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DESIGNER BABIES, ROBOT MALPRACTICE, AND THE CURES FOR CANCER: A LEGAL SURVEY OF SOME MEDICAL INNOVATIONS

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INTRODUCTION

One of the elegant aspects of law is that it enables society to apply simple but robust rules to complex phenomena.[1] Although lawyers are not doctors,[2] they are often required to distill simple and essential facts from complex medical phenomena to apply rules of law to resolve disputes between parties. Similarly, although legislators are not doctors, their regulatory schema and legislative prescriptions affect medical research. This process has the power to retard or support the progress of medical innovation.

Recent advances in computer science and genetic research have made certain medical phenomena more complex, yet more promising. A group of new innovations – CRISPR, immunotherapy, and artificial intelligence – has been touted as fundamentally changing the nature of medicine. Whether these claims will turn out to be true is not for us to answer here. Instead, this article hopes to demonstrate both that none of these advances pose insoluble legal quandaries and that the perennial debates that exist in the medical law literature today graft nicely onto these new breakthroughs.

The purpose of this article is two-fold – first it aims to introduce these breakthroughs to the legal community. Although lawyers and judges can rarely participate in basic scientific research, except as subjects, lawyers are generally smart people who can contribute in other ways. For example, they can render relevant judicial opinions, help craft model laws and regulations, or espouse certain bioethical views in the court of public opinion. As will be mentioned below, medical research does not occur in a social vacuum, and legislative

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[1] See Richard A. Epstein, *Simple Rules for a Complex World* 21 (Harv. U. 1995) (arguing that basic legal principles can and should govern a complex, industrial society).
[2] See generally Barak Richman, *On Doctors and Judges*, 58 Duke L. J. 1731 (2009).

and regulatory barriers can often be as large as scientific ones. Former head of the National Cancer Institute Dr. Vincent DeVita wrote, "Too often, lives are tragically ended not by cancer but by the bureaucracy that came with the nation's investment in the war on cancer . . . ."[3] This article hopes to arouse excitement in the legal community around these advances to spur legislative and regulatory reform.

Second, we hope to show how these breakthroughs fit into the existing legal framework. Medical innovations do not require innovative jurisprudence or novel regulatory schemes. If there are areas where there are difficulties fitting technology into existing legal and regulatory frameworks, this is a mark against the framework, not against the technology. In those areas where updates are necessary, they do not need to go far beyond existing frameworks.[4] A theme of the article is that areas of the law which derive from the casuistry of common law – case-by-case reasoning – such as medical malpractice, have legal standards that are robust and capable of dealing with a novelty such as a robot doctor. Areas of the law that have been created relatively recently in response to political vicissitudes, such as the Food and Drug Administration, have more difficulty dealing with a phenomenon like the personalized medicine of new immunotherapies. We hope to show where the law gets it right and where there are issues.

As a general matter, innovation and experimentation in medicine is not as easy as in other fields, and thresholds for adoption are much

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[3] Vincent DeVita, *The Death of Cancer* 32 (Sarah Crichton Books 2015).

[4] Compare Frank H. Easterbrook, *Cyberspace and the Law of the Horse*, 1996 U. Chi. Legal F. 207 (1996) (arguing that the best way to learn and craft the law of a particular field is to study general rules) with Lawrence Lessig, *The Law of the Horse: What Cyberlaw Might Teach*, 113 Harv. L. Rev. 501 (1999) (arguing that the nature of cyberspace is unique and can reveal general principles of law)

higher. This is because the stakes are often much higher. Experimentation often requires trial and error and large data sets to derive statistically meaningful data. This is simply not possible because humans do not, as a general matter, want to be guinea pigs. There are certainly patients who elect to have risky procedures or try experimental drugs, and federal law recently extended them the courtesy to allow them to take such risks with passage of the Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017.[5] But these risks are generally taken only in the direst of circumstances. Medicine benefits from perfectly healthy non-human animals that are experimented upon and used as practice for procedures. Medical progress is not the sole value of our society. Because the stakes are so high, many, both in the government and outside, are cautious when it comes to health treatments. Additionally, doctors do not want to experiment for fear of liability. This means that the benefits sometimes must demonstrate overwhelming improvement over the *status quo* for the innovation to be adopted; treatment paradigms must shift before there is widespread adoption of a new innovation.[6]

Each of the innovations discussed in this article has the potential to be such a paradigm shifter, even recognizing that such shifts are rare and that most science is incremental.[7] This article will be divided into three sections, each dealing with the aforementioned medical innovations that have captured the imagination of researchers, practitioners, and financiers.

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[5] Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017, Pub L No 115-176, codified at 12 USC § 360bbb-0a.
[6] E.g. insulin, penicillin, etc.
[7] See generally Thomas Kuhn, *The Structure of Scientific Revolutions* (U. Chi. 4th ed. 2012).

The article will begin with CRISPR, an acronym for clustered regularly interspaced short palindromic repeats. At base, this technology is a new way of conducting genetic research and implementing genetic therapies. It allows researchers and clinicians to locate and alter segments of a genome. This raises a host of legal issues. Specifically, patent law, ethical considerations, privacy, and drug approval will all be addressed.

The next innovation, although not technically something new, is immunotherapy. Immunotherapy is a branch of medicine that seeks to treat diseases through processes that in some way alter the body's natural immune system. The therapy has been around for over a hundred years, but with recent advances in genetic understanding, there is a renewed interest and demonstrated capability in its therapeutic potential.[8] As with CRISPR, regulatory concerns over drug approval predominate here, specifically over personalized medicine. The article proposes that a more liberal approach be taken towards approval of immunotherapies than towards typical new drug applications for certain structural reasons.

Finally, artificial intelligence will be addressed, specifically as it relates to diagnosis and treatment. Machine learning is a technique that allows a computer to draw inferences and correlations from data that it consumes. This opens the possibility of using computers to diagnose and suggest treatments for diseases based on collections of past data. This also raises the possibility of pursuing legal action against a robot. Medical malpractice in this context will be discussed.

One of the goals of this paper and hopefully this symposium is to arouse some excitement in the legal community around these breakthroughs that have such promise.

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[8] See William K. Decker, et al, *Cancer immunotherapy: Historical Perspective of a Clinical Revolution and emerging Preclinical Animal Models*, 8 Frontiers in Immunology (2017).

