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GENETICALLY-ENGINEERED BEGOTS, HAVE-NOTS, AND TINKERED TOTS: (HIGH SCORING POLYGENIC KIDS AS A HEREDITY-CAMELOT)-AN INTRODUCTION TO THE LEGALITIES AND BIO-ETHICS OF ADVANCED IVF AND GENETIC TESTING

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GENETICALLY-ENGINEERED BEGOTS, HAVE-NOTS, AND TINKERED TOTS: (HIGH SCORING POLYGENIC KIDS AS A HEREDITY-CAMELOT)—AN INTRODUCTION TO THE LEGALITIES AND BIO-ETHICS OF ADVANCED IVF AND GENETIC EDITING

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I. INTRODUCTION

It has now been almost three years since the first humans with edited genes were created. Using the Nobel prize-winning CRISPR-Cas9 technology, Chinese researcher, He Jiankui, genetically engineered embryos of twin girls, aiming (but failing in one) for resistance to HIV.[1] The event triggered a litany of cries from the Bioethics community.[2] While the CRISPR-Cas technology has been heralded by some as the magic bullet that could cure,[3] prevent, or even eliminate genetic diseases from the human population,[4] no less than sixty bioethical manifestos furnished responses ranging from caution to absolute moratorium.[5] Others, however, disagreed.[6] In the scientific

1. An unpublished paper, found about year after He Jiankui's "experiment" reveals various ethical flaws perpetrated by Dr. He. *See* Jakki Magowan, *Unpublished paper surfaces about the Chinese genome-edited babies*, BIONEWS (Dec. 9, 2019), https://www.bionews.org.uk/page_146644 [https://perma.cc/A4GM-D4SJ] (citing to MIT Technology Review).

2. One bioethicist who sounded in in favor of allowing the technique on human embryos since the risks of genome editing are "now so low that it is both ethically justifiable and highly desirable" to do so. *See* Mason Boycott-Owen, *'Designer babies' might not be as tall or smart as parents expect*, THE TELEGRAPH (Nov. 19, 2019), https://www.telegraph.co.uk/news/2019/11/21/designer-babies-may-not-smart-tall-parents-expect-study-warns/ [https://perma.cc/G349-G46K].

3. *See* Julianna Photopoulas, *Diabetes revered in mice using CRISPR and stem cell technology*, BIOEDGE (Apr. 27, 2020), https://www.bionews.org.uk/page_149260 [https://perma.cc/33EA-HUJX]; *see also* Jay Stone, *CRISPR helps uncover new leukemia genes*, BIOEDGE (Apr. 27, 2020), https://www.bionews.org.uk/page_149281 [https://perma.cc/2EFD-HQPQ].

4. *See generally*, JENNIFER DOUDNA & SAMUEL STERNBERG, A CRACK IN CREATION GENE EDITING AND THE UNTHINKABLE POWER TO CONTROL EVOLUTION (2017).

5. Carolyn Brokowski, *Do CRISPR Germline Ethics Statements Cut It?*, 2 CRISPR J. 1 (2018).

6. A few bioethicists have even argued that research on editing human embryos is a "moral imperative," since roughly 6% of all babies have "serious birth defects. Kyle Peterson, *The Gene Editors Are Only Getting Started*, WALL ST. J. (July 7, 2017), https://www.wsj.com/articles/the-gene-editors-are-only-getting-started-1499461756 [https://perma.cc/LMZ9-C8J9]. *See also* Alexander Ware, *Podcast Review: Humanity's Awesome, Terrifying Take-Over of Evolution*, BIONEWS (May 10, 2021), https://www.bionews.org.uk/page_155852 [https://perma.cc/H3ZS-6YPF].

community, many approved its use—at least to cure dangerous diseases—albeit requiring safety assurances.[7] Here, too, others disagreed.[8] The legal community, however, was relatively silent—initially. Medically speaking, in the aftermath of He Jiankui's genetic tampering we are still ignorant of the accuracy,[9] efficacy,[10] and dangers of the technique;[11] problems have surfaced,[12] and solutions, legal, bioethical, and medical, are still missing.[13]

Synchronous with advances in genetic editing ("geniting"), In Vitro Fertilization (IVF) has marched on since Louise Brown, the first "test-tube' baby created by this technology, was born forty-two years ago.[14] While mostly enjoying uniform support to address heart-breaking cases of infertility, a few IVF babies have been born with medical problems. In some cases,

7. Tina Rulli, *Gattaca or life-saving? Can we—should we—use CRISPR to edit human embryos, sperm or eggs to cure diseases?*, GENETIC LITERACY PROJECT (Jan. 22, 2021), https://geneticliteracyproject.org/2021/01/22/gattaca-or-life-saving-can-we-should-we-use-crispr-to-edit-human-embryos-sperm-or-eggs-to-cure-diseases/ [https://perma.cc/98TV-QJ5B] (noting "A 2017 report by the U.S. National Academy of Sciences and the National Academy of Medicine recommending that, once the technology is ready and safe, genetic modification of embryos could be allowed when there is a "serious disease or condition" to be addressed and no "reasonable alternatives" exist.").

8. Michael Cook, *CRISPR-edited embryos should not be used. Not for the moment, that is*, BIOEDGE (Sept. 6, 2020), https://www.bioedge.org/bioethics/crispr-edited-embryos-should-not-be-used.-not-for-the-moment-that-is/13540 [https://perma.cc/476S-N282].

9. Kimberly Bryon-Dodd, *CRISPR base-editing linked to off-target effects*, BIONEWS (Mar. 4, 2019), https://www.bionews.org.uk/page_141685 [https://perma.cc/6T9Q-B4MH] (reporting on an article in Science that showed "a large number of off-target mutations," in animal studies).

10. *Researchers get better at tweaking the genomes of human embryos*, THE ECONOMIST (Aug. 5, 2017), https://www.economist.com/science-and-technology/2017/08/05/researchers-get-better-at-tweaking-the-genomes-of-human-embryos [https://perma.cc/LWK6-BTS4] (noting problems with the quality of DNA repair, as well as noting the existence of mosaicism, thereby nullifying the effects of the gene-editing modification attempts).

11. *See* Alex Pearlman, *Biohackers are using CRISPR on their DNA and we can't stop it*, NEW SCIENTIST (Nov. 15, 2017), https://www.newscientist.com/article/mg23631520-100-biohackers-are-using-crispr-on-their-dna-and-we-cant-stop-it/ [https://perma.cc/8WHB-9DFK]. *See also* Dov Greenbaum, *Nobel Prize for CRISPR inventors re-sparks the debate on science's ethical boundaries*, CALCALIST (Oct. 9, 2020), https://www.calcalistech.com/ctech/articles/0,7340,L-3855990,00.html [https://perma.cc/ZB3T-2SWM] (one well-known biohacker, Josh Zayner, who" publicly injected himself with a CRISPR concoction in the hopes of treating herpes.").

12. Whether intentionally or not, the gene tampered with by He Jiankui also would affect recovery from stroke and would likely affect the child's cognition. *See* Isabel Steer, *Gene-deleted in genome-edited babies linked to better recovery from stroke*, BIONEWS (Feb. 25, 2019), https://www.bionews.org.uk/page_141598 [https://perma.cc/8BLT-L7PZ] (reporting on an article lead-authored by Alcina Silva and published in Scientific American). The genetic engineering of the twins might have also enhanced cognition and memory. *See* Antonio Regalado, *China's CRISPR twins might have had their brains inadvertently enhanced*, MIT TECH. REV. (Feb. 21, 2019), https://www.technologyreview.com/2019/02/21/137309/the-crispr-twins-had-their-brains-altered/ [https://perma.cc/N3LS-38CC]. One wonders if this experiment wasn't the beginning of an attempt at intellectual enhancement under the cover of something more benign, such as HIV immunity.

13. Gary Marchant et al., *From Genetics to Genomics: Facing the Liability Implications in Clinical Care*, 48 J.L. MED. & ETHICS 11 (2020).

14. *See generally*, ANVER KULIEV, SVETLANA RECHITSKY, & JOE LEIGH SIMPSON, PRACTICAL PREIMPLANTATION GENETIC TESTING (2000).

these are due to rank negligence on the part of IVF laboratories; in others they may arise due to inherent side-effects of the procedure.[15] Legal efforts to compensate injured children, even those harmed due to laboratory malfeasance,[16] have largely failed as some of the articles in this issue discuss.[17] Hard and precise regulation over both industries, IVF and hereditary human geniting (HHG), is absent in the U.S.[18]

"Soft" regulation for both technologies does exist in the form of limiting federal research funding in the United States and a self-imposed moratorium in the research community with little teeth. All the while, some researchers are chafing to continue the work.[19] Recent reports indicate that once the safety concerns are addressed, bioethicists and scientists will support HHG,[20] a position supposedly embraced by much of the laity—according to some studies.[21] That eventuality will unleash a tsunami of questions of social

15. *See e.g.*, *Science Update: In vitro fertilization may increase cancer risk among children with birth defects, NIH-funded study suggests*, NIH NEWSROOM (Nov. 10, 2020), https://www.nichd.nih.gov/newsroom/news/111020-IVF [https://perma.cc/9GPX-E6TA]; Annick Delvigne & Serge Rozenberg, *Epidemiology and Prevention of Ovarian Hyperstimulation Syndrome (OHSS) A Review*, 8 HUM. REPROD. UPDATE 559–577 (2002).

