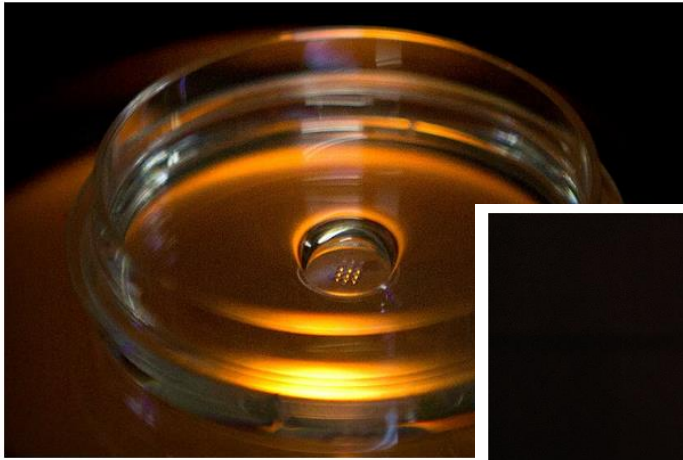






Chinese Scientist Claims to Use Crispr to Make First Genetically Edited Babies

The researcher, He Jiankui, offered no evidence or data to back up his assertions. If true, some fear the feat could open the door to “designer babies.”



He Jiankui, at a Hong Kong meeting in November 2018 where he presented his work, has not been seen in public since then. ANTHONY KWAN/BLOOMBERG/GETTY IMAGES

Chinese scientist who produced genetically altered babies sentenced to 3 years in jail

By Dennis Normile | Dec. 30, 2019, 8:15 AM

In U.S. First, Scientists Edit Genes of Human Embryos



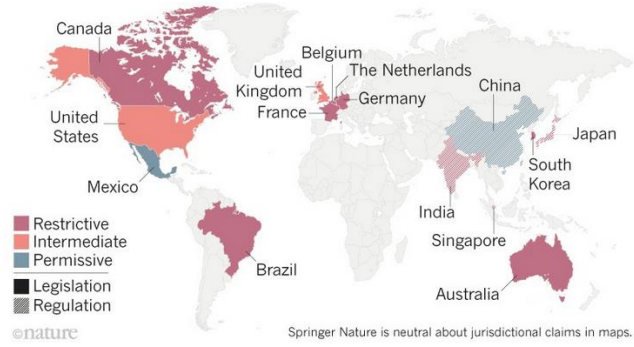
By The Associated Press

July 27, 2017

For the first time in the United States, scientists have edited the genes of human embryos

THE LEGAL LANDSCAPE

A 2016 survey in *Science* examined existing laws (legislation) and documented policies (regulation) that explicitly govern gene editing or might be applied to such activities. The survey labelled countries as restrictive, permissive or something in between. But specialists disagree over whether rules in some nations might be interpreted to permit gene editing.



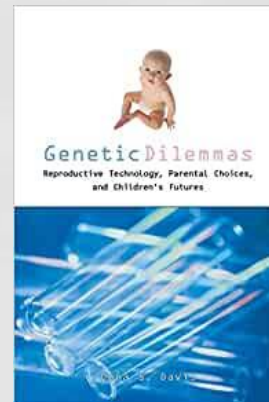
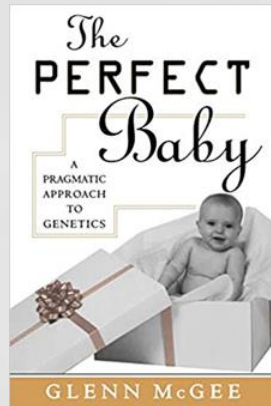
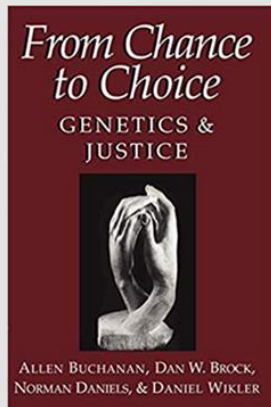
Source: R. Isasi et al. *Science* 351, 337–339 (2016).