I. CRISPR

A. OVERVIEW OF CRISPR-CAS9[9]

The CRISPR-Cas9 system is a tool to edit genes. Genes are the basic building blocks of an organism's genome, which is the basic genetic material of that organism. This genetic material is the blueprint from which structures and processes of an organism are created. The blueprint is made up of deoxyribonucleic acid (DNA)[10], which is composed of base pairs, whose initials are G, C, A, and T. Although not fully causally understood, this blueprint has a role to play in everything from certain diseases to certain character traits in humans. An ability to edit this blueprint opens the possibility of eradicating certain diseases as well as more dystopian applications.

CRISPR was originally described by Japanese researchers in 1987.[11] A series of short, repeating DNA sequences was noticed in *Escherichia coli* (*E. Coli*) bacteria. It was eventually discovered that within these sequences there were sequences that matched those of the viruses that were threats to *E. Coli* bacteria. These sequences were described as clustered regularly interspaced short palindromic repeats, or CRISPR, for short. It was hypothesized that CRISPR and its associated genes (*cas*), were a defense system that helped form a

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[9] See *CRISPR Guide* (addgene 2017), online at https://www.addgene.org/crispr/guide/ (visited Sept. 25, 2018) (Perma archive unavailable).

[10] This is true of most organisms, although some viruses have a ribonucleic acid (RNA) genome.

[11] Yoshizumi Ishino, et al, *Nucleotide Sequence of the Iap Gene, Responsible for Alkaline Phosphatase Isozyme Conversion in Escherichia Coli, and Identification of the Gene Product*, 169 J. Bacteriol. 5429 (1987).

bacterium's immune system.[12] CRISPR is what allows a bacterium to recognize an invader.

From this insight, researchers began to repurpose the CRISPR-Cas system so that instead of recognizing threats to a bacterium, they could recognize threats to a genome. Just as a virus is recognizable by a series of base pairs, so too are certain genetic malfunctions, such as Tay-Sachs disease. By "inputting" these genetic mutations into the CRISPR-Cas system, researchers can target these mutations. Once targeted, however, scientists wanted to discover ways to alter the sequences that they found.

When an individual is editing a document and wants to change some aspect of the paper throughout, he will use the "Control-F" function to find and then replace the word or series of words he wishes to change. Such a similar replacement method, using CRISPR, takes place using the Cas9 enzyme, which first unzips a DNA strand and engages in a cutting process, which makes insertion possible. Afterwards, a ribonucleic acid sequence, known as guide RNA, binds to the DNA strand and inserts the new sequence. This new insertion can take place using two methods, nonhomologous end joining (NHEJ) or homology-directed repair (HDR).[13] This system is not completely manipulable because, for instance, a target sequence must be around 20 nucleotides long and it cannot be identical to any

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[12] Hannah K. Ratner, Timothy R. Sampson, and David S. Weiss, *Overview of CRISPR-Cas9 Biology*, Cold Spring Harbor Lab Press 1023, 1029 (Oct 16, 2018).

[13] HDR is favored where precise editing is desired. "The expected alterations in the target DNA were observed, indicating that site-specific DSBs by RNA-guided Cas9 had stimulated gene editing by nonhomologous end joining repair or gene replacement by homology directed repair." Jennifer A. Doudna and Emmanuelle Charpentier, *The New Frontier of Genome Engineering with CRISPR-Cas9*, 346 Science Magazine 1077, 1081 (Nov. 2014).

other sequences in the genome. This means that not all sequences in a genome can be targeted and edited. Although not perfect, and research here is evolving, this method of gene editing has captured the imagination of scientists, in part because of its lower cost and greater effectiveness in comparison to other methods.[14]

B. INTELLECTUAL PROPERTY

Because there were few legal barriers to the kind of research that was foundational to the discovery of CRISPR,[15] a number of teams made unique and sometimes overlapping advancements, as is often the case with scientific discovery. As these advances began to lead to a product of economic value, disputes arose over ownership and discovery of the CRISPR-Cas system. The two primary teams to discover CRISPR were led by Dr. Jennifer Doudna and Dr. Emmanuel Charpentier, on the one hand, and Dr. Feng Zhang, on the other. Dr. Zhang and his team from the Massachusetts Institute of Technology filed their first patents before the America Invents Act's relevant provisions became active in 2013.[16] These provisions moved America from a first-to-invent to a first-to-file patent system. In the old first-to-invent regime, courts were asked to conduct a proceeding to determine whether another later-to-file party was actually the first to invent and therefore entitled to patent protection.

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[14] See, for example, Tomislav Meštrovic, *How Does CRISPR Compare to Other Gene-Editing Techniques* (News-Medical.net), online at http://www.news-medical.net/life-sciences/How-Does-CRISPR-Compare-to-Other-Gene-Editing-Techniques.aspx (visited Sept. 25, 2018).

[15] For instance, the animal rights organization People for the Ethical Treatment of Animals (PETA) does not currently include protection of bacteria as a goal in their mission statement. *Our Mission Statement* (PETA), online at http://www.peta.org/about-peta/ (visited Sept. 25, 2018).

[16] See American Invent Act, 35 U.S.C. § 321 (2012).

This proceeding, known as an interference proceeding, is bounded by certain conditions, such that not everyone would be able to challenge the patent. Still, many have criticized the system for creating inefficiencies.[17] As such, patent applications filed after March 16, 2013 are no longer subject to interference proceedings. Thus, while the outcome of the interference proceeding and current disputes over CRISPR may be of great importance to the parties, because of the America Invents Act, they are of less consequence to the broader scientific community.[18] More important is the broader question of intellectual property in pharmaceuticals.

In *Association for Molecular Pathology v. Myriad Genetics* (2013),[19] the Supreme Court held that while naturally-occurring DNA sequences cannot be patented, artificially-created sequences can be. The CRISPR-Cas system is based on naturally-occurring elements. As mentioned above, the palindromic repeats were first discovered in bacteria. But once discovered, the sequences of DNA have been manipulated to change their function. Additionally, scientists have devised novel ways of delivering new sequences, which do not occur in nature. This would seem to lend support to the idea that the CRISPR-Cas system is patentable.[20] This issue has yet to come before a court, however.

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[17] See Richard A. Epstein, *Patent Respect* (Defining Ideas, Nov 20, 2017), archived at https://perma.cc/P7JU-YEMF.

[18] But see James W. Sanner, *The Struggle for Crispr: A Billion Dollar Question in Intellectual Property*, 2016 U. Ill. J. L. Tech. & Pol. 431, 436-37 (Fall 2016) (arguing that the case leads to important implications about what constitutes an obvious advance in evaluating patentability).

[19] *Association for Molecular Pathology v. Myriad Genetics*, 569 U.S. 576, 589-95 (2013).