16. *Chelmsford fertility clinic gave woman wrong sperm*, BBC NEWS (Oct. 3, 2019), https://www.bbc.com/news/uk-england-essex-49923125#:~:text=A%20woman%20was%20given%20the,up%22%2C%20a%20report%20said.&text=But%20the%20mistake%20by%20the,the%20woman%2C%20the%20HFEA%20said [https://perma.cc/HE5Y-CBRB]. In the UK, which does have regulation, laboratory errors are said to be rare, "affecting less than 1% of fertility treatment cycles - but have risen by 6% in the last year and 18% in three years." *See also* Barbara Pfeffer Billauer, *The Sperminator as a Public Nuisance: Redressing Wrongful Life and Birth Claims in New Ways (a.k.a. New Tricks for Old Torts)*, 42 U. ARK. LITTLE ROCK L. REV. 1 (2019–2020) [hereinafter Billauer, *The Sperminator*].

17. *See generally* Yaniv Heled et al., *A Wrong Without a Remedy: Leaving Parents and Children with a Hollow Victory in Lawsuits Against Unscrupulous Sperm* Banks, 96 CHI.-KENT L. REV. 115 (forthcoming 2021); David Heyd, *Embryonic Injuries: Can You Sue if You Wouldn't Have Been Born, or Born Different?* 96 CHI.-KENT L. REV. 145 (forthcoming 2021); Dov Fox, *Causation and Compensation for Intergenerational Harm*, 96 CHI.-KENT L. REV. 139 (forthcoming 2021).

18. NAOMI CAHN, TEST-TUBE FAMILIES, WHY THE FERTILITY MARKET NEEDS LEGAL REGULATION 17 (2009); Naomi Cahn & Sonia Suter, *The Art of Regulating ART*, 96 CHI.-KENT L. REV. 29 (forthcoming 2021).

19. David Cyranoski, *Russian 'CRISPR-baby' scientist has started editing genes in human eggs with goal of altering deaf gene*, NATURE (Oct. 18, 2019), https://www.nature.com/articles/d41586-019-03018-0 [https://perma.cc/MCH3-MCCE].

20. Sheldon Krimsky *The Moral Choices on CRISPR Babies*, 19 AM. J. BIOETHICS 15–16 (2019).

21. Dietram A. Scheufele et al., *U.S. Attitudes on human genome editing*, 357 SCIENCE 553–554 (2017) (N.B. this research was done prior to He Jiankui's research); *see also* S.Hendrik et al., *Reasons for being in favour of or against genome modification: a survey of the Dutch general public,* 2018 HUM. REPROD. OPEN 1–12 (2018); Pete Shanks, *Manufacturing Opinion: What's Not to Like About a Perfect Technology?*, BIOPOLITICAL TIMES (Aug. 25, 2020), https://www.geneticsandsociety.org/biopolitical-times/whats-not-about-perfect-technology [https://perma.cc/DV95-XFFT]. *Genetics experience impacts attitudes towards germline gene editing: a survey of over 1500 members of the public*, J. HUM. GENETICS, July 31, 2020. A survey by advocates of human germline gene editing finds some support for medical (but not enhancement) applications—except among women, the religious, and anyone with professional or personal knowledge of genetics or genomics. Parents and people with college degrees are more

justice, resource allotment and availability, bioethics, raising regulatory and liability issues including the need for legal redress, triggering a panoply of cultural concerns as well. Conflicting resolutions among various medical specialties,[22] countries, and cultures[23] have already surfaced[24] and divergent international results[25] further complicate matters.

We start with the recognition that using CRISPR-Cas as a human and hereditary gene-editing tool also may cause harms (e.g., off-target injuries) which have yet to be identified.[26] This deficit may result in children born with unanticipated defects, highlighting the legal lacuna in redressing and preventing such harms[27] surfacing in novel reproductive technologies.[28] Holdings from cases addressing less dramatic reproductive technological accidents[29] or arising in the context of IVF facilities[30] demonstrate that if harm

skeptical than those without children or degrees. There are, however, cultural variation in views. *See* Emily L. Howell, *What Do We (Not) Know About Global Views of Human Gene Editing? Insights and Blind Spots in the CRISPR Era.*, 3 CRISPR J. (2020).

22. Who makes the decision what to regulate? Lawyers, scientists, doctors, theologians, or as one commentator claims, ethicists. *See* Brendon Parent, *CRISPR lit the Fire: Ethics Must Drive Regulation of Germline Engineering*, 3 SCITECH LAWYER CHI. 18–21 (2016).

23. For example, deaf mothers in the U.S. sought to select for deaf children via enhanced reproductive technologies in several countries, where the case was widely reported, and publicly denied. JUDITH DAAR, THE NEW EUGENICS: SELECTIVE BREEDING IN AN ERA OF REPRODUCTIVE TECHNOLOGIES 5, 19, 185 (2017).

24. Michael Cook, *Tandem IVF: anything to guarantee a baby*, BIOEDGE (Aug. 26, 2017), https://www.bioedge.org/bioethics/anything-to-guarantee-a-baby/12404 [https://perma.cc/6MXD-ANN5].

25. In Israel, I could only find an obscure reference to the event, with no indication of the resolution. Gideon Weitzman, *Who Is Normal?* TORAH TIDBITS, Oct. 23, 2019, at 63.

26. Heidi Ledford, *CRISPR gene editing in human embryos wreaks chromosomal mayhem Three studies showing large DNA deletions and reshuffling heighten safety concerns about heritable genome editing,* NATURE (June 25, 2020), https://www.nature.com/articles/d41586-020-01906-4 [https://perma.cc/6KBT-TVUW].

27. *See generally* Dov Fox, *Reproductive Negligence*, 117 COLUM. L. REV. (2017) (discussing the litany of harms occasioned by various forms of reproductive negligence, and the paucity or unavailability of legal remedies).

28. Sigal Samuel, *Is it time to regulate biohacking? California thinks so. A new law warns biohackers not to edit their genes at home*, VOX (Aug. 13, 2019), https://www.vox.com/future-perfect/2019/8/13/20802059/california-crispr-biohacking-illegal-josiah-zayner [https://perma.cc/84CL-QBYD] (noting the " notorious [Californial] biohacker, Josiah Zayner,. . . runs a company . . . the Odin [which is] selling biohacking supplies ranging from $20 DNA to a $1,849 DIY genetic engineering kit. In 2017, he injected himself with CRISPR DNA at a biotech conference, live-streaming the stunt. That same year, he started selling a CRISPR kit to target a human gene, the removal of which could theoretically make muscles bigger. The FDA soon released a notice saying the sale of DIY gene-editing kits for use on humans is against the law.").

29. Barbara Pfeffer Billauer, *Re-Birthing Wrongful Birth Claims in the Age of IVF and Abortion Reforms*, 50 STETSON L. REV. (2020).

30. Barbara Pfeffer Billauer, *Wrongful Life in the Age of CRISPR-CAS: Using the Legal Fiction of 'The Conceptual Being' to Redress Wrongful Gamete Manipulation*, 124 PENN ST. L. REV. 435 (2020).

occurs to resultant children, tort liability is virtually unavailable.[31] International regulation is uneven, ineffective, or absent, promoting reproductive tourism, which generates legal issues of its own. And while precise regulations do exist in the U.K. governing use of IVF, these regulations seem not to have prevented or curtailed errors and accidents.[32] In the U.S. effective regulation does not exist, as discussed by Professors Cahn and Suter in their article which immediately follows (along with their suggestions for improvement and legislative revitalization).[33] Israel provides a middle-of-road scenario—some regulations exist but are complicated by cultural and religious tensions.[34] Common law remedies, discussed in the articles following, are also deficient. Before even addressing the legal landscape, an overview of the moral and societal issues presented by these technologies must be unveiled.

While IVF flies under the banner of benign acceptability—obscuring some serious issues the technology provokes, CRISPR-Cas and other forms of HHG, raise hackles—perhaps deflecting more particularized and incisive examination. Some suggest that CRISPR-Cas might provide a less legally and bioethically fraught endeavor—at least to produce healthy children—than does IVF.[35] Nevertheless, I suggest that the issues presented by both technologies are quite similar and attempts to dissect out differences turn on artificially contrived platforms. Hence, I begin by suggesting that redressing legal and bioethical problems on a technology-by-technology basis is inefficient and confusing. Rather, a new nomenclature with a systems-oriented approach is required. I therefore propose addressing all relevant issues presented by advanced reproductive technologies be they CRISPR, its improvements,[36] or IVF-based technologies, under the umbrella of *hereditary human*

31. *Id. See also* CA 1326/07 Hammer v. Macabbi Health SServices; ACBv. Thomson Med. Pte. Ltd., [2017] SGCA 20 (Sing.) (a Singapore case addressing switched sperm, depriving parents of their biological offspring and reviewing the world-wide literature on the subject).

