

Key Issues in Reproductive Technologies – Marcy Darnovsky (CGS) and Silvia Yee (DREDF)

- I. Show Clip from GATTACA
 - Minutes 9 to 13
 - 10-15 minutes of reaction and discussion
- II. Marcy on Pre-implantation Reproductive Technologies

Slide 1 – title

Slide 2 – GATTACA

Slide 3 – GATTACA (low-tech wheelchair and spiral (i.e., DNA helix) staircase)

Slide 4 – GATTACA (in-valids)

Slide 5 – Embryo screening (PGD)

The mechanism that enabled the world shown in *GATTACA* was, at least implicitly, the embryo screening technology known as pre-implantation genetic diagnosis or PGD. I know some of you are familiar with it, but I'll take a minute to explain how it works.

This slide shows a sketch of how it works. The embryo that's shown here as an oval was created outside the body, by combining eggs and sperm in a petri dish, and allowed to grow and divide for three days until what started after fertilization as a single-celled zygote became an eight-celled embryo. Then one of the 8 cells is physically removed—which the embryo seems to tolerate pretty well—and that removed cell is genetically analyzed. It is tested for the presence or absence of certain genes, toward the end of de-selecting for disfavored conditions—that is, those considered disabilities, or selecting for a desired sex, almost always for a particular sex. Embryos that don't make the grade are discarded, one or more of those that do pass are transferred into a woman's womb.

PGD came into use in 1990. It was initially envisioned as a way to prevent the births of children with fatal diseases like Tay Sachs or debilitating conditions that manifest in early childhood, like cystic fibrosis. By the early 2000s it was being used for a range of additional conditions, such as sickle cell anemia and Down syndrome. Then came adult-onset diseases. In 2001, some fertility doctors began using PGD for sex selection. The scope of conditions for which it is used continued to expand, in a classic case of mission creep, well into the hundreds.

Most PGD use is to select against disabilities. It is also widely advertised by fertility clinics for sex selection, often under the rubric of “family balancing.” The *GATTACA* scenario (selecting for “the best of both of you” – that is, selecting for traits that the prospective parents or that society values) isn’t currently widespread. That’s because first, few complex traits are caused in any straightforward way by one or a few genes, and second, the number of available embryos from which to choose isn’t typically that large.

However, several years ago a fertility doctor in Los Angeles did launch a program in which he offered PGD to select for eye color, hair color and skin color. Technically this was dubious, but in marketing terms it was a stroke of genius: although the outcry in response to his offer persuaded him to shelve the program (“for now,” as he put it), his practice and use of PGD for other types of selection and de-selection are booming.

PGD policies vary in different countries:

- from countries like the US, where it’s basically anything goes,
- to the UK, where a quasi-governmental body, the Human Fertilisation and Embryology Authority, provides a list of conditions – now over 200 – for which it is permissible for fertility clinics to test (similar in France, India, the Netherlands),
- to countries where PGD is prohibited as illegal: Germany, Austria, and Switzerland.

Slide 6 – 23andMe inheritance calculator

PGD is a pre-pregnancy selection technology, but not the only one. A newer pre-pregnancy technology is, in a sense, an updated version of carrier testing—genetic testing that’s typically done when people are considering having children and have a family history of a serious disease like Tay Sachs.

This new technology also involves genetic tests of prospective parents. But instead of checking for one or a few specific gene variants associated with a particular disease, these new tests claim to report on the probability of a particular man and woman producing a child with or without certain traits.

The drop-down menus shown in this next slide is an illustration that is part of an application for a patent that was recently awarded to the direct-to-consumer genetic testing company 23andMe. At the top left, it says, “I prefer a child with”, and then there are sets of choices on different menus. You can select “low risk” or “high probability” of colorectal cancer, congenital heart disease, or breast cancer. Or you can select “low risk” or “high probability” of a child with blue, green or brown eyes, or a child with risk / probability of being able to taste bitter.

At the bottom, the display shows a table of “preferred donors” – these are sperm or egg donors – and the probabilities of a child with a particular trait being

produced by each one, when combined with another genome (presumably the customer's).

News about this patent broke last year, and as in the case of the fertility doctor who offered PGD for hair, eye and skin color, it generated enough controversy that the company wound up disavowing it. 23andMe said that when the patent was filed 5 years previously, it had envisioned partnering with sperm banks and fertility clinics to offer the product to people undergoing in vitro fertilization. But it said it now has no intention of developing it.

Slide 7 – GenePeeks

Another company, a brand new one that launched just this month, has decided to make a run at the pick-a-donor to select your child's traits idea that 23andMe backed away from.