[20] "The patents directed at CRISPR avoid this pitfall because, despite CRISPR itself being an arguable product of nature, the claims are directed at methodologies for introducing the CRISPR-Cas9 system into cells and using it to accomplish gene-editing

If patentable, CRISPR falls into the preexisting debate over intellectual property protection for pharmaceuticals. There is a rich literature and public discussion debating the appropriate level of this protection.[21] Public scrutiny about drug costs has brought the issue to the forefront. There is both a moral and utilitarian calculus to the intellectual property debate. On the moral front, there are those who claim that it does not make sense to talk about a property right in a non-scarce good, like an idea, while there are others who claim that an inventor has an absolute property right in his idea. Then there is the utilitarian debate between those who think that intellectual property protection incentivizes invention and those who believe that the patent system is stifling. While there are absolutist positions, many fall along a spectrum where intellectual property is to be protected, but only to a certain extent.

Without a doubt, intellectual property protections increase the price of drugs in the United States. For small molecule drugs, the reduction in price when a generic is allowed on the market is 80 percent and for biologics this could be 20 percent.[22] The cost of producing an FDA-approved drug is estimated to be over $2.5 billion and can take more than a decade.[23]

This article does not purport to solve these problems, but merely says that CRISPR does not pose any unique problems to the extant

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tasks beyond the cells' normal natural function." Sanner, 2016 U. Ill. J. L. Tech. & Pol. at 437 (cited in note 18).

[21] See Dean Baker, et al, *Should the Government Impose Drug Price Controls?*, (N.Y. Times Jan 10, 2016), archived at https://perma.cc/M7D5-SZCU.

[22] See Jeremy A. Greene and Kevin R. Riggs, *Why Is There No Generic Insulin? Historical Origins of a Modern Problem*, 372 New England J. Medicine 1171, 1173 (2015).

[23] See Rick Mullin, *Tufts Study Finds Big Rise in Cost Of Drug Development*, Chemical & Engineering News (Nov. 20, 2014), online at https://cen.acs.org/articles/92/web/2014/11/Tufts-Study-Finds-Big-Rise.html (visited Sept. 25, 2018).

system of intellectual property regulation in this country.[24] The only unique issue posed by genetics, as such, was resolved by the Supreme Court in the *Myriad* case. This is because therapeutics that stem from CRISPR will not be naturally occurring. The central issue for patent law will be about the obviousness and uniqueness[25] of the methods of these artificial treatments; but this is a central question for patent law and not unique to CRISPR.

Much more unique are issues involving the FDA, as genetic therapeutics and especially precision and personalized medicine pose challenges to the Administration's regulatory framework, which was designed to deal with diseases that target millions.

C. THE FOOD AND DRUG ADMINISTRATION

Much has been written about the FDA and its drug approval process. Some claim the FDA is too liberal in its approval process, while others claim the agency is too restrictive.[26] Many of these arguments, however, were written about drugs that are wholly different from the kinds of therapeutics that CRISPR can enable.

The FDA has yet to lay out a comprehensive approach to addressing CRISPR, but then-Commissioner Robert Califf wrote a note posted on the Administration's website outlining some of his thoughts. The note said that while the Administration is used to

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[24] Nor do either of the other two advances to be discussed below.

[25] *Regents of the University of California v. Broad Institute, Inc.*, 903 F3d 1286, 1291 (Fed Cir 2018).

[26] DeVita, *The Death of Cancer* at 190-215 (cited in note 3); see Leah Isakov, Andrew W. Lo, and Vahid Montazerhodjat, *Is the FDA Too Conservative or Too Aggressive?: A Bayesian Decision Analysis of Clinical Trial Design* *1 (draft paper, MIT, Jan. 24, 2016), online at http://alo.mit.edu/wp-content/uploads/2015/08/FDA_26.pdf (visited Sept. 25, 2018).

dealing with new drugs, "the potential breadth of applications and the fundamental nature of altering the genome call for the participation of multiple constituencies in considering the most effective regulatory policies to address any potential risks."[27] The note suggested that CRISPR-Cas would be regulated as a biological product, and thus be evaluated by the Center for Biologics Evaluation and Research (CBER), an arm of the FDA. This is a center within the FDA that is tasked with evaluating the use of biologics, including vaccines, blood transfusions, and gene therapies.[28] According to Califf, there were no objections to CRISPR therapeutics, but there were still risks worth addressing: "Proposals for NIH-funded human gene therapy clinical trials are discussed and reviewed for scientific, clinical, and ethical issues by the NIH's Recombinant DNA Advisory Committee (RAC). The RAC recently discussed (and did not find any objections to) the first clinical protocol to use CRISPR/Cas9-mediated gene editing.[29] The potential for 'off-target' effects such as insertions or deletions at unintended genetic loci has been identified by experts in the field as a key concern."[30]

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[27] Robert M. Califf and Ritu Nalubola, *FDA's Science-based Approach to Genome Edited Products* (U.S. Food & Drug Administration, Jan. 18, 2017), online at http://blogs.fda.gov/fdavoice/index.php/tag/crispr/ (visited Sept. 25, 2018), archived at https://perma.cc/DK6L-WSJU.

[28] See, for example Food and Drug Administration, Proposed Approach to Regulation of Cellular and Tissue-Based Products; Availability and Public Meeting, 62 Fed. Reg. 9721 (1997) (announcing proposed regulation).

[29] See Jocelyn Kaiser, *First Proposed Human Test of CRISPR Passes Initial Safety Review* (Science, June 21, 2016), archived at https://perma.cc/VG7Z-TMY4.

[30] Robert M. Califf and Ritu Nalubola, *FDA's Science-based Approach to Genome Edited Products* (cited in note 27). See also BioPharm International Editors, *FDA Describes Its Approach to Genome-Edited Products* (BioPharm, Jan 18, 2017), archived at https://perma.cc/D43B-TUUH.

While approval by the RAC is a step forward for both testing and clinical trials, this committee is not dispositive and the FDA will be able to weigh in independently. Some have speculated that because this is a novel issue, the "CBER would take a very conservative approach toward the first approval of a human biological product that is a nucleic acid-nuclease complex intended to permanently change the phenotype of the target tissue . . . [and] FDA would also need to consider the probability of off-target effects of the CRISPR/Cas system, even if the scientific literature states that this probability is low."[31]

Whether this is correct as a positive matter, there are some good reasons why the FDA should actually be more liberal in its cost-benefit analysis of CRISPR-Cas therapies than in those of more traditional medicine. These reasons primarily stem from the unique nature of gene therapies.