המערערת בע"א פלוני (קטין), מכבי שירותי בריאות, ליאור המר נ' מדינת ישראל 2896.09,3856/09,3828/10; ACB v. Thomson Med. Pte. Ltd., [2017] SGCA 20 (Sing) 1326/07,572/08,8776/08,2600/09

32. Billauer, *The Sperminator*, *supra* note 16.

33. Cahn & Suter, *supra* note 18.

34. Guy Rosner et al., *Genetic Testing in Israel: an overview*, 10 ANN. REV. GENOMICS & HUM. GENETICS 175–92 (2009) (noting that "[c]ulturally appropriate genetic programs have been initiated in religious Jewish and non-Jewish communities in an attempt to overcome cultural barriers and reduce the frequency of severe genetic diseases nationwide"). *See also* Barbara Pfeffer Billauer, *Joshua, Son of None: When the Rabbinate Becomes Guardian of the Genes,* TIMES ISR. (Nov. 25, 2019), https://blogs.timesofisrael.com/author/barbara-pfeffer-billauer/ [https://perma.cc/R59T-YJMH].

35. Giulia Cavaliere, *Genome editing and assisted reproduction: curing embryos, society or prospective parents*?, 21 MED., HEALTH CARE AND PHIL. 215–225 (2018).

36. Rachel Siden, *Retron genome editing approach is faster and easier than CRISPR*, BIONEWS (May 10, 2021), https://www.bionews.org.uk/page_156297 [https://perma.cc/FYD3-ZQPD].

genetic manipulation (HHGM).[37] One objective of a unified terminology would allow exploration of a unified paradigm to protect children harmed by these modern genetic/reproductive technologies.[38] This approach would also provide for an overarching exploration of the impacts of genome-tinkering on society, rather than fragmenting the questions on a technology-by technology basis. Coalescing the societal, moral, and legal question under a single nomenclature also allows us to incorporate or coalesce different cultural views surrounding reproductive issues in a single assessment.[39]

II. THE NEW MORALITY WROUGHT BY HHGM

We start by noting that genetic tampering invites concerns of eugenics: For example, one attempted use of Pre-Implantation Genetic Testing (PGT) is to select *for* genes that produce deafness. This effort has triggered conflicts between the hearing and non-hearing communities regarding whether deafness constitutes a disability or a unique culture, as noted by Dean Judith Daar.[40] The conundrum also raises issues such as whether we should sanction creating deaf children on the premise that deafness is not a disability, but rather a culture to be nurtured and fostered? Or, alternatively, will we require deafness to be eradicated on the grounds that caring for deaf children depletes the public health budget, or that creating deaf children violates some parental duty (called parental beneficence)[41] to produce children who will likely lead the best life, as suggested by some bioethicists? [42] Of course, the meaning of "the best life" is open to all sorts of unresolvable moral, religious, and cultural interpretations.

37. Which would include newer forms of genetic editing, including Retron Library Recombineering (RLR), which uses segments of bacterial DNA called retrons that can produce fragments of single-stranded DNA. *See* Mariella Moon, *Harvard scientists create gene-editing tool that could rival CRISPR*, ENDGADGET (May 1, 2021), https://www.engadget.com/harvard-gene-editing-tool-rlr-214700187.html [https://perma.cc/2P96-K5LF].

38. Helen C. O'Neill & Jacques Cohen, *Live Births Following Genome Editing in Human Embryos: A Call for Clarity, Self-Control and Regulation*, 38 REPROD. BIOMEDICINE ONLINE 131, 131 (2019).

39. David Nelken, *Law, Liability and Culture*, *in* FAULT LINES, TORT LAW AS CULTURAL PRACTICE 1, 25 (David M. Engel & Michael McCann eds., 2009) (noting: "[l]egal culture, like all culture is a product of the contingencies of history and is always undergoing change."). *See also* OLIVER WENDELL HOLMES, THE COMMON LAW 22 (1881) ("The history of what the law has been is necessary to the knowledge of what the law is.").

40. DAAR, *supra* note 23, *see also* Bernard M. Dickens, *The New Eugenics—Selective Breeding in an Era of Reproductive Technologies: A Review Essay*, 44 POPULATION & DEV. REV. 627 (2018).

41. P. Herissone-Kelly, *Procreative beneficence and the prospective parent,* 38 J. MED. ETHICS (2006).

42. Hannah Bourne et al., *Procreative beneficence and* in vitro *gametogenesis*, 30 MONASH BIOETHICS REV. 29–48 (2012); Michael Cook, *Savulescu interviewed on 'procreative beneficence'*, BioEdge (Nov. 10, 2019), https://www.bioedge.org/bioethics/savulescu-interviewed-on-procreative-beneficence/13273 [https://perma.cc/CT7R-FDF4].

And then we have the question of creating designer children—which to a certain extent, can be done right now and will be discussed in Part IV.[43] Certainly traits like height or strength can be selected at the test-tube level by parents who perhaps selfishly or egotistically want their children to be like—or unlike—them. Perhaps this technique also might be used for the greater good, since usually we think of genetic engineering as a means to design uber-children—brighter, taller, healthier. But perhaps there might be uses some may claim as nefarious: someone wishing to create depressed children on the premise that some of our greatest writers and artists created great works under the cloud of depression? What about engineering abnormally short children because some short people become wonderful actors or comedians precisely because of their diminished physical stature? Julian Savulescu says it would be unacceptable to create children prone to depression, but manic depressiveness could be okay.[44] The basis seems to be his knowledge of the productivity of those so diagnosed—in his opinion.

Another issue is differing cross-cultural sensibilities. One might assume that countries of similar levels of development, both economic and scientific, might be governed by similar views of ethics, fairness, and morality, but that is no longer the case. Cultural morés from technologically-advanced Eastern and Middle Eastern countries may differ from sensitivities of the West—generating yet an additional layer of problems and tensions.[45] The value of boys outweighs girls in certain cultures; in others the opposite tendency occurs. Politically, too, culture matters. One China expert[46] suggested that a Chinese dream is to genetically engineer their children with superior

43. An issue I first presented for discussion before the legal community at the SEALS conference of 2020.

44. Julian Savulescu & Guy Kahane, *The Moral Obligation to Create Children with the Best Chance of the Best Life*, 23 BIOETHICS 274–290 (2009).

45. For example, recently, a team of researchers from the American-based Salk Institute produced a monkey-human chimera, an organism whose cells come from two different organisms. "The research was conducted in China 'to avoid legal issues. . . .'" Nicola Davis, *First human-monkey chimera raises concerns among scientists*, THE GUARDIAN (Aug. 3, 2019), https://www.theguardian.com/science/2019/aug/03/first-human-monkey-chimera-raises-concern-among-scientists [https://perma.cc/A2YB-GMAF]. *See also* Yvonne Collins, *Human-monkey hybrid embryos grown in China, claim researchers,* BIONEWS (Aug. 12, 2019), https://www.bionews.org.uk/page_144312 [https://perma.cc/MNN2-TCSV] (stating, that "this type of research had previously raised technical and ethical concerns and is currently heavily restricted in Spain and the USA."). A second monkey-human chimera experiment was reported in April of 2021. *See* Barbara Pfeffer Billauer, *Of Mice And Men, Monkeys, And Pigs. The Ethics of Chimeric Research*, AM. COUNCIL ON SCI. & HEALTH (Apr. 29, 2021), https://www.acsh.org/news/2021/04/29/mice-and-men-monkeys-and-pigs-ethics-chimeric-research-15517 [https://perma.cc/54UD-Z4FK]; Tao Tan et al., *Chimeric contribution of human extended pluripotent stem cells to monkey embryos ex vivo*, 184 CELL 2020–2032 (2021); *Fantastic Beasts and how to Make Them*, THE ECONOMIST, Apr. 17, 2021, at 63–64.

46. Personal communication with "Spengler," a noted Columnist for The Asia Times (Nov. 11, 2019).

intelligence[47] which might have motivated He Jiankui's experiments.[48] The above illustrates the importance of cultural influence—be it geographic, political, religious, or tribal—in influencing public perception and solutions regarding genetic interventionism.

Finally, we have the issue of elevating genetic legacy to a form of determinism, minimizing the conjoint effects of environment, metabolism, lifestyle, or multiple interactions, the effects of which we are, at least as yet, unable to predict.[49]

In this introductory precis, I will begin by providing a conference overview, including noting the presentations which are not included in this written volume. In Part IV raise a novel dilemma which was not addressed at the conference—as a thought-experiment for the reader or fodder for classroom or dining table discussion: the dilemmas of using polygenic scoring to create "uber-children." I hope that the solutions raised in the papers contained in this Symposium issue provide some solutions to this vexing and current problem or at least provide "food for thought" and launch-points for further discussion. Finally in Part V I will revisit the morality-driven issues presented by these vexing problems.

III. CONFERENCE OVERVIEW

The Chicago-Kent Symposium on *Embryonic Injuries and Nascent Injuries in the Age of CRISPR-Cas*, held November 18–19, 2020, presented an opportunity for legal scholars who had previously done research in these areas to present their works to the legal public and to interact with one another. Some papers presented at the conference are presented in this limited volume. But the conference also included the perspectives of scientists,

47. "In this ever more competitive global pursuit of applications for gene editing, we hope to be a stand-out," He and his team wrote in an ethics statement. "The genetic editing of a speck-size human embryo carries significant risks, including the risks of introducing unwanted mutations or yielding a baby whose body is composed of some edited and some unedited cells. Data on the Chinese trial site indicate that one of the fetuses is a 'mosaic' of cells that had been edited in different ways. The National Academy of Sciences in the US gave guarded support for gene-edited babies, although only if they could be created safely and under strict oversight." Antonio Regalado, *EXCLUSIVE: Chinese scientists are creating CRISPR babies A daring effort is under way to create the first children whose DNA has been tailored using gene editing*, MIT TECH. REV. (Nov. 25, 2018).