Treatment / enhancement distinction

- Breaks down practically, conceptually
 - Consider silicone breast implants
 - Breast reconstruction following cancer surgery or injury
 - Breast augmentation
 - Breast reduction for back pain, posture, self-esteem
 - Ritalin for attention deficit disorder, studying
 - Beta-blockers for hypertension, angina, heart rhythm disorders, performance anxiety
- Breaks down practically, scientifically
 - Enhancement at different levels
 - Cellular → physiological → whole organism

Myths of merit

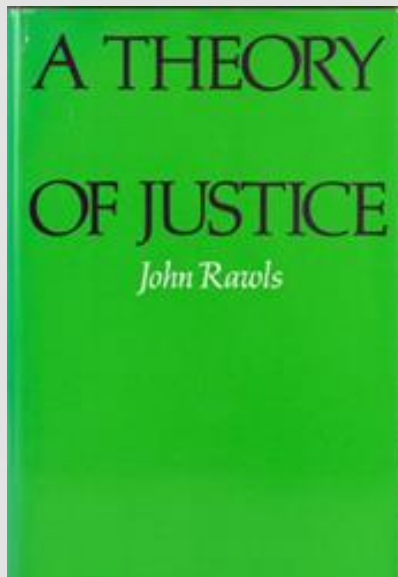
- Genetic enhancement threatens merit by undermining the value of exerting effort on a level playing field
 - Perhaps we misvalue effort & merit
- Assuming responsibility & exercising choice necessarily lead to the hubris of playing God
 - Can we act responsibly but not pridefully?



Justice as fair equality of opportunity

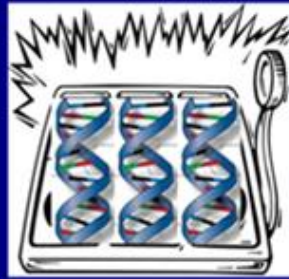
Those with the same level of **talent and ability**, and the same level of **motivation** to use them, should have the same prospects of success in life, regardless of their initial social situation.

--John Rawls



A just society ensures the conditions of fair equality of opportunity.

The Natural Lottery



The Social Lottery

Social
Lott

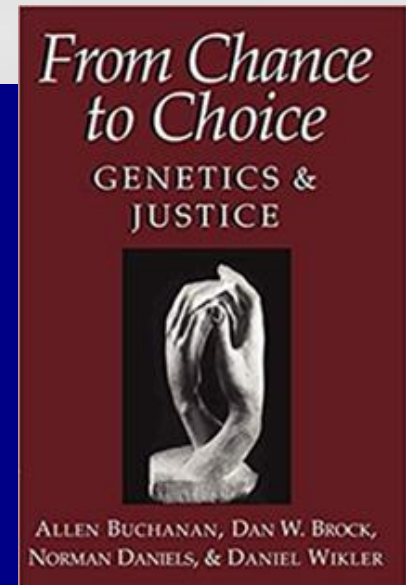


If the playing field is level (equal opportunity), then
natural ability + effort \rightarrow fair outcomes

● Which inequalities require redress?

- Formal and informal discrimination
- Social lottery's effects resulting from **unjust social structures**
- Social *and natural* lotteries' effects resulting from what is **beyond the individual's control (brute luck)**

What happens when the natural lottery is no longer beyond human control?
No longer a matter of luck?



Gene doping

Repoxygen is a new way to artificially enhance an athlete's performance — one that is hard to detect and with potentially permanent effects

How it works

Repoxygen was developed as a gene therapy treatment for severe anemia. A patient is injected with a harmless virus carrying a modified gene that encodes erythropoietin, a protein that boosts red blood cell production. The host's cells can translate that gene into active proteins as if the foreign gene were the cells' own.

1 Delivery

DNA packaged in a virus is injected into the athlete and flows through the bloodstream into muscle.

Danger: Altered viruses can trigger dangerous reactions from the immune system.

Alternatives: Viruses are not the only way to deliver performance-enhancing genes to cells. Fat molecules or naked DNA can be injected directly into muscle.