Genetic diseases lie along a spectrum of complexity in their causes. On one end of the spectrum are disorders that are caused by a single point mutation of a single gene and on the other end of the spectrum are polygenic mutations, combined with environmental variables that contribute to the development of disease. An example of a monogenic disorder is Tay-Sachs disease, which is caused by a mutation of the gene that regulates an enzyme on chromosome 15. An example of a more complex disease is breast cancer, which may have an identifiable genetic component, but also is thought to be influenced by environmental factors.[32]

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[31] Jay W. Cormier and Ricardo Carvajal, *Ready or Not, CRISPR and Gene Editing Have Arrived and Are Here to Stay*, Update 8 (Aug. 2016).

[32] See Devra Lee Davis, et al., *Rethinking Breast Cancer Risk and the Environment: The Case for the Precautionary Principle*, 106 Envir. Health Perspectives 523, 523-24 (Sept. 1998).

On this spectrum, it would make sense that, although monogenic disorders can be highly penetrant and significantly affect disease risk, more conditions are likely to be the result of oligogenic or polygenic, lower penetrance gene disorders. In thinking about evolutionary selection, it would follow that those genes not expressed may not have evolutionary selection pressure equivalent to those that are more frequently expressed; genes not expressed tend to fade from cosmic presence over time. If a gene does not manifest, then it cannot be selected for. This makes sense on a logical level and is borne out by specific and general empirical research. Podder and Ghosh demonstrate "that [polygenic disorder] genes are under weaker selection pressure than [monogenic disorder] genes . . . ."[33] And diseases like Tay-Sachs affect fewer individuals than diseases like breast cancer.[34] Additional traits of the gene, such as location on an autosomal versus sex chromosome and dominant versus recessive inheritance pattern, also combine to affect the prevalence of gene expression. Biomedicine's initial forays into gene manipulation with CRISPR likely will focus on monogenic targets for reasons described below.

For the discussion below, what is important to take from the above is that there are biological reasons why monogenic diseases

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[33] Soumita Podder and Tapash C. Ghosh, *Exploring the Differences in Evolutionary Rates between Monogenic and Polygenic Disease Genes in Human*, 27 Molecular Biology and Evolution 934, 935 (Dec. 2, 2009), online at http://mbe.oxfordjournals.org/content/27/4/934.full.pdf+html (visited Sept. 26, 2018).

[34] 1 per 320,000 newborns is affected (Tay-Sachs). Stephen L. Nelson, *GM2 Gangliosidoses* (Medscape Apr. 25, 2018), online at http://emedicine.medscape.com/article/951943-overview (visited Sept. 26, 2018); About 1 in 8 U.S. women (about 12%) will develop invasive breast cancer over the course of her lifetime. *U.S. Breast Cancer Statistics* (Breastcancer.org Jan. 9, 2018), online at http://www.breastcancer.org/symptoms/understand_bc/statistics (visited Sept. 26, 2018).

are going to be less prevalent in a population than polygenic diseases.

While treatment of polygenic diseases is certainly within the capability of CRISPR-Cas therapies, many researchers have focused their attention on monogenic disease. In laying out a development program, Hsu, Lander, and Zhang specifically note, "For a monogenic recessive disorder due to loss-of-function mutations (such as cystic fibrosis, sickle-cell anemia, or Duchenne muscular dystrophy), Cas9 may be used to correct the causative mutation."[35] It is telling that this is where they have decided to initiate their program.

There are also bioethical considerations here that militate toward first focusing on catastrophic monogenic diseases. In February 2017, the National Academy of Sciences released a report making a number of suggestions with respect to human genome editing. It concluded that "clinical trials of genome editing in somatic cells for the treatment or prevention of disease or disability should continue, subject to the ethical norms and regulatory frameworks . . . ." On the other hand, "somatic genome editing for purposes other than treatment or prevention of disease and disability should not proceed at this time."[36] In other words, tackling diseases – and specifically relatively simple genetic ones – is less problematic than pursuing enhancement beyond a baseline of normal health. The concept of "enhancement" is a much broader one than curing specific diseases and likely covers more of the population. For now, because these

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[35] Patrick D. Hsu, Eric S. Lander, and Feng Zhang, *Development and Applications of CRISPR-Cas9 for Genome Engineering*, 157 Cell 1262, 1274 (June 5, 2014).

[36] *Report Highlights: Human Genome Editing Science, Ethics, and Governance* *2-3 (National Academy of Sciences and National Academy of Medicine, Feb. 2017), online at http://www.nationalacademies.org/cs/groups/genesite/documents/webpage/gene_177260.pdf (visited Sept. 26, 2018).

therapeutics that deal with specific diseases are thought to treat smaller populations, this is something that should militate toward a more liberal approach to approval.

This research program is no longer merely theoretical. In 2016, the FDA approved the first clinical trial in humans for the treatment of Duchenne's disease. There are a number of recently-established public companies that are using CRISPR-Cas to develop therapies for the treatment of diseases. In their prospectuses, the primary diseases they are developing their cures for are monogenic ones. While research and funding for more complex disorders certainly sits on the horizon, this is the state of research today.

The implications for the law are clear when understood in light of both the FDA's governing statute and its *raison d'etre*.

After passage of the Drug Efficacy Amendment in 1962, also known as the Kefauver-Harris Amendment,[37] drug companies were required to prove efficacy in addition to safety. As a practical matter, this meant a new requirement for randomized clinical trials. These trials add a cost of both time and money to the drug approval process. Calls to reform this process abound and there have been numerous changes to the original formulation in response to the demand for new drugs from patients and their advocates.[38] Indeed, the situation is becoming so drastic that a former NCI director pathologized the FDA's over-conservatism, calling it Frances Kelsey Syndrome.[39] This "disease" is present where government officials are

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[37] An Act to Protect the Public Health by Amending the Federal Food, Drug, and Cosmetic Act to Assure the Safety, Effectiveness, and Reliability of Drugs, Authorize Standardization of Drug Names, and Clarify and Strengthen Existing Inspection Authority; and for Other Purposes of 1962, Pub. L. No. 87-781, 76 Stat. 780.

[38] See, for example Richard A. Epstein, *The Other Drug War* (Hoover Institution, Jan. 25, 2016), online at https://www.hoover.org/research/other-drug-war (visited Sept. 26, 2018).