48. G Owen Schaefer, *China may be the future of ay be the future of genetic enhancement*, BBC FUTURE (Aug. 8, 2016), https://www.bbc.com/future/article/20160804-china-may-be-the-future-of-genetic-enhancement [https://perma.cc/HD8K-GCUV].

49. Lisa Rapaport, *Genetic markers not the best way to predict disease risk*, JERUSALEM POST, Jan. 12, 2020, at 8 (quoting researcher David Wishart: "What we found was quite shocking. . . Based on our result mor than 95% of diseases or disease risks (including Alzheimers's disease, autism, asthma, juvenile diabetes. psoriasis, etc.) could NOT be predicted accurately," with genetic markers); *see also* Rosie Gilchrist, *Alternative framework for heredity proposed*, BIONEWS (Apr. 27, 2020), https://www.bionews.org.uk/page_149272 [https://perma.cc/SJ8A-JMYC].

ethicists, and disability rights advocates whose work is not included here due to limitations of time and space—but whose importance must not be overlooked, and whose input is reflected in the solutions, legal and legislative, proposed in the papers that follow.

The Symposium began with a panel of scientific experts starting with Professor Neville Sanjana[50] of the NYU Grossman School of Medicine, who introduced the scientific aspects of genetic engineering and the CRISPR-Cas technology. We proceeded to Professor Amit Choudhary[51] of the Broad Institute, whose current work involves advancing and perfecting CRISPR-Cas and who outlined some of the problems with the technique. Finally, we were treated to Dr. Svetlana (Lana) Rechitsky[52] of Reproductive Genetic Innovations of Illinois, a pioneer in IVF, whose work involves detecting genetic markers for disease including delayed onset illnesses for the purposes of deselecting embryos carrying deleterious genetic information. Professor Jessica Roberts[53] of Houston Law Center, an expert in her own right on discrimination and privacy issues presented by these technologies, thoughtfully moderated the session.

Two highlights of the conference were our Opening and Closing Speakers, Dean Judith Daar[54] of Northern Kentucky University School of Law, and Bioethicist, Professor Arthur Caplan[55] of the NYU Grossman School of Medicine. Both have long been involved in the law and ethics of reproductive engineering, and both are regarded as pre-eminent advisors to both the legal and medical communities. Because of their long-standing interest, expertise, and writings in the field, they were able to present to us an invaluable history, perspective, and future outlook.

With this background, the panels that followed crystalized current problems and tackled on potential solutions. Because technology advances faster than law or ethical constructs can fathom,[56] clear conceptualization and resolution of the issues continue to elude the bioethical and legal communities,

50. *Neville Sanjana*, N.Y. GENOME CENTER, https://www.nygenome.org/labs/sanjana-lab/ [https://perma.cc/GZ6E-NZ2T].

51. *Amit Choudhary*, BROAD INSTITUTE, https://www.broadinstitute.org/scientific-community/science/programs/csoft/chemical-biology/group-wagner/wagner-group-group-members [https://perma.cc/YG53-3BEY].

52. *Svetlana Rechitsky*, REPROD. GENETIC INNOVATIONS, https://rgiscience.com/meet-our-team/ [https://perma.cc/CXC2-8F7Q].

53. *Jessica L. Roberts*, U. HOUSTON L. FACULTY, https://www.law.uh.edu/faculty/main.asp?PID=4797 [https://perma.cc/CYE8-39UX].

54. *Judith Daar*, NORTHERN KENTUCKY U., https://chaselaw.nku.edu/faculty/full-time-faculty-bios/JudithDaar.html [https://perma.cc/GG34-5ZSB].

55. *Arthur Caplan*, N.Y.U. LANGONE HEALTH, https://med.nyu.edu/faculty/arthur-l-caplan [https://perma.cc/Z7MA-49NL].

56. Cook, *supra* note 24.

a fact the judiciary concedes.[57] Even delineating or identifying present or potential problems has defied legal analysis. One problem in conceptualization is that issues arise from a host of technologies which trigger varying degrees of invasiveness and "indelibility" (permanence),[58] including, but not limited to, those with the potential for cloning gametogenic materials.[59] CRISPR-Cas, the technology employed in He Jiankui's gene editing, is being supplanted by newer, supposedly safer technologies with even broader possibilities.[60] To date, no mechanism exists for resolving, reconciling, or even identifying the broad-spectrum of dilemmas presented by these technologies.[61] In that the sensitivities involved will transcend the current legal and bioethical paradigms, we can expect—and indeed should invite—input from consumers and stakeholders, who, at the end of the day, will have immense freedom to make their own decisions regarding how they will choose to implement these technologies in their own lives.

The goal of the conference and this Symposium volume is to provide the lay-legal audience with a broad panorama of approaches to addressing issues involving hereditary human genetic manipulation (HHGM) illustrated via issues (and harms) arising from genetic engineering through CRISPR-Cas and Advanced IVF technologies. Indeed, the second panel examined the current legislative framework (or the lack thereof) as an explanation for the current situation and presented novel means of addressing current and future problems via the legislative mode. Addressing the health, safety, and damage aspects of the technology in a joint presentation were Professors

57. "Science has once again—as it always does—outstripped the law . . . the direction from the higher courts and the Legislature is clear—perhaps a half-step behind today's science, but clear—and until it is changed, it controls the outcome of this case." (opinion written by Judge Robert McBurney) Collins v. Xytex Corp., No. 2015CV259033, 2015 WL 6387328, at *3 (Ga. Super. Ct. Oct. 20, 2015).

58. These technologies include: In Vitro Fertilization (IVF), Pre-implantation Genetic Testing (PGT), and in vitro gametogenesis ("IVG") via somatic cell nuclear transfer (SCNT). *See* Bourne et al., *supra* note 42 (noting "[r]ecent research suggests that it may become possible to derive gametes (eggs and sperm) from human stem cells in vitro, a process which we will term in vitro gametogenesis (IVG). IVG would allow the creation of stems cells from a patient's somatic (body) cells, and these stems cells could then be used to generate a plentiful supply of eggs or sperm in the laboratory.").

59. For example, mitochondrial transfer (colloquially known as "three-parent-children"), is allowed in the UK, but prohibited in the U.S. Paula Amato et al., *Three-Parent IVF: Gene Replacement for the Prevention of Inherited Mitochondrial Diseases*, 101 FERTILITY & STERILITY 31, 31–35 (2014) (discussing the technique involved in implanting the nuclear genome from the pronuclear stage zygote of a woman affected with mitochondrial disease in an enucleated donor zygote).

60. Moon, *supra* note 37.

61. Carolyn Brokowsky & Mazhar Adil, *CRISPR Ethics, Moral Considerations for Applications of a Powerful Too*l, 431 J. MOLECULAR BIOLOGY 88–101 (2018).

Naomi Cahn[62] of the University of Virginia School of Law and Sonia Suter[63] of the George Washington University School of Law. Professors Cahn and Suter's contribution to the written symposium expands upon their presentation and delves into the history of existing regulations for Assisted Reproductive Technology ("ART") and the continuum of regulatory approaches. They conclude that all forms of ART should be regulated together and set out predictions of what this would look like. Raising additional conundrums presented by genetic engineering techniques, such as evading current DNA detection tools used by crime-fighting agencies and addressing the intellectual property issues of these discoveries, was Professor Dov Greenbaum[64] of the Interdisciplinary Center School of Law of Herzliya. Professor Greenbaum's article brings up powerful questions regarding genetic manipulation. Specifically, he focuses on sperm donation and changing landscape of donor anonymity as it relates to CRISPR technology. Coalescing the key points of the session was Discussant Dean Amy Campbell[65] of UIC John Marshall School of Law.

The third panel, directed by Discussant Professor I. Glenn Cohen[66] of Harvard Law School, addressed tort issues presented when negligence is committed by reproductive laboratories. Professor Yaniv Heled[67] of Georgia State University, who wrote one of the earliest papers in the field and who, along with colleagues Professor Timothy Lytton[68], also of Georgia State and Professor Liza Vertinsky[69] of Emory University School of Law, authored an amicus brief in the latest case discussing the matter, gave a historical overview of the lacuna in law. Their written contribution provides a more detailed look at the seminal *Xytex* case and its impact on wrongful birth causes of action. The authors explore the complicated political nature of the case as it relates to abortion and the impact of limiting an entire avenue of liability

62. *Naomi R. Cahn*, U. VA. L. SCHOOL, https://www.law.virginia.edu/faculty/profile/nrc8g/2915359 [https://perma.cc/Q336-MMVT].

63. *Sonia M. Suter*, GEO. WASH. L., https://www.law.gwu.edu/sonia-m-suter [https://perma.cc/WB7D-E4QY].

64. *Dov Greenbaum*, IDC HERZLIYA, https://www.idc.ac.il/en/pages/faculty.aspx?username=dgreenbaum [https://perma.cc/N446-RS5F].

65. *Amy T. Campbell*, U. IL. CHI., https://law.uic.edu/profiles/campbell-amy/ [https://perma.cc/3SPF-NDJJ].

66. *I. Glenn Cohen*, HARV. L. SCHOOL, https://hls.harvard.edu/faculty/directory/10176/Cohen [https://perma.cc/5HR5-YV2S].

