that permitted genetic diagnosis to be performed on an embryo *before* implantation into a woman's body.

The technique relies on a peculiar idiosyncrasy of human embryology. When an embryo is produced by in vitro fertilization (IVF), it is typically grown for several days in an incubator before being implanted into a woman's womb. Bathed in a nutrient-rich broth in a moist incubator, the single-cell embryo divides to form a glistening ball of cells. At the end of three days, there are eight and then sixteen cells. Astonishingly, if you remove a few cells from that embryo, the remaining cells divide and fill in the gap of missing cells, and the embryo continues to grow normally as if nothing had happened. For a moment in our history, we are actually quite like salamanders or, rather, like salamanders' tails—capable of complete regeneration even after being cut by a fourth.

A human embryo can thus be biopsied at this early stage, the few cells extracted used for genetic tests. Once the tests have been completed, cherry-picked embryos possessing the correct genes can be implanted. With some modifications, even oocytes—a woman's eggs—can be genetically tested before fertilization. The technique is called "preimplantation genetic diagnosis," or PGD. From a moral standpoint, preimplantation genetic diagnosis achieves a seeming impossible sleight of hand. If you selectively implant the "correct" embryos and cryopreserve the others without killing them, you can select fetuses without aborting them. It is positive and negative eugenics in one go, without the concomitant death of a fetus.

Preimplantation genetic diagnosis was first used to select embryos by two English couples in the winter of 1989, one with a family history of a severe X-linked mental retardation, and another with a history of an X-linked immunological syndrome—both incurable genetic diseases only manifest in male children. The embryos were selected to be female. Female twins were born to both couples; as predicted, both sets of twins were disease-free.

The ethical vertigo induced by those two first cases was so acute that several countries moved immediately to place constraints on the technology. Perhaps understandably, among the first countries to put the most stringent limits on PGD were Germany and Austria—nations scarred by their legacies of racism, mass murder, and eugenics. In India, parts of which are home to some of the most blatantly sexist subcultures in the world, attempts to use PGD to "diagnose" the gender of a child were reported as early as 1995. Any form of sexual selection for male children

was, and still is, prohibited by the Indian government, and PGD for gender selection was soon banned. Yet the government ban seems to have hardly staved the problem: readers from India and China might note, with some shame and sobriety, that the largest "negative eugenics" project in human history was not the systemic extermination of Jews in Nazi Germany or Austria in the 1930s. That ghastly distinction falls on India and China, where more than 10 million female children are missing from adulthood because of infanticide, abortion, and neglect of female children. Depraved dictators and predatory states are not an absolute requirement for eugenics. In the case of India, perfectly "free" citizens, left to their own devices, are capable of enacting grotesque eugenic programs—against females, in this case—without any state mandate.

Currently, PGD can be used to select against embryos carrying monogenic diseases, such as cystic fibrosis, Huntington's disease, and Tay-Sachs disease among many others. But in principle, nothing limits genetic diagnosis to monogenic diseases. It should not take a film such as *GATTACA* to remind us how deeply destabilizing that idea might be. We have no models or metaphors to apprehend a world in which a child's future is parsed into probabilities, or a fetus is diagnosed before birth, or becomes a "previvor" even before conception. The word *diagnosis* arises from the Greek "to know apart," but "knowing apart" has moral and philosophical consequences that lie far beyond medicine and science. Throughout our history, technologies of knowing apart have enabled us to identify, treat, and heal the sick. In their benevolent form, these technologies have allowed us to preempt illness through diagnostic tests and preventive measures, and to treat diseases appropriately (e.g., the use of the *BRCA1* gene to preemptively treat breast cancer). But they have also enabled stifling definitions of abnormalcy, partitioned the weak from the strong, or led, in their most gruesome incarnations, to the sinister excesses of eugenics. The history of human genetics has reminded us, again and again, that "knowing apart" often begins with an emphasis on "knowing," but often ends with an emphasis on "parting." It is not a coincidence that the vast anthropometric projects of Nazi scientists—the obsessive measurement of jaw sizes, head shapes, nose lengths, and heights—were also once legitimized as attempts to "know humans apart."