This slide shows the image from the home page of that company, GenePeeks. Along with the company logo and an adorable baby in a diaper, who looks like he or she might be African American, and who is certainly precocious (which we can tell because he's playing with alphabet blocks). The web page says in large type, "Protecting our children." The rest of the copy reads, "It's what gets us up in the morning (and keeps us up at night). A revolution in the life sciences has made it possible to keep our kids healthy with tools that were unimaginable even a few years ago."

Of course, none of these repro-genetic technologies "keep our children healthy." They are all about various forms of selection and de-selection.

23andMe's patent and GenePeeks suggest that a lot of technical and business and marketing ingenuity is being put into the effort to make selecting the traits of future children seem modern, high tech, and desirable. But these, and PGD, are aimed at the relatively small number of people who have their children with assisted reproduction.

Slide 8 – Early fetal gene tests

There's another new prenatal testing technology today, one that any pregnant woman can use: early fetal gene tests. This next slide shows a troubled-looking wide-eyed white baby with a bar code on its forehead.

Early fetal genetic testing, or screening, works by taking a small amount of a woman's blood very early in a pregnancy, and isolating fetal DNA from it. You'd simply give a little extra blood at the lab at your prenatal checkup at 8, 9 or 10 weeks, maybe your first one. There would be no risk to you or the fetus. You'd get the results before you were visibly pregnant, before you'd told your mother or your friends.

Since the end of 2011, four U.S. companies have introduced slightly different versions of these tests, sometimes called “non-invasive prenatal tests” or “non-invasive prenatal screens”—for chromosomal conditions. More companies are eyeing what has already become a lucrative market for a product that insurance companies seem to like very much. Companies outside the U.S. including the behemoth Chinese genomics company BGI have also launched products.

Until now, the predominant prenatal genetic test has been amniocentesis, which is invasive and carries some risk. Only about 2% of pregnant women in the US agree to it, roughly 100,000 per year. NIPTs are expected to expand that number by more than an order of magnitude – to push the number to several millions.

Several flagship medical organizations – associations that represent obstetricians, genetic counselors and medical geneticists – have issued recommendations that NIPTs *not be used* as part of routine prenatal care. The National Society of Genetic Counselors’ statement recommends that when they are used, the women undergoing them always be given full and non-directive information by trained genetic-health counselors.

But this go-slow advice by medical professionals and genetic counselors is up against a growing commercial force. As a commercial product, which is one unavoidable way to evaluate it, non-invasive prenatal tests are in a rare and sought-after category: this is a product whose introduction creates a new demand, and a large new consumer base.

The fetal gene tests that are currently being marketed and sold count chromosomes. They clearly have the potential to further reduce the number of babies born with Down syndrome, and to reinforce the assumption that Down syndrome is a dread disease to be prevented.

I want to say a few words about how these tests are being marketed, which tells us a lot about how they could change, perhaps dramatically, how our society thinks about what kinds of children should be welcomed into the world.

The observations I’ll share are drawn from a series of wonderful articles by George Estreich, which are part of the advance reading list, and I highly recommend them to you. George points out that the websites of the companies selling early fetal gene tests:

are slick, expensive-looking, carefully worded. These are acts of persuasion, subordinate to the goal of making a profit; and whether we like it or not, they are a part of our society’s conversation about biomedicine, not outside it.

And persuasion, as George points out, is “by definition *directive*” and “as such, conflicts with the injunction for genetic counselors to be *nondirective*.”

Slide 9 – Sequenom’s MaterniT21

This next slide is a web page from the company Sequenom, which calls its early fetal gene test MaterniT21. Here is George’s description:

They look like models from a *Cialis* ad: healthy, prosperous, white, late thirties or early forties. If you were guessing, you’d say the man was an executive in a nonmedical field, that the wife has a professional degree but scaled her career back for family, and that they drove to the office together in a silver Lexus SUV. His hobby is golf, hers is scrapbooking. You see them over the doctor’s shoulder – he’s a blurred white coat in the foreground – and they look concerned but reassured, as if they have just received good news about a solvable problem.

The problem is Down syndrome, and the solution is Sequenom’s test, MaterniT21. The website describes Down syndrome in a way that, George comments, is:

“more than a superficial improvement upon the slanted language, factual errors, and long lists of possible disease features that are fading, but still common, in contemporary descriptions of the condition.”

Nonetheless, he points out, the description still uses the language of risk, and mentions “birth defects.”

“Though it speaks with the bland rhetoric of health and choice, and though it’s subtly done, at root it works the way most advertisements work: it engages our fears, then seeks to allay them. Down syndrome, in the world of the ad, is an abstract world of randomness and risk; *MaterniT21plus* is the answer.

What, then, is left out? As ever, the actual lives of people with Down syndrome.”