2 Change

Viruses bind to muscle cells and deposit the foreign gene inside, where it integrates into the cell's chromosomes. The gene stimulates the production of the protein erythropoietin (EPO).

Danger: Inserting foreign DNA can damage the cell's own genes, risking cancer.

Detection: Presence of a foreign gene in the athlete's DNA.

Other gene doping possibilities

■ In 1988, H. Lee Sweeney and colleagues at the University of Pennsylvania School of Medicine injected mice with a virus carrying a gene that boosted production of insulin-growth factor 1 (IGF-1). The injected mice had 15% more muscle mass than untreated mice.

■ In 2004, Ronald Evans and colleagues at California's Salk Institute for Biological Studies engineered mice to have extra copies of the gene encoding a protein called peroxisome proliferator-activated receptor delta (PPAR-delta). These mice could run twice as far as unaltered mice.

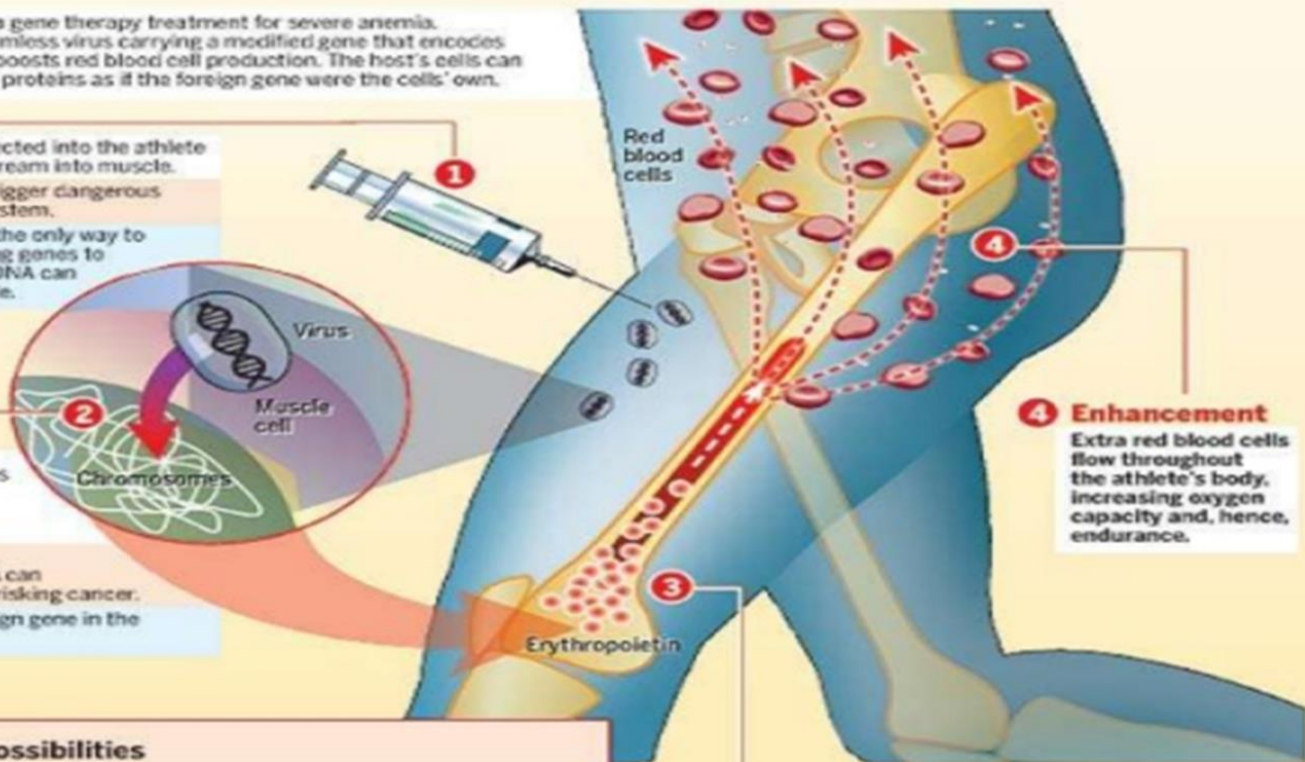
3 Dispersal

Erythropoietin (EPO), produced by the altered muscle cells, flows through the bloodstream to bone marrow, stimulating production of red blood cells, the body's main transporter of oxygen.