67. *Yaniv Heled*, GA. STATE L. SCHOOL, https://law.gsu.edu/profile/yaniv-heled/ [https://perma.cc/CK7B-DK4W].

68. *Timothy D. Lytton*, GA. STATE L. SCHOOL, https://law.gsu.edu/profile/timothy-d-lytton/ [https://perma.cc/LP77-FYTN].

69. *Liza Vertinsky*, EMORY U. L. SCHOOL, https://law.emory.edu/faculty/faculty-profiles/vertinsky-profile.html [https://perma.cc/C6HB-X8NB].

exposure. Noting the refusal of virtually all courts to countenance wrongful life claims and the predilection to limiting wrongful birth claims, Professor Heled illustrated that children born injured as a result of reproductive laboratory negligence are effectively barred from remedy. Expanding on the philosophical underpinnings for these holdings and detangling the tortured misapplication of Derrick Parfit's Non-Identity Problem to the issue was Philosophy Professor David Heyd[70] of the Hebrew University, an international expert on the intersection of law and philosophy, especially in reproductive and family law issues. His article focuses further on the philosophy of the "Non-identity problem," both in cases of abortion (being born vs. not being born) and genetic manipulation via CRISPR (being born differently). He then discusses different conceptions of identity and how each may be used to overcome this problem as it relates to wrongful birth claims. Finally, Professor Dov Fox[71] of the University of San Diego School of Law, who has also written extensively on the tort aspects of "reproductive negligence," identified for us yet other unimagined harms sure to ensue, such as statute of limitations and causations issues. Professor Fox's written contribution details the history of DES litigation and how those lessons can apply to modern-day CRISPR gene editing. He also discusses various compensation schemes that could help victims of gene editing injury generation after generation.

The fourth panel integrated bioethical and legal issues generated by these new technologies. Professor Scott Burris[72] of Temple Law School served as the Discussant and Professors Michele Goodwin[73] of the University of California Irvine School of Law and Hank Greeley[74] of Stanford Law School, also long-standing pioneers in the field, gave a historical perspective. Professor Goodwin's presentation, entitled "Cultural Enhancement or Medical Manipulation," reminded us of the racial dilemmas that may emerge and require cognition to address, detailing current problems, along with mining cultural and historical wisdom to furnish additional wisdom.

70. *David Heyd*, HEBREW U. JERUSALEM, https://en.philosophy.huji.ac.il/people/david-heyd [https://perma.cc/H964-2MZ6].

71. *Dov Fox*, U. SAN DIEGO, https://www.sandiego.edu/law/about/directory/biography.php?profile_id=3332 [https://perma.cc/6VME-NY3V].

72. *Scott Burris*, TEMP. U. BEASLEY SCHOOL L., https://law.temple.edu/contact/scott-burris/ [https://perma.cc/QQ3P-EP5W].

73. *Michele Bratcher Goodwin*, U.C. IRVINE L., https://www.law.uci.edu/faculty/full-time/goodwin/ [https://perma.cc/SY8V-82HN].

74. *Henry T. Greely*, STAN. L. SCHOOL, https://law.stanford.edu/directory/henry-t-greely/ [https://perma.cc/W9Y3-TMZ9].

My[75] presentation on Savior Siblings, a technology involving selecting genetically compatible siblings to provide organ or tissue donation for already existing sick children, highlights the conflicts between cultural bioethics and U.S. law, and reiterated the need for greater legal oversight is needed for children subjected to genetic manipulation. My written contribution to the symposium provides an in-depth analysis of the ethical conundrums related to savior sibling creation, raising essential questions of consent, the best interests of savior siblings, and reproductive liberty. Here I explore the gap between the legal and ethical paradigms and highlight the necessity of biological and societal input in order to create consistent and effective regulation.

The final panel discussed considerations of the historically disenfranchised: the disabled, women, and social justice concerns, under the direction of Discussant Professor Myrisha Lewis[76] of William and Mary University School of Law. Professor Robert Dinerstein[77] of American University presented a paper on the impact of reproductive technologies on the disabled, and Professor Seema Mohapatra[78] of Southern Methodist University discussed the importance of social justice concerns. Professor Pamela Laufer-Ukeles of Sha'ari Mishpat College of Law[79] topped off the program with an impassioned talk on the need to consider the impact of informed consent, especially as it affects women and women's rights. Professor Laufer-Ukeles expands upon this discussion of consent in her written symposium contribution. She discusses the necessity of informed consent as it relates to embryonic genetic design and the difficulties in obtaining this consent. She employs feminist theory to discuss what consent should look like—emphasizing collaboration and empowerment.

75. *Barbara Pfeffer Billauer*, THE INSTITUTE OF WORLD POLITICS, https://www.iwp.edu/faculty/barbara-p-billauer/ [https://perma.cc/8SEN-UA4T].

76. *Myrisha S. Lewis,* WM. & MARY, https://law2.wm.edu/faculty/bios/fulltime/mslewis01.php [https://perma.cc/EB79-TNXX].

77. *Robert Dinerstein*, AM. U., https://www.wcl.american.edu/community/faculty/profile/dinerstein/bio [https://perma.cc/Z64P-2QM8].

78. *Seema Mohapatra*, SMU, https://www.smu.edu/Law/Faculty/Profiles/Mohapatra-Seema [https://perma.cc/9Z4Y-KK4N].

79. *Pamela Laufer-Ukeles*, TIMES OF ISRAEL, https://blogs.timesofisrael.com/author/pamela-laufer-ukeles/ [https://perma.cc/8TGN-JTPL].

IV. A DILEMMA: POLYGENIC SCORES TO CREATE ENHANCED UBER-KIDS

A. Whole-Genome Sequencing and Holistic Gene Health

Thus far, HHGM has focused on selecting against single genes causing specific diseases or conditions, or "improving" a single trait such as sex or immune expression. But now we can evaluate the holistic health of a person or even an embryo/prospective child. By tallying all the genetic risks recorded on a genome, "a whole-genome selection" study, we can calculate "a polygenic score"[80] or health quotient (HQ), to determine the overall likelihood of health,[81] and the risk of contracting specific diseases. Using genome-wide genetic data to assess millions of genetic variations of common (and not-so common disease) a person's inherited susceptibility can be assessed for each disease. This is accomplished by "computational algorithm that combines information from all of the variants into a number, or PRS, that reflects a person's inherited susceptibility to these diseases."[82] "Under the banner of 'wellness genomics,' scientists are already identifying natural genomic variants they see as helping their carriers resist disease, tolerate environmental extremes, and rebound from injuries more quickly."[83] At present, use of polygenic scores in clinical practice is enjoying robust debate.[84]

More controversial, however, is that the same technology can calculate an HQ or polygenic health score for an embryo. Coupled with IVF, this information has been touted as allowing selection of an embryo with the best

80. Shing W. Choi et al., *Tutorial A Guide to Performing Polygenic Risk Score Analysis*, 15 NATURE PROTOCOLS 2759 (2020). *See also* CDC, *Polygenic risk scores: What are they and what can public health do with them?* (Aug. 13, 2020), webinar_Polygenic Risk_Janssens.mp4 ("While the development and validation of polygenic risk scores may hold considerable promise to impact disease prevention and health promotion in the future, the present value of applying such models in clinical medicine and public health practice remains debatable.").

81. ROBERT PLOMIN, BLUEPRINT: HOW DNA MAKES US WHO WE ARE 70 (The MIT Press 2018).

82. *Polygenic Risks: What's the score?*, NATURE PORTFOLIO, https://www.nature.com/articles/d42473-019-00270-w [https://perma.cc/34PX-MQ8G] (last visited Aug. 9, 2021).

83. Eric T. Juengst, "*Prevention" and Human Gene Editing Governance*, 23 AMA J. ETHICS 49–54 (2021) (citing RAHUL Koul,*Wellness genomics: genomics for health and wellness*, BIOSPECTRUM (Dec. 15, 2014), https://www.biospectrumindia.com/features/73/7050/wellness-genomics-genomics-for-health-and-wellness.html [https://perma.cc/6EA7-JMMH]).

84. *See* Muin J. Khoury, *Is it Time to Integrate Polygenic Risk Scores into Clinical Practice? Let's Do the Science First and Follow the Evidence Wherever it Takes Us!*, CDC BLOG (June 3, 2019), https://blogs.cdc.gov/genomics/2019/06/03/is-it-time/ [https://perma.cc/5S6A-VRCN].

holistic genetic blueprint,[85] claiming to present the would-be child (and its parents) with a semi-prophetic view of that child's health-related life.[86]

Currently, commercially available technology exists to calculate an HQ or polygenic score for health—allowing parents to select the healthiest embryo. At first glance this sounds marvelous. Upon reflection, discussed in Part IV, this might not be so wonderful. Yet, at least one U.S. company advertises services for determining whether an embryo "has an increased probability of becoming a child with a variety of health difficulties by creating "polygenic risk scores," (PGS), claiming they want every family to have a healthy baby.[87] Other countries are trying to catch up.[88] At least one U.S. company reportedly also tests for "Low IQ"[89] boasting that they can devise an HQ for intelligence,[90] and that "once high-quality genetic and academic achievement data from a million individuals becomes available, expected to be within five to ten years, it will be able to predict IQ to within 10 points."[91] This would mean parents soon should be able to select the smartest embryo

85. *Modern genetics will improve health and usher in "designer" children*, THE ECONOMIST, Nov. 7, 2019.