Slide 10 – Natera

Let’s take a quick look at one more web page. This one is from an early fetal gene testing company called Natera. Like many of the other websites of these companies, this one’s aesthetic is what George describes as “sunlit clinical: lots of white, lots of hope.” But Natera, George comments:

is still sorting out their messaging. The home page banner features a sun rising over a field of flowers. When you look closer, the sun is actually a clump of cells. In the sky is the company's motto: *Conceive. Deliver.* It sounds almost military, as does the company's former name, the Gene Security Network.

From *Gene Security Network* to *Natera* may be the most extreme name change in the history of American corporate governance: what used to sound like a shadow organization in one of the Bourne movies now sounds like a shampoo.

Natera's home page features an explanation of the name change: "The name Natera is drawn from the terms: natal, nature, and earth. Our new name better reflects our mission to help couples around the world manage pregnancies and reduce the risk of genetic disease."

George points out that as a matter of medical fact, Down syndrome is not, in fact a disease. And, he goes on to say, "as for their mission, to "reduce the risk of genetic disease" is as close to openly eugenic as any of these companies get."

Down syndrome is the most frequent target of today's early fetal gene tests. In the works are tests that report the entire genetic sequence of an early fetus. In other words, a just-pregnant woman might soon be able to get the kind of genetic information about her nine-week-old fetus that you or I can get today by sending a hundred dollars and a wad of spit to one of the "direct-to-consumer" gene test companies like 23andMe.

If or when those are developed, most of the results will be presented as risk probabilities about conditions for which few, if any, therapies are available. So what will parents do if they are told that their 10-week-old fetus has a five times higher-than-average chance of being diagnosed with breast cancer later in life, or a 34% higher-than-average risk of developing Alzheimer's 70 years from now?

I think early fetal gene tests—the ones already on the market included—are game changers. Disability rights advocates and scholars have been asking hard questions about prenatal testing for decades. Now they are going to be squarely on the table, in an even more challenging way, for everyone.

Slide 11 – DREDF

Slide 12 – CGS

III. Silvia on the American Eugenics Movement and Discussion Themes

I would like to turn now from the discussion of pre-genetic technologies themselves to look at the history of eugenics in the United States. Pre-genetic technologies and the

impact on the birthrates of people with certain disabilities have prompted comparisons with eugenics so let us together flesh out that analogy a little more.

The American Eugenics Movement remains a little-known chapter of U.S. history. It doesn't appear to be formally studied as an educational topic, even though compulsory sterilization laws were adopted in over 30 states. This is ironic since the introduction of eugenics as a legitimate "science" topic in early 20th century American education was one of the main factors in legitimizing compulsory sterilization. American eugenics programs were implemented at the beginning of the 20th century and the laws remained on the books as late as the 1970s in a few states. Over 60,000 people with disabilities were sterilized without any effective consent as a result of the laws. Just to provide a sense of scale, in Delaware, at the peak of sterilizations in the late 1920s to the 1940s, individuals were sterilized under the laws at a rate of 18/100,000 residents. Compare this rate with 75-80/100,000 residents, which is the rate of sterilization of individuals with disabilities in Germany between 1934 and 1939. There is a clear difference in rates of course, but also keep in mind that this is a direct comparison between one small U.S. state, in a country with democratically elected leaders, recognized constitutional rights, and the intended safeguard of a balance between legislative, judicial and administrative powers.

At this point, I would like to take a closer look at California, where 20,000 sterilizations or approximately one-third of the national total took place. California's first eugenics law was introduced in 1909. There was a relatively low rate of around 12 sterilizations/year until 1921, when the rate soared to 450/year, or about 13/100,000 residents. There were about the same number of men sterilized as women, broken down in to the following general categories: 60% were considered mentally ill, 35% were considered mentally deficient, and there was some over-representation of people of Mexican or African-American descent. For example, African-Americans comprised 1% of the general population, but 4% of those who were sterilized. This racial over-representation was in part due to the fact that the original eugenics targets of people in prisons (considered delinquent), and those who were considered mentally ill or feebleminded, was expanded to include groups that were socially feared by the white middle and upper socio-economic classes that controlled the laws. As a consequence, Mexican immigrants who came seeking employment and who also traditionally had large families were subject to sterilization laws along with deportation.

In the first decades of California eugenics laws, due process was entirely absent. Prior or subsequent notice of the sterilization operation was not given. No consent was required beforehand from affected individuals or their families. While an apparent giving of consent was sometimes recorded in an individual's institutional file, consent may have been the condition for getting out of an institution where they would otherwise have been forced to stay. No records or reports of sterilizations were required of those who performed them, and there was no way to challenge an order of sterilization or appeal the decision to a body higher than the institution that was going to perform the operation.