Detection: Changes in the concentration of multiple proteins in the blood or urine.

4 Enhancement

Extra red blood cells flow throughout the athlete's body, increasing oxygen capacity and, hence, endurance.



In sports, what is valued is superior “developed ability” and winning

Innate Ability



Unearned, unmeritorious, lucky advantages



Developed Ability



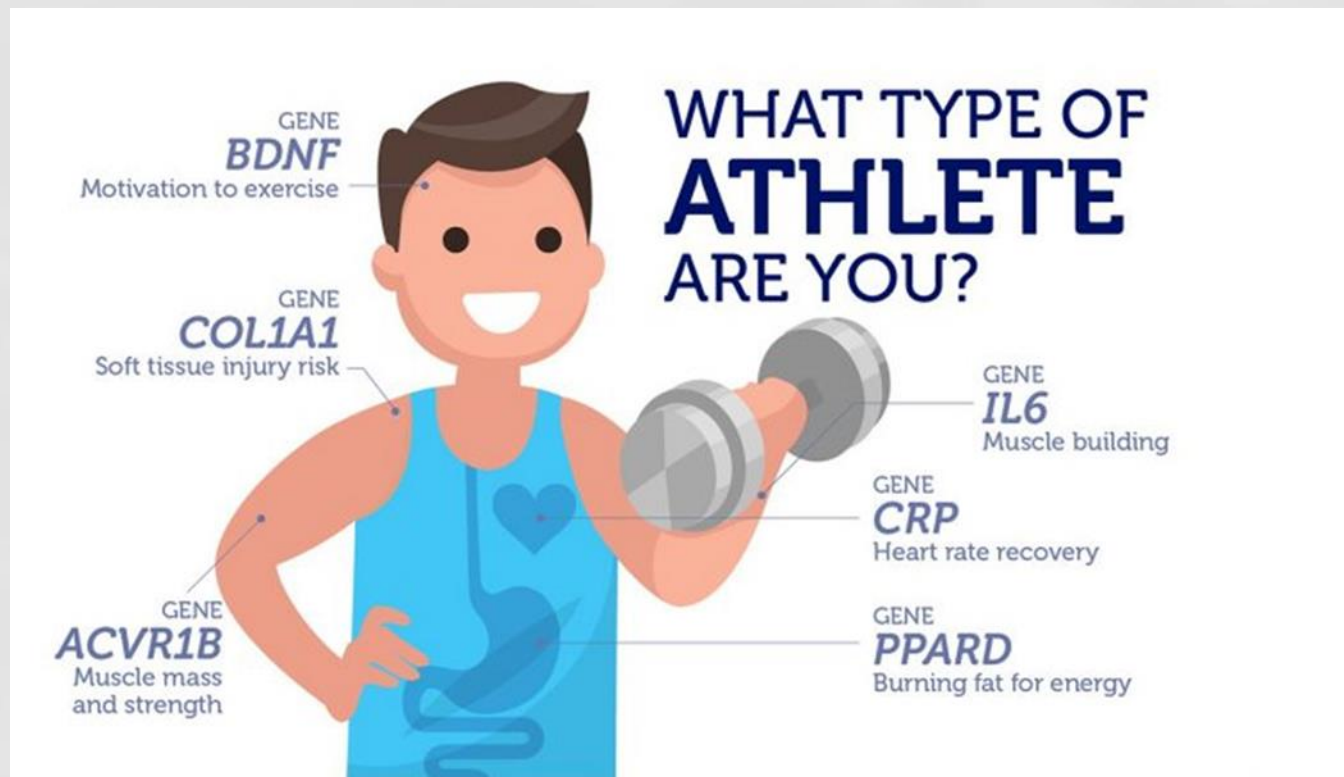
Success

Individual Effort



The “earning,” the source of the merit

Merited, not just lucky



- Genes related to muscle mass, heart rate recovery, oxygenation, risk of soft tissue injury
- Genes related to motivation

But, it's not just genes

GENE
BDNF
Motivation to exercise

WHAT TYPE OF
ATHLETE
ARE YOU?