[39] DeVita, *The Death of Cancer* at 190 (cited in note 3).

irrationally risk averse because they do not want to see any negative headlines that jeopardize their careers or funding. Exhibit A of such headlines are those from the thalidomide episode and its protagonist, Frances Kelsey. Because newspapers rarely print stories about the individuals who die because of drugs that were not approved fast enough, there is a systemic bias to overweight the risk of dangerous drugs and not dangerous delays.

Sensing that its procedures are often not effective in responding to patients' demands, the FDA has expedited procedures for allowing their use in certain circumstances. These procedures, known as expanded access or compassionate use, allow for the use of investigational new drugs (IND) outside of the traditional clinical trials that are required for new drug approval.[40] Expanded use is available only where, *inter alia*, the patient or patients to be treated "have a serious or immediately life-threatening disease or condition, and there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition."[41] This system has come under fire for the burden it places on doctors and patients to justify their decisions.[42]

A more liberalized regime was implemented with great success in the oncology field during the 1980s. The program, known as the Group C drug distribution system, had the approval of drugs fall within the purview of the National Cancer Institute, with a tripartite system created for classifying drugs. Drugs classified in Groups A and B were given to investigators in early-stage trials. If they

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[40] 21 CFR § 312.300 et seq.

[41] *IND Applications for Clinical Treatment (Expanded Access): Overview* (FDA, June 2, 2016), archived at https://perma.cc/X5XX-H6NY.

[42] Recent attempts to rectify this situation include passage of the aforementioned Right to Try Act of 2017.

demonstrated any efficacy in more than one trial, they would be categorized into Group C and be made available to any patient whose doctor filled out the brief Form 1572.[43] The NCI would track any adverse reactions reported by doctors. As Dr. DeVita notes, "During its existence, more than twenty anticancer drugs were categorized as Group C and made available to cancer patients who needed them." [44] The program also had buy-in from the pharmaceutical companies and from doctors.

The success of the Group C program led to the creation of the IND process, which sought to formalize this program. The IND request process has been noted for its ineffectiveness due to multiple layers of bureaucracy and paperwork, which create a temporal and dispositional disincentive for doctors to proceed through that route.

What this article proposes is that CRISPR-Cas inspired drugs be subject to some version of the Group C drug distribution system on a prima facie basis. Given the above structural reasons that indicate monogenic disorders are more likely to be the subject of CRISPR-Cas trials and experiments in the near future, the FDA should approach the CRISPR-Cas therapy approval process in a different manner than they approach that of other drugs.

One central reason for treating genetic disorders as different from conditions like high cholesterol is that the patient characteristics are inherently different. It can be known from birth when people have crippling genetic disorders, and their lives are immediately and permanently altered. In the case of high blood pressure, while patients certainly experience symptoms, the condition does not play as central a role in their lives. Because of the centrality of genetic disorders, patients and their doctors are forced to learn more about

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[43] DeVita, *The Death of Cancer* at 206 (cited in note 3).
[44] Id. at 207.

the diseases. Patients' knowledge of their condition when suffering from chronic diseases like hemophilia differs from that of those suffering from conditions like high blood pressure, although as we move toward complete genome sequencing at birth, these predispositions could be known in utero.

Along this line of reasoning, because individuals with these disorders are likely going to be a smaller portion of the population that has more knowledge about their conditions, their consent is likely to be more informed and the risks of a bad decision are lowered in this instance. Public health catastrophes seem less likely to occur in defined populations with altered risk tolerances because of preexisting understanding of their conditions. These genetic diseases are wholly different from morning sickness and thalidomide. This fact is a counterargument to the position that there should always be a case-by-case analysis of drugs enabled by CRISPR and that any thumb on the scale will hinder this process.

D. HIPAA

One final area where this new method of research abuts regulations is in the dissemination of genetic information for research purposes. The Health Insurance Portability and Accountability Act of 1996 (HIPAA) is the primary federal law regulating the use and dissemination of protected health information. HIPAA's Privacy Rule sets certain requirements for both covered entities that collect patient data and entities that wish to use that data for clinical and epidemiological research. Covered entities, including health care providers and laboratories, are generally only able to share personal health information, including genetic information, if the patient consents. One exception, relevant for our discussion, comes with respect to de-identified data. A data set may be shared with researchers without a patient's consent if that data excludes 16 unique identifiers, including names, zip codes, and social security numbers. Another method by which information can be shared is by

having a qualified statistician determine that there is no way the information could be used to determine an individual patient's identity.[45]

Although this will be discussed below, progress in machine learning has made it possible for those not associated with the medical profession to use large datasets to draw relevant clinical correlations. The correlations drawn here would be of particular relevance to genomics. The reason why is that computer power is able to minimize the difficultly of drawing correlations that involve multi-factor inputs. In the above spectrum of polygenic and monogenic disorders, one of the reasons why monogenic disorders have been easier to understand is because the correlation between any input to be altered and the phenotypic output is better understood – this has led to effective screening networks, such as those in the Ashkenazi community for preventing Tay-Sachs disease. If researchers were better able to draw correlations from large data sets, polygenic disorders would be easier to treat.

But as will be shown below, these correlations can only be understood using massive data sets. The strength of modern neural networks is in the data that they are trained on. In many areas of society, data are not protected as stringently as in the health care setting.[46] It is not a coincidence, however, that it is often easier to

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[45] 45 CFR § 164.514(a)–(c).

[46] As privacy scholars such as Daniel Solove have observed, the current regulation of individual privacy in the United States is an unwieldy patchwork of common law, constitutional law, and federal and state regulation. As such, privacy has become too amorphous and broad a doctrine to provide reasonable rules for the research use of genetic data. The next section describes how the privacy framework conceptualizes risk associated with the use of genetic data and how the overstatement of risk contributes to the propertization of this data under current law. Jorge L. Contreras, *Genetic Property*, 105 Georgetown L.J. 1, 18-28 (2016). See also Daniel J. Solove, *A*

conduct research in areas like traffic regulation or actuarial sciences where data is more freely available.

The situation in preventing the dissemination of genetic information has been described as a tragedy of the anti-commons.[47] The tragedy of the commons is that in a system of undefined property rights, no one is incentivized to care for common areas and they will fall into disrepair. This is the classic argument for well-defined property rights. [48] The tragedy of the anti-commons, however, exists where property rights are so defined and expansive that they stifle innovation by granting an individual the right to exclude others from something that he ought not have a right to exclude others from. So, to give an absurd example, if the state were to declare that an individual has a property right in the letter "e" and royalties must be paid for its use, then science would be severely limited. This debate is an analogue to the above debate in patent law as between strong and weak protection designed to encourage either inventors or innovators.