As the political theorist Desmond King puts it, "One way or another, we are all going to be dragged into the regime of 'gene management' that will, in essence, be eugenic. It will all be in the name of individual health

rather than for the overall fitness of the population, and the managers will be you and me, and our doctors and the state. Genetic change will be managed by the invisible hand of individual choice, but the overall result will be the same: a coordinate attempt to 'improve' the genes of the next generation on the way."

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Until recently, three unspoken principles have guided the arena of genetic diagnosis and intervention. First, diagnostic tests have largely been restricted to gene variants that are singularly powerful determinants of illness—i.e., highly penetrant mutations, where the likelihood of developing the disease is close to 100 percent (Down syndrome, cystic fibrosis, Tay-Sachs disease). Second, the diseases caused by these mutations have generally involved extraordinary suffering or fundamental incompatibilities with "normal" life. Third, justifiable interventions—the decision to abort a child with Down syndrome, say, or intervene surgically on a woman with a *BRCA1* mutation—have been defined through social and medical consensus, and all interventions have been governed by complete freedom of choice.

The three sides of the triangle can be envisioned as moral lines that most cultures have been unwilling to transgress. The abortion of an embryo carrying a gene with, say, only a ten percent chance of developing cancer in the future violates the injunction against intervening on low-penetrance mutations. Similarly, a state-mandated medical procedure on a genetically ill person without the subject's consent (or parental consent in the case of a fetus) crosses the boundaries of freedom and noncoercion.

Yet it can hardly escape our attention that these parameters are inherently susceptible to the logic of self-reinforcement. *We* determine the definition of "extraordinary suffering." *We* demarcate the boundaries of "normalcy" versus "abnormalcy." *We* make the medical choices to intervene. *We* determine the nature of "justifiable interventions." Humans endowed with certain genomes are responsible for defining the criteria to define, intervene on, or even eliminate other humans endowed with other genomes. "Choice," in short, seems like an illusion devised by genes to propagate the selection of similar genes.

Even so, this triangle of limits—high-penetrance genes, extraordinary suffering, and noncoerced, justifiable interventions—has proved to be a useful guideline for acceptable forms of genetic interventions. But these boundaries are being breached. Take, for instance, a series of startlingly provocative studies that used a single gene variant to drive social-engineering choices. In the late 1990s, a gene called *5HTTLRP*, which encodes a molecule that modulates signaling between certain neurons in the brain, was found to be associated with the response to psychic stress. The gene comes in two forms or alleles—a long variant and a short variant. The short variant, called *5HTTLRP/short*, is carried by about 40 percent of the population and seems to produce significantly lower levels of the protein. The short variant has been repeatedly associated with anxious behavior, depression, trauma, alcoholism, and high-risk behaviors. The link is not strong, but it is broad: the short allele has been associated with increased suicidal risk among German alcoholics, increased depression in American college students, and a higher rate of PTSD among deployed soldiers.

In 2010, a team of researchers launched a research study, called the Strong African American Families project, or SAAF, in an impoverished rural belt in Georgia. It is a startlingly bleak place overrun by delinquency, alcoholism, violence, mental illness, and drug use. Abandoned clapboard houses with broken windows dot the landscape; crime abounds; vacant parking lots are strewn with hypodermic needles. Half the adults lack a high school education, and nearly half the families have single mothers.

Six hundred African-American families with early-adolescent children were recruited for the study. The families were randomly assigned to two groups. In one group, the children and their parents received seven weeks of intensive education, counseling, emotional support, and structured social interventions focused on preventing alcoholism, binge behaviors, violence, impulsiveness, and drug use. In the control group, the families received minimal interventions. Children in the intervention group and in the control group had the *5HTTLRP* gene sequenced.

The first result of this randomized trial was predictable from prior studies: in the control group, children with the short variant—i.e., the "high risk" form of the gene—were twice as likely to veer toward high-risk

behaviors, including binge drinking, drug use, and sexual promiscuity as adolescents, confirming earlier studies that had suggested an increased risk within this genetic subgroup. The second result was more provocative: these very children were also the *most likely* to respond to the social interventions. In the intervention group, children with the high-risk allele were most strongly and rapidly "normalized"—i.e., the most drastically affected subjects were also the best responders. In a parallel study, orphaned infants with the short variant of *5HTTLRP* appeared more impulsive and socially disturbed than their long-variant counterparts at baseline—but were also the most likely to benefit from placement in a more nurturing foster-care environment.