86. The claims of usefulness and accuracy of using polygenic scores as a health risk predictor is fraught with difficulty, and minimizes not only environment- heredity interaction, but the complicated interactions of the genetic signature itself. *See* Judy Siegel, *Israeli-led international team discovers 72 genetic changes that cause breast cancer*, JERUSALEM POST, Oct. 24, 2017, at 10 (reporting on a study published in Nature and Nature Genetics). Most geneticists opine that these predictions are only useful on a population level. *See e.g.*, Denis Alexander *infra* note 114, at 143–144, 160, 211; R.C. LEWONTIN, BIOLOGY AS IDEOLOGY 27, 45, 64 (1992) (noting the contribution of randomness, (developmental noise), social contributions, to expression of human traits, noting the scientists at the Genome Projected explicitly rejected genetic determinism. R.C. LEWONTIN ET AL., NOT IN OUR GENES: BIOLOGY, IDEOLOGY AND HUMAN NATURE 8, 247, 251, 269, 287 (2d ed., 2017); *see also* SIDDHARTHA MUKERGEE, THE GENE (2016).

87. GENOMIC PREDICTION CLINICAL LAB., https://www.lifeview.com/ [https://perma.cc/2TZU-23SR].

88. Michael Cook, *Ukraine clinic seeks to genetically engineer babies*, BIOEDGE (May 2, 2021), https://www.bioedge.org/bioethics/ukraine-clinic-seeks-to-genetically-engineer-babies/13783#:~:text=Our%20Medical%20Center%20based%20on,skin%20quality%20and%20breast%20size [https://perma.cc/5S69-D4ZE] (noting that a recent advertisement from Medeus Medical Center read: "Hello! Our Medical Center based on the Institute of Quantum Medicine is opening its own laboratory for genetic editing of stem cells. Our long-term goals include working with humans using edited stem cells. We plan to edit grey hair colour, skin quality and breast size.").

89. O CARTER SNEAD, WHAT IT MEANS TO BE HUMAN 190 (2020); *see also* HANNAH CRITCHLOW, THE SCIENCE OF FATE (2019).

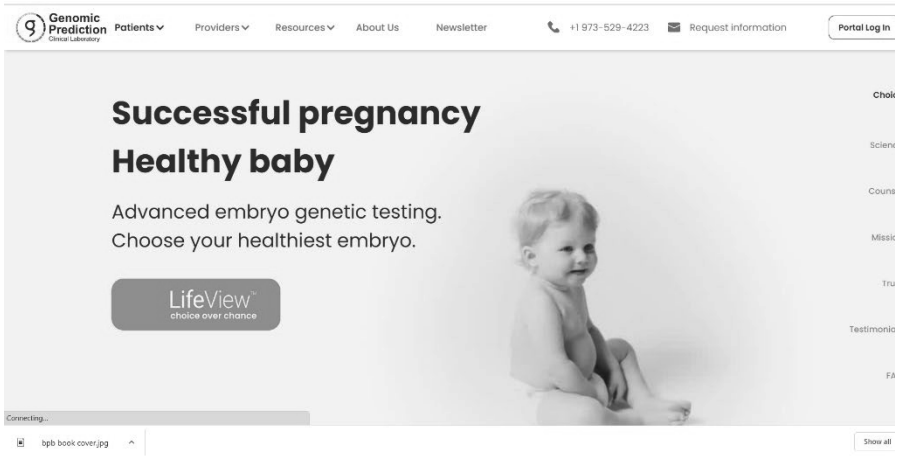
90. The claim has been called into question by researchers, noting that the improvement would be variable and would only reach 2.5 IQ points above average. *See* Ehud Karavani et al., *Screening Human Embryos for Polygenic Traits Has Limited Utility*, CELL, Dec. 19, 2019. *See also* Boycott-Owen, *supra* note 2 (quoting Dr. Liz Ormondroyd) (noting "It has long been feared that genetic information might be used to select embryos based on desire for characteristics such as increased height or intelligence. This computer simulation study shows that, for these complex characteristics 'designer babies' remain in the realm of science fiction.").

91. Hannah Devlin, *IVF Couples Could be Able to Choose the "Smartest Embryo',* THE GUARDIAN (May 24, 2019), https://www.theguardian.com/society/2019/may/24/ivf-couples-could-be-able-to-choose-the-smartest-embryo [https://perma.cc/M6RN-TAH2].

amongst those culled following hormonal stimulation—a practice assuming a premature but overarching belief in genetic determinism.[92] And we are not far from calculating even an aesthetic index (AI), which might comprise height, weight, and skin coloring integrated into an algorithm premised on conventional ideals of beauty (based on Fibonacci proportions). Indeed, the data and technology to select for height, purportedly already exists.[93]

B. Truth in Advertising

As noted above, at least one company markets their technology as enabling parents to choose "their healthiest embryo." That representation facially appears to be overly simplistic in that it seemingly ignores the impact of the environment, including the in-utero environment and epigenetic changes which influences how behaviors and environment can cause changes that affect the way genes work.[94]



95

92. A belief not subscribed to by prominent geneticists and evolutionary biologists. *See supra* note 86.

93. Barbara D. Bitarello & Iain Mathieson, *Polygenic Scores for Height in Admixed Populations* 10 G3: GENES, GENOMES, GENETICS, Nov. 1, 2020, at 4027–4036 (noting that "a major barrier to the use of PRS is that the majority of GWAS come from cohorts of European ancestry. The predictive power of PRS constructed from these studies is substantially lower in non-European ancestry cohorts. . . .Our results suggest that there is no simple statistical solution to the PRS transferability problem and emphasize the importance of performing GWAS in diverse populations.").

94. Unlike genetic changes, epigenetic changes are reversible and do not change your DNA sequence, but they can change how your body reads a DNA sequence. *What is Epigenetics?*, CDC, https://www.cdc.gov/genomics/disease/epigenetics.htm#:~:text=Epigenetics%20is%20the%20study%20of,body%20reads%20a%20DNA%20sequence [https://perma.cc/S7AV-UXHX].

95. GENOMIC PREDICTION, Screen shot taken May 14, 2021.

The embryo which might be "genetically" superior at selection—when it is eight cells old—may well not be so physically healthy years later. Indeed, recent evidence indicates that late-onset Alzheimer's disease is driven by epigenetic changes occurring after birth.[96] Furthermore, even direct genetic prediction of phenotypic expression is complicated. "For example, it has been estimated that approximately 100,000 independent loci are causal for height in humans."[97] And it is hardly likely we've identified all of them.

The polygenicity of certain traits, meaning the influence of multiple genes to affect one trait, is reflective of another genetic situation—that of pleiotropy, which might be considered the converse—meaning one gene impacts multiple traits. Horizontal pleiotropy is the causal effect of one genetic locus on multiple traits, such as occurs with schizophrenia and low body mass index;[98] vertical pleiotropy is indirectly causal of multiple traits (e.g., increased low density cholesterol which in turn impacts heart disease risk). at present, "it is unknown to what extent horizontal pleiotropy affects genetic variation in the human genome at the genome-wide level."[99] The more loci associated with a trait, such as height, means there are more chances for associations with multiple traits to interact. Choosing the would-be tallest child would mean there may be other unanticipated or unwanted "go-alongs."

Further, what might be considered "ideal" in one culture, might be considered abhorrent in another. And what a parent chooses for a child might not be what the child would choose for him or herself. Allowing the parent to select a genetic signature for the child tramples on established notions of autonomy. Does the parent have the right to make these choices? What redress does the child have if he is unhappy with parental choice? Can s/he sue the parents, as Dr. Sivan Tamir presciently asked?[100]

Dr. Tamir raises questions of the child's right *not* to be enhanced vs. their right "to an open future."[101] Indeed, consideration of existing ethical

96. *Alzheimer's epigenetic drivers identified*, GENETIC ENG'G & BIOTECH. NEWS (Sept. 29, 2020), https://www.genengnews.com/news/alzheimers-epigenetic-drivers-identified/ [https://perma.cc/RY5Y-HPU9].

97. Evan A. Boyle et al., *An Expanded View of Complex Traits: From Polygenic to Omnigenic*, 169 CELL 1177–86 (2017).

98. Shahram Bahrami et al., *Shared Genetic Loci Between Body Mass Index and Major Psychiatric Disorders: A Genome-wide Association Study*, 77 JAMA PSYCHIATRY 503–512 (2020) (there seems to be a link between BMI and SCZ).

99. Daniel M. Jordan, *HOPS: a quantitative score reveals pervasive horizontal pleiotropy in human genetic variation is driven by extreme polygenicity of human traits and diseases*, 20 GENOME BIOLOGY (2019).

100. Sivan Tamir, *Postnatal Human Genetic Enhancement – A Consideration of Children's Right to Be Genetically Enhanced*, FRONTIERS SOCIO. (Nov. 8, 2016), https://www.frontiersin.org/articles/10.3389/fsoc.2016.00015/full [https://perma.cc/M2BT-7ABC].