But unlike in the above debate, the answer with respect to genetic privacy seems more straightforward. Whatever the case for an individual inventor's ownership in his invention, the case for the individual's ownership in material that he willingly parts with is on shakier moral and utilitarian grounds. There does not seem to be an inalienable right to one's own genetic information that cannot be contracted away. Just as an individual may contract with a company

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Taxonomy of Privacy, 154 U. Pa. L. Rev. 3 (2006) (articulating different conceptions of privacy).

[47] Contreras, *Genetic Property* at 7 (cited in note 46); Michael A. Heller, *The Tragedy of the Anticommons: Property in the Transition from Marx to Markets*, 111 Harv. L. Rev. 621, 624 (1998) (defining the "tragedy of the anticommons").

[48] See Harold Demsetz, *Toward a Theory of Property Rights* 57 Am. Econ. Rev. 347, 355 (1967).

to give up identifiable personal information in exchange for free services, like email or social networking, so too should an individual be allowed to exchange his genetic information with genetic testing companies that then use that data for research. Instead of being subject to the requirements of the Privacy Rule, genetic material should be subject to the same contract law principles that governs an individual customer's relationship with an Internet company like Google or Facebook.

II. IMMUNOTHERAPY AND PERSONALIZED MEDICINE

Long before the discovery of DNA and modern gene therapy, doctors had been experimenting with the body's immune system as a method of combatting disease. The basic idea of immunotherapy is that bioengineers supplement the body's immune system, including lymphocytes that recognize and kill pathogens, to fight previously incurable diseases. This idea is not new. In 1893, William Coley published a paper detailing his attempts at treating cancer through injecting the bacteria *streptococcus* into his patients.[49] Dr. Coley noticed that one of his patients saw a total remission of his cancer after he became infected with the bacterium.[50] Throughout the last century, immunotherapy saw its popularity ebb and flow, but in recent years the field has seen an explosion of academic and clinical interest.[51]

Although two distinct fields, gene editing is used in new immunotherapy techniques. In 2016, the National Institute of

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[49] William B. Coley, *The Treatment of Malignant Tumors by Repeated Inoculations of Erysipelas. with a Report of Ten Original Cases*, Clin. Orthop. Relat. Res. 3 (1991).
[50] Id.
[51] Decker, et al, 8 Frontiers in Immunology (cited in note 8).

Health's Recombinant DNA Advisory Committee was presented with a proposal to use CRISPR-Cas to alter T cells, which are integral lymphocytes that destroy antigens. The Committee was unanimous in its approval, with one abstention.[52] In the presentation to the Committee, the investigators noted that CRISPR-Cas has the potential to enhance T cell therapies.[53] The NIH is not the only federal body whose approval is necessary for such testing; its mandate only applies to institutions receiving NIH funding.[54] The FDA has said that the NIH's recommendations, "may be considered during our overall review of investigational new drug applications (INDs) submitted to FDA."[55]

The question, however, is: how does immunotherapy that incorporates gene editing techniques fit into the existing regulatory structure? In some ways, very well, but in other ways not at all. As a matter of positive law, the FDA can and has claimed that it has authority to regulate these immunotherapy drugs because they are

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[52] Laura McGinley, *Federal Panel Approves First Test of CRISPR Editing in Humans* (Washington Post, June 21, 2016) online at https://www.washingtonpost.com/news/to-your-health/wp/2016/06/21/federal-panel-approves-first-test-of-crispr-editing-in-humans/?utm_term=.ecafe797e44f (visited Sept. 26, 2018) (Perma archive unavailable).

[53] *June RAC Briefing Slides* *13 (National Institute of Health, Recombinant DNA Advisory Committee, June 21, 2016), online at https://osp.od.nih.gov/wp-content/uploads/2016/08/1524_RAC_Briefing_Slides.pdf (visited Oct. 1, 2018) (Perma archive unavailable).

[54] "Institutions that receive NIH funding for any research involving recombinant or synthetic nucleic acids, unless such research is specifically exempted by the NIH Guidelines, must comply." *Frequently Asked Questions: NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules* *2 (National Institute of Health, April 2013), online at https://osp.od.nih.gov/wp-content/uploads/2013/11/Synthetic_FAQs_April_2013.pdf (visited Oct. 1, 2018) (Perma archive unavailable).

[55] Robert M. Califf and Ritu Nalubola, *FDA's Science-based Approach to Genome Edited Products* (cited in note 27).

just like any other new drug. The governing statute of the FDA, the Federal Food, Drug, and Cosmetic Act defines a drug as any "article[] intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease" or "intended to affect the structure or any function of the body."[56]

Modern immunotherapy requires that the patient's cells be altered in different ways with other substances. This makes the procedure akin to the stem cell procedure addressed in *Regenerative Sciences*. In that case, the D.C. Circuit held that the FDA had authority to regulate the mixture that would be reinjected into the patient. The FDA's position in that case has come under much criticism for a failure to understand the nature of law or demonstrate a basic understanding of how medicine progresses.[57]

The court rejected a number of claims, such as the claim that purely intrastate commerce is not covered by the interstate commerce clause, but most relevant was its discussion of the FDA's

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[56] 21 U.S.C. § 321(g)(1); see also 21 C.F.R. § 201.128.

[57] See, e.g., Richard A. Epstein, *The FDA's Misguided Regulation of Stem-Cell Procedures: How Administrative Overreach Blocks Medical Innovation*, (Manhattan Institute, September 24, 2013), online at https://www.manhattan-institute.org/pdf/lpr_17.pdf (visited Sept. 27, 2018) (Perma archive unavailable) ("The record in Regenerative Sciences demonstrates that the FDA has neither the medical insight nor the legal expertise to justify the extraordinary new powers that it claims for itself over the practice of medicine."). This criticism of the FDA is misplaced if one reconsiders the purpose of the agency. Some have speculated that the purpose of the FDA is to in some way further the practice of medicine or improve public health. This is certainly one plausible motivation, but others have been advanced. One of these theories is that the FDA exists to facilitate rent-seeking behavior, avoid competition, and raise barriers to entry. See generally Gabriel Kolko, *The Triumph of Conservatism* 5—6 (Quadrangle Books 1967); See Marc T. Law and Gary D. Libecap, *The Determinants of Progressive Era Reform: The Pure Food and Drugs Act of 1906* *5 (National Bureau of Economic Research Working Paper No. 10984, Dec. 2004), online at http://www.nber.org/chapters/c9989.pdf (visited Oct. 1, 2018) (Perma archive unavailable).

rules regarding the production of "human cells, tissues, and cellular or tissue-based products (HCT/Ps) used for therapeutic purposes."[58] Those regulations, codified in 21 C.F.R. part 1271, had a regulatory exemption for "minimally manipulated" cells.[59] While the plaintiffs created a genuine issue of fact in disputing the government's claim that altering genes is more than minimally manipulating cells, they failed to respond to the government's other claims, not meeting their burden.[60]

What is most telling here is that future litigants are not foreclosed from asserting this claim – they simply have a burden to meet. This burden does not appear to be a difficult one, especially considering the nature of new immunotherapies. These therapies by their very nature are simply designed to amplify the functions of lymphocytes. There are no fundamental changes to the cells where they become a new type with a new purpose. This allows future immunotherapy litigants to distinguish their case from *Regenerative Sciences*.