In both cases, it seems, the short variant encodes a hyperactive "stress sensor" for psychic susceptibility, but also a sensor most likely to respond to an intervention that targets the susceptibility. The most brittle or fragile forms of psyche are the most likely to be distorted by trauma-inducing environments—but are also the most likely to be restored by targeted interventions. It is as if *resilience* itself has a genetic core: some humans are born resilient (but are less responsive to interventions), while others are born sensitive (but more likely to respond to changes in their environments).

The idea of a "resilience gene" has entranced social engineers. Writing in the *New York Times* in 2014, the behavioral psychologist Jay Belsky argued, "Should we seek to identify the most susceptible children and disproportionately target them when it comes to investing scarce intervention and service dollars? I believe the answer is yes." "Some children are—in one frequently used metaphor—like delicate orchids," Belsky wrote, "they quickly wither if exposed to stress and deprivation, but blossom if given a lot of care and support. Others are more like dandelions; they prove resilient to the negative effects of adversity, but at the same time do not particularly benefit from positive experiences." By identifying these "delicate orchid" versus "dandelion" children by gene profiling, Belsky proposes, societies might achieve vastly more efficient targeting with scarce resources. "One might even imagine a day when we could genotype all the children in an elementary school to ensure that those who could most benefit from help got the best teachers."

Genotyping all children in elementary school? Foster-care choices driven by genetic profiling? Dandelions and orchids? Evidently, the conversation around genes and predilections has already slipped past the

original boundaries—from high-penetrance genes, extraordinary suffering, and justifiable interventions—to genotype-driven social engineering. What if genotyping identifies a child with a future risk for unipolar depression or bipolar disease? What about gene profiling for violence, criminality, or impulsivity? What constitutes "extraordinary suffering," and which interventions are "justifiable"?

And what is normal? Are parents allowed to choose "normalcy" for their children? What if—obeying some sort of Heisenbergian principle of psychology—the very act of intervention reinforces the identity of abnormalcy?

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This book began as an intimate history—but it is the intimate future that concerns me. A child born to a parent with schizophrenia, we now know, has between a 13 to 30 percent chance of developing the disease by age sixty. If both parents are affected, the risk climbs to about 50 percent. With one uncle affected, a child runs a risk that is three- to fivefold higher than the general population. With two uncles and a cousin affected—Jagu, Rajesh, Moni—that number jumps to about tenfold the general risk. If my father, my sister, or my paternal cousins were to develop the disease (the symptoms can emerge later in life), the risk would again leap severalfold. It is a matter of waiting and watching, of spinning and respinning the teetotum of fate, of assessing and reassessing my genetic risk.

In the wake of the monumental studies on the genetics of familial schizophrenia, I have often wondered about sequencing my genome, and the genomes of selected members of my family. The technology exists: my own lab, as it turns out, is equipped to extract, sequence, and interpret genomes (I routinely use this technology to sequence the genes of my cancer patients). What is missing, still, is the identity of most of the gene variants, or combinations of variants, that increase the risk. But there is little doubt that many of these variants will be identified, and the nature of risk conferred by them quantified, by the end of the decade. For families such as mine, the prospect of genetic diagnosis will no longer remain an abstraction, but will transform into clinical and personal realities. The triangle of considerations—penetrance, extraordinary suffering, and justifiable choice—will be carved into our individual futures.

If the history of the last century taught us the dangers of empowering

governments to determine genetic "fitness" (i.e., which person fits within the triangle, and who lives outside it), then the question that confronts our current era is what happens when this power devolves to the individual. It is a question that requires us to balance the desires of the individual—to carve out a life of happiness and achievement, without undue suffering—with the desires of a society that, in the short term, may be interested only in driving down the burden of disease and the expense of disability. And operating silently in the background is a third set of actors: our genes themselves, which reproduce and create new variants oblivious of our desires and compulsions—but, either directly or indirectly, acutely or obliquely, influence our desires and compulsions. Speaking at the Sorbonne in 1975, the cultural historian Michel Foucault once proposed that "a technology of abnormal individuals appears precisely when a regular network of knowledge and power has been established." Foucault was thinking about a "regular network" of humans. But it could just as easily be a network of genes.