101. *Id.*

proclamations such as the *Convention on the Rights of the Child* (1989)[102] does not even seem to have been probed before embarking on this *Oryx and Crake*-like adventure.[103] And once we have the ability to select against "unhealthy," "stupid," or "ugly" children, will a parent be required to employ such technology, as Savelescu's doctrine of "Procreative Beneficience" [104] implies?[105] This paradigm "holds that when a couple plans to have a child, they have significant moral reason to select, of the possible children they could have, the child who is most likely to experience the greatest wellbeing—that is, the most advantaged child, the child with the best chance at the best life."[106] One wonders if this paradigm trespasses on a competing cultural notion that every child is a gift, healthy or not.[107]

Even for those subscribing to Savelescu's notion—who gets to choose whether the embryo is primarily selected (bred) for beauty, brains, or brawn, and on what basis? Will the state be allowed to mandate that determination? Is beauty better than brains? Will the choice be based on whether the embryo is sexed as male or female, unwittingly reviving hopefully bygone stereotypes? Are will we be forced to revert back to Justice Holmes' unfortunate assumptions that "three generations of imbeciles are enough" if we can eliminate "imbeciles" entirely?[108] Surely, this procreative beneficence imperative reeks of Mengele-derived eugenics, a philosophy based on the Volk-public health imperative—that the health of the population is the most important focus of a physician—a concept rooted in and driving the practice of Nazi medicine.[109]

> Most . . . reports concentrate on immediate research ethics questions False of any new biomedical innovation: questions about physical risk, informed consent, and fair distribution of research benefits and burdens. But behind those deliberations, the memory of the Holocaust

102. *See also* Eur. Parl. Ass., *The Recommendations of the Council of Europe on Genetic Engineering*, RECOMMENDATION 934 (1982) (similarly invoking the "right to inherit a genetic pattern, which has not been artificially changed.").

103. MARGARET ATWOOD, ORYX AND CRAKE (Anchor Books 2003) (speculative fiction about a genius who seeks to genetically re-engineer a new humanoid society).

104. Michael Cook, *Savulescu interviewed on 'procreative beneficence',* BIOEDGE (Nov. 10, 2019), https://www.bioedge.org/bioethics/savulescu-interviewed-on-procreative-beneficence/13273 [https://perma.cc/YD54-T8WV].

105. Herissone-Kelly, *supra* note 41 ("Savelescu's 'principle of procreative beneficence' (PPB) holds that parents or single reproducers are at least prima facie obliged to select the child, out of a range of possible children they might have, who will be likely to lead the best life.") The author of this article disagrees. *See also* B. Saunders, *Is procreative beneficence obligatory?*, 41 J. MED. ETHICS. 175–8 (2015).

106. Bourne, *supra* note 42.

107. SNEAD, *supra* note 89, at 103.

108. Buck v. Bell, 274 U.S. 200 (1927).

109. DAVID G. MARWELL, MENGELE: UNMASKING THE "ANGEL OF DEATH" 9–10 (W.W. Norton & Company 2020).

> surfaces more fundamental ethical questions about where this research leads and the worry that we could repeat the mistake of creating genetic hierarchies from social prejudices and try again to remake our species against the backdrop of a fundamentally unjust vision of human health.[110]

Indeed, differing biological considerations occasioned via genotypic modification or phenotypic enhancement also have not been considered, including commingling objectives of disease prevention versus trait enhancement.[111]

The same questions arising regarding the propriety of gene-editing for phenotypic enhancement or genotypic editing also arise in the context of poly-genic scoring and selecting for (or against) uber-kids. These are not merely questions that must be asked before proceeding with, or permitting, or regulating HHGM, these are questions that probe the fundamental determination of what is it about humans that we value? And what do these technologies and their wanton promotion say about society at large?[112] The polygenic score assessment dilemma crystallizes these issues, even calling into question, or at least raising for consideration the use of HHGM for promoting health or selecting for the super-healthy.

C. Creating Uber-kids:

The concept of creating uber-kids by HHGM (either by genetically engineering them or selecting among available embryos for the "prettiest" present in the IVF store) and commercially advertising this service presumes an absolute faith in genetic determinism. That a child might have a lesser predisposition to disease—at least according to her or his genetic signature block—does not mean that a sibling-embryo with a lower HQ who has a greater (and undetected) genetic propensity for self-discipline might not enjoy greater health, as a result of her avoidance of sweets and devotion to regular exercise, while the child winning the genetic lottery has uncontrolled weaknesses and cravings, over-subscribing to these delights such that that he or she becomes victim to non-genetically driven obesity or diabetes, is not even considered.

110. Juengst, *supra* note 83.

111. Phenotypic prevention involves modifying the expression of pathogenic DNA variants to forestall their clinical effects in at-risk patients. Genotypic prevention involves controlling transmission of pathogenic variants between generations to avoid the birth of affected offspring. Preventive strengthening seeks to improve normal human traits to resist disease. These distinctions have been neglected in human gene editing governance discussions. *Id.*

112. *See, e.g.*, MICHAEL SANDEL, THE CASE AGAINST PERFECTION: ETHICS IN THE AGE OF GENETIC ENGINEERING (Harvard Uni. Press 2007).

One must even question allowing advertising of a technology that buys into the GATTACA-like vision of the future.[113] While identifying (and selecting against or "fixing") single gene diseases is a reliable and effective means of eliminating disease, using polygenic scores have far less reliability. Further, these tests predict (or try to) health conditions that might arise in the future, in many cases, conditions that are also environmentally mediated. Current estimates indicate that polygenic traits (those with more than one genetic effector) might have a 55% degree of accuracy, at best, at a population level.[114] Knowledge of an HQ also imposes a fore-knowledge the child may not wish to know, along with possible obligations of disclosure, possibly triggering discriminatory actions.[115]

Other questions involve informed consent, and whether this information imparts on the parent a duty to shield the child from exposure to risks exacerbating genetic proclivities. Thus, simply stated, in addition to the dangers of "too much knowledge," polygenic health scores are far from 100% predictive; an intelligence predictor would be even less reliable and would resurrect old tropes arguably better left buried.[116]

V. MORALITY IN SOCIETAL MOTION

A. Bioethical Issues and Social Justice:

While eradicating disease is a noble result of HHGM, the ancillary capacity of providing human improvement or enhancement also requires social justice considerations.[117] Will poor people have the same access to the technology? Will uneducated people have the same knowledge of possibilities? Will powerful people and regimes restrict access to the elite? While

113. GATTACA is a film about a culture dependent on genetic superiority as achieved via parents with the financial capacity to genetically engineer their children, and the flaws of such reliance on genes for advancement. The film is available online and worth a watch. GATTACA (Columbia Pictures 1997). The screenplay is also available. *See also* Antonio Regalado, *The World's First Gattaca Baby Tests Are Finally Here*, MIT TECH. REV. (Nov. 8, 2019), https://www.technologyreview.com/2019/11/08/132018/polygenic-score-ivf-embryo-dna-tests-genomic-prediction-gattaca/ [https://perma.cc/465W-BKHZ].

114. DENIS ALEXANDER, GENES, DETERMINISM AND GOD 138 (2018).

115. *See, e.g.*, Chadam v. Palo Alto School District, D.C. No. 4:13-cv-04129-CW (9th Cir. 2016). The decision is in limbo as "[t]he court has ordered mediation to resume before March 14, 2017 and has since appointed a mediator to the case." Jennifer K. Wagner, *Update on Chadam v. Palo Alto Unified School District,* THE PRIV. REP. (Jan. 24, 2017), https://theprivacyreport.com/2017/01/24/update-on-chadam-v-palo-alto-unified-school-district/ [https://perma.cc/GBN7-4K8D].

116. *See* (or better yet, don't see) generally, RICHARD HERRNSTEIN & CHARLES MURRAY THE BELL CURVE (1994) (explaining the variations in intelligence in American society as genetically governed).

117. "There has been a shifting of our longing for legal justice to social justice and—it must be noted—also a waning respect for law." Justice Louis D. Brandeis, *Remarks to the Chicago Bar Association* (Jan. 3, 1916).

Professor Doudna, the co-creator of the CRISPR technology, champions its use—she predicates her position on wide-spread availability, thereby bypassing social justice concerns.[118] But merely couching the issue as assuming broad availability of costly and optional health services is "wishful thinking." Health disparities based on socioeconomics are not addressed by merely wishing them away. That rich parents will be allowed to select a better health-future for their child merely highlights the disparity in health care we now find between rich and poor, along with the often-accompanying racial divide.

Heightened intelligence selection might be expected to be the most sought-after trait[119] and presents even worse problems than selection for better health. What appears to elude recognition or consigned to the back burner of cognition is the fact that high intelligence is not predictive of great achievement,[120] and that environmental factors—including unmodifiable ones such as birth order or geo-politics or economics—play a role in a gene's phenotypic expression.[121]

Even a raw intelligence score is the product of many genes, although soon we may be able to identify all of them. Once that happens, perhaps we can expect creation of a super-race of intellectual giants. Of course, if that technology becomes restricted to the rich or powerful, we will only increase genetic and wealth disparities. The super-achieving rich people, a product of both good genes and a better environment, will select for smarter children, leaving the poorer segment of the population (either because of lesser genetic endowment and/or lamentable environments) to wither, with the intellectual disparity becoming greater with each generation.