Stress of racism,
sexism, anti-
semitism, ...
violence, stigma ...

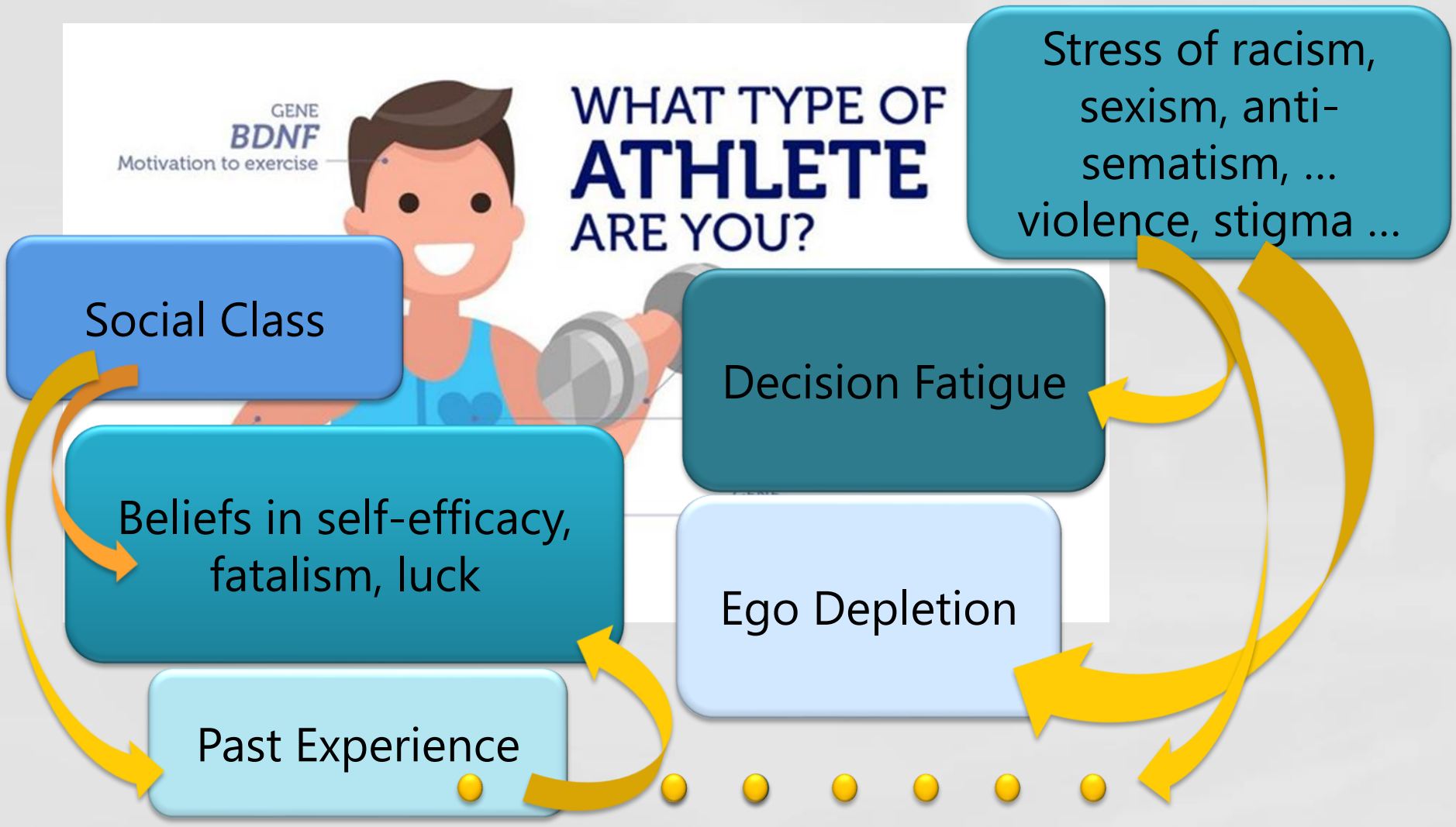
Social Class

Decision Fatigue

Beliefs in self-efficacy,
fatalism, luck

Ego Depletion

Past Experience




And, it's not just athletic ability

Social Psychology of Education
<https://doi.org/10.1007/s11218-021-09632-z>



Pygmalion in the genes? On the potentially negative impacts of polygenic scores for educational attainment