But beyond the positive question of how a future court will rule is the normative question of what regulatory regime is appropriate for this therapy. The current regime of FDA rules is not appropriate for the very personalized nature of immunotherapy, and calls to regulate this as the practice of medicine have much merit.

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[58] See *United States v. Regenerative Sciences, LLC*, 741 F.3d 1314, 1321 (D.C. Cir. 2014).
[59] See 21 C.F.R. §1271.10(a)
[60] *United States v. Regenerative Sciences*, LLC, 741 F3d 1314, 1322 (DC Cir 2014) ("For example, appellants admit that the culturing process is designed to 'determine the growth and biological characteristics of the resulting cell population.' It is also undisputed that, in at least some cases, appellants add substances to the cell culture that affect the differentiation of bone marrow cells. These concessions are fatal to appellants' attempt to claim refuge under § 1271.10(a). Given that § 1271.10(a) is an exemption from the otherwise applicable provisions of the FDCA, appellants ultimately bear the burden of establishing that it applies to the Mixture. See *United States v. First City Nat'l Bank of Houston*, 386 U.S. 361, 366 (1967)").

When drugs were manufactured with few deviations and did not target particular groups or individuals, the FDA may have been justified in taking a conservative approach to drug approval. This is because the consequences of their decisions would affect a larger number of people. The advent of personalized medicine obviates this risk.

The FDA has established the double-blind clinical trial as the gold standard for drug approval. It is worth noting that these studies are not a requirement of any enabling legislation by Congress, but rather an invention of the FDA promulgated through regulations. This regime may make sense for drugs that are targeting diseases that affect large populations in mostly the same ways but should be rethought when dealing with personalized treatments of diseases such as cancer.

One of the reasons this regime of forced testing has come under fire is that doctors are sometimes able to determine fairly early whether a drug is effective. Forcing patients to participate in a control group, when it is known that there is a better treatment is questionable from an ethical standpoint. The above being said, newer clinical trials are aiming to isolate specific biologic and molecular targets that can be used as surrogates for disease response and drug efficacy. This newer form of clinical trial necessarily will mean smaller numbers of patients. Such smaller, more involved patient populations are a basis of translational medicine. Most newly developed trials are done through a multidisciplinary approach, with clinicians administering trial agents to patients and bench scientists analyzing the identified molecular targets that are intermediaries in disease response thought to represent end-point patient survival.

Additionally, there is some question about whether drugs should be tested individually, especially if they are intended to be

used in conjunction with other drugs.[61] Cancer is a *sui generis* disease for a number of reasons.[62] Doctors are often in a better position than administrators to understand the intricacies of their patients' situations.

To be sure, there is potential for abuse in any situation where there is asymmetric knowledge, but there are other branches of the law that are perfectly capable of dealing with these. For instance, the doctrine of informed consent ensures that a patient knows and understands the risks that he is taking when he embarks on any medical decision. There is a growing movement of doctors, patients, academics, and government officials who are calling for a rethinking of the double-blind study.[63] It is difficult to conduct a large randomized double-blind study in the U.S., especially for niche diseases. Most are being done in other countries, and translational trials in the U.S. are replacing the older model. With personalized medicine, it may be the case that a person's unique immune system responds to drugs differently than another person's, and a doctor should have some leeway in determining how best to act in light of this fact.

Finally, it is worth mentioning one final evolving area of the law giving weight to this argument. In *Abigail Alliance for Better Access to Developmental Drugs v. von Eschenbach*, a group of patients and their doctors had leveled a claim against the FDA, asserting that the Due Process Clauses of the Fifth and Fourteenth Amendments conferred

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[61] DeVita, *The Death of Cancer* (cited in note 3).
[62] See generally Douglas Hanahan and Robert A. Weinberg, *The Hallmarks of Cancer*, 100 Cell 57 (2000).
[63] See John J. Cohrssen and Henry I. Miller, 39 Regulation 22, 22 (2016-2017).

on terminally ill patients a right to try potentially life-saving drugs.[64] The D.C. Circuit did not find this claim compelling, applying the Supreme Court's *Washington v. Glucksberg* test, which looks at two primary features when assessing their claim: a) whether the alleged right is "deeply rooted in this Nation's history and tradition" and b) whether a "careful description" of the asserted right is put forward.[65] The Supreme Court declined to hear the appeal. This case was decided before the Court's Substantive Due Process jurisprudence began to change, and there may be a colorable argument to reconsider the case, given the Court's recent reconsideration of the Fourteenth Amendment.[66]

III. ARTIFICIAL INTELLIGENCE AND ROBOT MALPRACTICE

Artificial intelligence is a term that refers to a host of applications ranging from simple handheld calculators to robots that are indistinguishable from humans. Many in the computer science community believe that general artificial intelligence, a point where computers have all the capabilities of humans, is far off. Instead, what has aroused so much excitement in recent years is a subset of artificial intelligence called machine learning. Machine learning has existed since the 1950s, but recent increases in computing power and the availability of data have made the technology more viable. IBM used machined learning to train a computer called Watson to beat human champions at the game of Jeopardy.[67]

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[64] *Abigail Alliance for Better Access to Developmental Drugs v von Eschenbach*, 495 F3d 695 (DC Cir 2007).
[65] *Washington v Glucksberg*, 521 US 702, 721 (1997).
[66] See, e.g., *Obergefell v Hodges*, 135 S.Ct. 2584 (2015).
[67] See David Ferucci, et al., *Building Watson: An Overview of the DeepQA Project*, 31 AI Magazine 59, 60 (2010).