The sterilization procedure was often justified as beneficial not only for society, but also a direct benefit for the patient. For instance, it was said that sterilization of male lifetime prisoners who were judged as showing sexual or moral perversions, or who were guilty of certain repeat offenses, would help curb and rehabilitate the men's destructive traits so that they could rejoin society. Women were subject to a less individualistic and more explicit eugenics perspective. For example, society was warned to 'beware of "the high grade moron" who could have the greatest negative effect on a race because, although they seemed mentally normal and would go undetected on intelligence tests, their sexual deviance could cause the procreation of more sexually deviant women.'

U.S. eugenics programs sought to control the procreation, birth, and ongoing presence of people with disabilities, and especially people with mental disabilities, in American society. In this conference, words like eugenics, extinction, and the right to life have been raised in response to assisted suicide policies, practices and laws, as well as medical practices that potentially or actually restrict the provision of healthcare services to people with disabilities. Pre-genetic and reproductive technologies directly implicate how, when, and whether people with disabilities will be born, and therefore offer a direct analogy to American eugenics laws and practices, which explicitly sought those same goals. But analogies are useful for both the similarities *and* the differences raised between the subjects of comparison. How far does this particular analogy go?

Here are some similarities. The American eugenics program and pre-genetic reproductive technologies have a similarity of purpose, to reduce the number of babies born with at least certain disabilities. People with mental disabilities were sterilized in the past so that they could not bear children. The commercial entities that promote pre-genetic technologies and non-invasive testing today emphasize the birth of "healthy babies" instead of the inverse message of choosing against bearing babies with disabilities but the results are generally the same. Another similarity is the overt co-opting of science as an ostensibly objective means of advancing a valuable social good such as reducing overall crime and "delinquency" or promoting informed parenting choices. In the case of eugenics, the scientific assumption that people with mental disabilities would necessarily bear children with disabilities was flawed, as was the assumption that disability could be eliminated through the controlled "breeding" of humans. As Marcy pointed out earlier, the new non-invasive prenatal tests use science to sell and subtly exaggerate the certainty of NIPT results. The information presented is not "purely" objective and the test results do not inherently dictate a particular decision, while underlying personal values and assumption that play an equal role in choice-making are downplayed.

Perhaps the biggest difference between eugenics programs and reproductive technologies is that the eugenics programs were approved by those in political authority, legally implemented, and widely justified in the press and public education programs. New reproductive technologies and testing procedures are not being pushed by the state. Private commercial entities have developed the technologies, profit motive in a capitalist system is driving the availability of media and information, and popularity is growing because of a primal human desire to procreate (at increasingly older ages).

Currently we know that 90% of fetuses *that test positive* for Down syndrome are aborted in the U.S., but not all fetuses are tested. Up to this point, many women have chosen not to undergo the risks and invasiveness of 2nd trimester amniocentesis. In our brave new world, NIPTs essentially eliminate the risks and timing of the older tests and will likely greatly increase the number of women – among those who can afford it - who are likely to test their fetus. The very latest reproductive technologies being researched, such as whole-genome fetal tests, could enable the manipulation of embryonic genes in *inheritable* ways. This could result not only in an impact on one particular fetus/baby/person, but on all the future inheritable genetic material that will be available in the world through that person, reducing the chances of inheritable genetic conditions, and perhaps even random genetic conditions. People with disabilities will be much less likely to be born, not because of a centralized state-sanctioned program of forced sterilization, but because of an entire series of individual, constitutionally-protected decisions made by women and their families.

We see at least four broad themes that can be addressed in our discussion today, and would welcome additional ones that you wish to raise. Consider the following, and take the “verses” with a grain of salt since there is usually more nuance involved than a single opposition.

- Commercially-motivated medical information verses “objective” professional medical information; the latter also raises red flags for a disability community that has fought for decades to free itself from the limitations and stereotypes imposed under a “medical model of disability” that wholly equates individuals with disabilities to their diagnoses
- Individual civil and human rights of privacy and free choice verses the needs of a civil society for diversity, tolerance and universal design
- Fear mongering and exaggeration, both among sellers of commercial NIPTs who raise the specter of bearing a child with a disability, and among opponents of NIPTs and reproductive technologies who speak of extermination and a pogrom against people with disabilities
- The ideal that scientific/medical advances will improve everyone’s lives verses the reality of how medical advances are actually “distributed” and made available in the U.S., and how healthcare and community-based services are actually provided under Medicare and Medicaid to low-income people with disabilities of all ages

IV. Discussion among Institute Attendees

Resource Websites

- 23andMe: <https://www.23andme.com/>
- Genepeeks: <https://my.genepeeks.com/genepeeks/displayhome.do>
- Sequenom MaterniT21:
<http://laboratories.sequenom.com/maternit21plus/maternit21-plus-knowing-about-your-pregnancy>
- Natera: <http://www.natera.com/>
- Site on American Eugenics, established by Lutz Kaelber, Associate Professor of Sociology, University of Vermont: <http://www.uvm.edu/~lkaelber/eugenics/>