Lucas J. Matthews¹  · Matthew S. Lebowitz¹ · Ruth Ottman^{1,2,3} · Paul S. Appelbaum¹

- Stigmatization, differential treatment by others
- Self-perception of competence, academic efficacy
- Fatalism, self-fulfilling prophesy

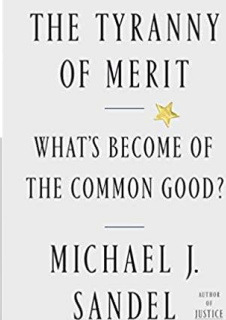
Recommendations

- Not to avoid genetic technologies, including judicious gene editing
 - Even genetic enhancement at some levels
- Not to avoid assuming responsibility or the shift from chance to choice
- Not to hide behind fears of “playing God”
 - We already do in myriad social, behavioral ways
 - As parents
 - As policymakers

Instead give up some myths of merit

- That effort is largely/mostly individual & meritorious
- That the result of effort is 100% earned, not at all a matter of fortune or luck
- That the moral universe aligns prosperity/success with merit (desert) & failure with wrongdoing

Protestant	Salvation	Earned and thus deserved, or a gift of grace?
Secular	Success	Earned and thus deserved, or beyond one's control?



“The Protestant work ethic began as a tense dialectic of grace and merit, helplessness and self-help. In the end, merit drove out grace. The ethic of mastery and self-making overwhelmed the ethic of gratitude and humility.”

“The fortunate [person] is seldom satisfied with the fact of being fortunate [but also] needs to know that he has a *right* to his good fortune ... that he ‘deserves’ it, and above all, that he deserves it in comparison with others. He wishes to be allowed the belief that the less fortunate also merely experience [their] due.”

--Sandel quoting Max Weber

“The notion that we are free human agents, capable of rising and succeeding by our own effort, is only one aspect of meritocracy. Equally important is the conviction that those who succeed deserve their success. This triumphalist aspect of meritocracy generates hubris among the winners and humiliation among the losers. ... This triumphalist aspect of meritocracy is a kind of providentialism without God, at least without a God who intervenes in human affairs. The successful make it on their own, but their success attests to their virtue.”

--Sandel

Ethic of fortune “appreciates the dimensions of life that exceed human understanding and control. It sees that the cosmos does not necessarily match merit with reward. It leaves room for mystery, tragedy, and humility.” –Sandel

Ethic of mastery places “human choice at the center of the spiritual order.” --Sandel quoting Jackson Lears

“A culture less intent on the individual’s responsibility to master destiny might be more capacious, more generous, more gracious. ...

[Recognition of the unpredictable character of fortune and fate might lead people] to imagine their own misfortune and transcend the arrogance of the meritocratic myth—to acknowledge how fitfully and unpredictably people get what they deserve.”

--Lears

- Sandel concludes that this “providentialist notion that people get what they deserve ... comes in two versions—one hubristic, the other punitive.” He rejects both.
- He also rejects the use of genetics to enhance people as hubristic.
- He distinguishes between genetic means and effortful means to improve or enhance oneself and one’s offspring.
- He most strongly rejects seeking “perfection” by any means—effort or genetic enhancement.



- But can we truly maintain there is an ethical distinction between employing genetic or social enhancement?
- Once genetic enhancement is possible, can we avoid the responsibility of using/not-using it?
- **Shift the focus from genetic enhancement to enhancing discourse & behavior.**
- Avoid the hubris, heartache, & harms of seeking *perfection*, while embracing the benefits of both exerting effort and using genomic tools to enhance capabilities and outcomes.
- Be more gracious, generous, empathetic, and cooperative.
- Reduce comparison, competition, and adherence to caste and hierarchy.