Alternatively, in the world of perfect social justice, if everyone is similarly enhanced, the intellectual disparities would still remain. Everyone might become smarter- but in the same comparative proportions. This situation conjures the intellectual wannabe who, seeking to cure her inferiority complex, discovers that we use only 10% of our brains. Coming upon an elixir enabling her to capture the unused 90% of cerebral capacity, she proudly boasts of her newfound prowess—at which point everyone takes the drug. And so, Ms. Super-Intellectual-Wannabe reverts to her original status at the low end of the newly enhanced IQ bell-curve. Furthermore, while

118. DOUDNA & STERNBERG, *supra* note 4.

119. Would-be mothers prioritize sperm from donors with high intelligence.

120. MALCOLM GLADWELL, OUTLIERS 10–18, 84–96,102 (2018) ("intellect and achievement are far from perfectly correlated.").

121. Michael Cook, *More protests over eugenics, this time at Michigan State*, BIOEDGE (June 20, 2020), https://www.bioedge.org/bioethics/more-protests-over-eugenics-this-time-at-michigan-state/13477 [https://perma.cc/UVD3-9KQJ].

everyone might be genetically enhanced—*all* who are now smarter—their environments still differ, leading to differences in phenotypic expression. The IQ-environment divide is further compromised by traits only indirectly related to intelligence, such as motivation, concentration, imagination, and creativity, and cross-right-brain left-brain thinking. All our predictive prowess and commercial promises, then, might amount to little, raising the importance of monitoring the commercial advertising and reporting.

B. The rights of society: the value of those who would not have been selected

Selecting for uber-health is also viewed as an attack on the disabled. And as disabilities scholars point out, one feature of genotypic prevention is the tacit judgment "that the burden of coping with new cases of genetic disease can outweigh any other value that individuals with the target genotypes might bring to a family or community."[122]

The dangers of the new technology also present us with the prime opportunity to commoditize humans, seeing humans as a type or functional unit, let's call then B-entities: the beautiful ones (the B-1's), the brainy ones (the B-2s), the brawny ones (the B-3s), reminiscent of the entities populating of *Brave New World*[123] who require periodic doses of Soma, a mild to potent amnesiac and euphoriant to allow them to tolerate the known limits of their persona. So, who wants to know that you will get cancer when you are forty-five, asks the child so genetically-determined?[124]

The deleterious social negatives of selecting for healthy children and deselecting the physically or psychologically compromised is highlighted when a parent has a choice between selecting the embryo with the healthiest genes or the smartest genes, as the two constructs do not go hand in hand. By selecting for the healthiest children-to-be, society would be selecting *against* the likes of certain great contributors to society who, with current technology available, would never have been born: physicist Stephen Hawking, with ALS; mathematician Charles Proteous Steinmetz, a dwarf with hip dysplasia; financial tech wizard, Fareida Bedioi, with cerebral palsy; or the blind astronomer Wanda Diaz Mersad, who discovered sonification. Mathematician, John Nash, was a schizophrenic (a genetic condition), whose son, a PhD in math, was similarly diagnosed giving us two generations of

122. Juengst, *supra* note 83 (citing ERIK PARENS, & ADRIENNE ASCH, PRENATAL TESTING AND DISABILITY RIGHTS (2000)).

123. ALDOUS HUXLEY, BRAVE NEW WORLD (Harper & Row 1932).

124. The issue also presents questions regarding insurability. *See The gene is out of the bottle*, THE ECONOMIST, Aug. 5, 2015, at 57.

schizophrenics—to paraphrase Justice Holmes. Others with serious psychological impairments such as Vincent Van Gogh and Sylvia Plath also made great contributions. And then we have those who are social or learning-challenged, including Dr. Carol Greider, a dyslexic and Nobel Prize Winner in biology (Agatha Christie was similarly dyslexic), and the autistic Dr. Temple Grandin, an autism activist.[125]

The uber-health proponents surely would claim genetic engineering could come to the rescue, allowing birth of these same personalities—minus their deficit. But as Stephen Hawking said, it was only the fear of imminent death that spurred him on to achievement,[126] and it was Dr. Mersad's blindness that enabled her discovery, using sound to compensate for her physical challenges. Dr. Grieder credits her dyslexia for enabling her to think in a different way, garnering her the Nobel prize. Other lesser-known persons who have suffered hereditable genetic injury such as inoperable breast cancer, credit the disease and the horrific journey they faced combatting it, with giving them a new sense of purpose and strengthening their marriage.[127]

On the flip side of the equation is the message we send devaluing those who have not attained uber B scores—the physically disabled,[128] the intellectually disadvantaged, or the phocomelic—missing an arm or a leg, the suicidal or the manic-depressive. What value do we ascribe to those "diminished" children when their siblings, blood-related or societally defined, are uber B's? Perhaps the lesser value assigned to creatures not attaining uber-B status devalues our humanity?[129] Certainly a sense of value, or a feeling of self-importance exists in these people, along with the happiness at being part

125. Geerat Verney was a blind paleontologist. Erwin Krebs, who discovered the Krebs cycle was hearing impaired. Kathiann Kowalski, *Disabilities don't stop these experts in science and tech*, SCI. NEWS FOR STUD. (Aug. 31, 2017), https://www.sciencenewsforstudents.org/article/disabilities-dont-stop-these-experts-science-and-tech [https://perma.cc/9VCZ-3H79].

126. Niall Firth, *Stephen Hawking: I didn't learn to read until I was eight and I was a lazy student*, MAIL ONLINE (Oct. 23,2010), https://www.dailymail.co.uk/sciencetech/article-1322807/Stephen-Hawking-I-didnt-learn-read-8-lazy-student.html [https://perma.cc/NW62-4UPV].

127. Personal communication JW now cured from inoperable cancer. Nov.30, 2019 (on file with author) ("What is life about? Without suffering what type of people would we be? Take my situation for instance. I carry the BRCA2 gene. It was probably passed down from my dad. If I hadn't had cancer, I don't know that I'd have had the life I've had. I don't know that I'd still be married (as cancer made my marriage so much stronger). I know that we would not have created the XXXX Foundation and raised over $4 million dollars and helped 4000 patients with cancer."). *See also* Dan Rather, *Gene editing will let us control our very evolution. Will we use it wisely?*, THE GUARDIAN (Dec. 8, 2019), https://www.theguardian.com/commentisfree/2019/dec/08/gene-editing-will-let-us-control-our-very-evolution-we-must-use-it-wisely [https://perma.cc/GM2X-EMN6].

128. "According to the WHO (1980), a person with a disability is not necessarily handicapped, if despite his/her limitations can have the fulfillment t of a respectable and livable life, without any kind of physical or mental barriers." Alessandra Pentone, *I am disabled but you make me handicapped*, DISABILITIES & BIOETHICS 19–20.

129. *See* Elie Klein, *The miracle of disability*, JERUSALEM POST, Dec. 22, 2019.

of a peer group, or contributing to the happiness of others, or the delight in partaking of nature even for those of limited talents, in some cases at higher levels than achieved by the genetically better-endowed. One only needs to read *Flowers for Algernon*[130] and follow the psychological journey and life experience of a profoundly retarded man who is suddenly given an elixir generating genius status, who then (sadly?) reverts to his former self, now happy in his station. This story, apparent when interacting with real persons similarly situated, demonstrates that those who may not have achieved uber B-status have value and worth—to themselves and to others, and that their life experience is profoundly determined by and reflected in the worth they feel by looking into someone else's eyes, especially a parent's.

The profitability of companies selling tinker-toy tots, gene-fixes, or eliminating embryos presenting lower genetic signatures (as opposed to their use to increase the likelihood of viability after birth or elimination of single gene-diseases) is a testament to the value society places on uber-B status.

VI. CONCLUSION

As new technologies emerge, it will be cumbersome to formulate laws or bioethical doctrine specific to each. It will be almost impossible not to be diverted from considering the moral, social, and human aspects of these technologies, technologies which superficially seem so magnanimous—curtailing disease, eliminating intellectual disability.

Unless we conceptualize the technologies more broadly, we will be scurrying to clean up the residues of societal conflict and the detritus of social concerns on a technology-by-technology basis. I, therefore, propose reclassifying HHGM technologies based on degrees of invasiveness, artificiality, and '*indelibility'* (ability to reverse results). Thus, *selecting for* certain traits by Pre-implantation Genetic Testing (PGT) may be considered an enhanced means of natural selection: if one wants tall or smart children, one used to marry a tall or smart spouse. Perhaps here, PGT might be akin to conventional reproductive choice and morally acceptable. *Selecting against* a trait (or disease) via PGT might be characterized as merely the inverse of *selecting for* a trait. Alternatively, it might be considered a public good, if it reduces disease. Editing genes *to correct for* nature's errors and mutations might be characterized as a form of surgical intervention, especially at a somatic level. This method of characterization enables us to understand the revulsion or fear generated by introducing hereditable changes to the population germline, as it is not akin to any "natural" means of

130. DANIEL KEYES, FLOWERS FOR ALGERNON (Harcourt, Brace & World 1972).

reproduction or evolutionary biological processes. Artificially duplicating genetic material or cloning gametes also might be antithetical to the natural order in that it, too, falls outside the natural order, either biologically, or conceived via cultural/biblical imperatives ("be fruitful and multiply") requiring inter-mixing of male and female genetic signatures.

Questions related to HHGM will force us to confront just what it means to be healthy as well as human. It will require us to ask whether we evaluate ourselves as individuals—or in comparison with other members of society. It will force us to delineate between health and uber-health—between baseline or enhancement. It will require us to balance easy availability of novel technology and acknowledgement of the dangers. This issue aims to provide a framework for answering these questions and developing solutions for some of them.