A formal definition of machine learning is a process whereby a computer can learn and perform certain tasks without being explicitly programmed to do so.[68] The way the computer "learns" is by creating and applying a model that is based on past data. This past data is known as a training set and can either be structured or unstructured. A structured dataset includes inputs and outputs, while an unstructured dataset only includes inputs. The training set creates the algorithm and in the inference phase that algorithm is applied to previously unseen inputs.

For instance, consider a machine learning program to recognize handwriting. The computer would be given thousands of examples of handwritten numbers. If the data were structured, then each of those handwritten number inputs would be paired with an output, i.e. the number it actually is. From this training set, the computer is able to create a model. This model will then be used to recognize future handwritten numbers. If it was given a handwritten '7' that was slightly different from one 7 in the training set, the computer would still be able to properly recognize that the pixels arranged in that order should be classified as a 7.

But the promise of machine learning is not that computers will be able to identify human handwriting from a training set,[69] but rather that computers will be able to recognize cancers from a training set.[70] With a large enough dataset, a computer would be able

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[68] See Arthur L. Samuel, *Some Studies in Machine Learning Using the Game of Checkers*, 44 IBM J. Research & Development 210 (1959) For a more formal definition, see Tom Mitchell, *Machine Learning* 2. (McGraw-Hill, 1997) ("A computer program is said to learn from experience E with respect to some class of tasks T and performance measure P if its performance at tasks in T, as measured by P, improves with experience E.").

[69] Although a system to recognize the notoriously illegible writing of doctors would be valuable.

[70] See, for example Andre Esteva, et al., *Dermatologist-level Classification of Skin Cancer with Deep Neural Networks*, 542 Nature 115 (2017).

to recognize correlations that humans do not necessarily know exist. As the underlying molecular and genetic basis of cancer is elucidated, old categorization, e.g. the stage description of cancer, is being revolutionized. It is becoming clear that our distinctions between, for example, lung and liver cancer, are gross and inaccurate. Cancers, regardless of their organ of origin, are being fingerprinted by their biology. The nuances of these molecular structures are highly complex and may well be more rapidly and effectively identified by computer programs than by scans and their appearance under a microscope. This could become the new method of tumor classification.

Both structured and unstructured datasets can be used as inputs. This means that certain images, for instance, can be labeled with certain diseases, and then a computer can try to find those diseases in future instances. To this end, many companies, have embarked on programs to bring machine learning to the field of medicine.

Much like the technology in this field, the legal literature is nascent. [71] Professor Price has termed such diagnostic methods "black-box medicine," which he defines as "the use of opaque computational models to make decisions related to health care." The reason that they are opaque is not malicious in any sense, but rather because the causal relationships that are derived from neural networks, for instance, are necessarily shown as outputs and cannot be divided into human-cognizable factors. This differs dramatically from simple linear relationships between, for example, weight and chance of heart disease.

These efforts have focused on a number of applications, including diagnostics, treatment, and drug discovery. The basic idea

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[71] For a helpful introduction, see W. Nicholson Price II, *Black-Box Medicine*, 28 Harv. J. L. & Tech. 419 (2015).

is that computers will be trained on the corpus of medical knowledge and will draw predictive models that can then be applied to a new set of facts when they are presented. For treatment, this means that correlations between certain disease inputs and certain treatment outcomes will be determined and then applied to new cases. For new drug discovery, this means looking at the structure of drugs and known interactions and qualities and drawing conclusions that would not have otherwise been seen. This is medical casuistry.

Like all casuistry it is subject to two types of errors – type I and type II errors. In diagnostics, the first type of error finds a disease where there is none; the second type of error does not find a disease when one exists. In treatment, the type I error gives a drug in a dosage where it should not and in a type II error it does not give a drug where it should.

These types of errors are the fundamental errors of malpractice. A doctor either does something he should not have done ("false positive") or does not do something he should have done ("false negative"). Similarly, inferences derived from machine learning can lead to either of these errors. The question becomes how the law should treat malpractice when it is not a human committing an error, but rather a machine. What is the degree of liability and who bears it? How far back does the chain go? For instance, can a programmer be liable if one of his algorithms is used to misdiagnose a patient? These are questions of tort and contract law.

The remainder of this section will give the current law of robot malpractice and then attempt to fit machine learning within its corpus.

Medical malpractice is a subset of tort law generally. It is a kind of professional negligence that requires the typical four elements to

be proven: duty, breach of duty, causation, and damages.[72] In most instances of negligence, a court will adopt either a strict liability or a reasonable person standard for determining whether there has been a breach of duty.[73] In the medical malpractice context, that determination is made by comparing the doctor's actions or inactions with those of the standards of his profession.[74] This usually means that there will need to be expert testimony that establishes what the appropriate standard of care is for any given situation.[75]

There are those who have doubted whether this is the appropriate regime for addressing private harms in the medical context. The fact that there is generally a preexisting contractual relationship between the tortfeasor and the victim makes this distinct from other cases of negligence.[76] Furthermore, given the mathematical nature of inferences derived from machine learning, there is an easier weighing mechanism for determining both *ex ante* decision making and *ex post* liability apportionment.[77] This means that negotiations about price and risk are grounded in a statistical

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[72] B. Sonny Bal, *An Introduction to Medical Malpractice in the United States*, 467 Clinical Orthopaedics and Related Research 339, 339 (2009).

[73] See *Robbins v Footer*, 553 F.2d 123, 126 (D.C. Cir. 1977) ("The conduct of a defendant in a negligence suit is usually measured against the conduct of a hypothetical reasonably prudent person acting under the same or similar circumstances.").

[74] See id. ("In a malpractice case, however, the question of whether the defendant acted in conformity with the common practice within his profession is the heart of the suit...As part of his prima facie case a malpractice plaintiff must affirmatively prove the relevant recognized standard of medical care exercised by other physicians and that the defendant departed from that standard when treating the plaintiff.").

[75] See id. at 126-27.

[76] Richard A. Epstein, *Medical Malpractice, Imperfect Information, and the Contractual Foundation for Medical Services*, 49 L. & Contemp. Probs. 201, 202 (1986).

[77] By this we mean that patients and doctors are in a position to know the likelihood of type I and type II errors because the machine learning protocols are designed to articulate what these different error rates are.

backdrop that allows for a range of potential outcomes. Insurance companies and providers can negotiate these offerings and provide patients with options depending on their risk tolerance and price sensitivity. Perhaps, for instance, a patient is willing to waive or cap certain medical malpractice claims because of the inherent riskiness of the procedure in order to secure a lower price.

That being said, as it currently stands, medical malpractice is not dealt with in the contracts context, but instead as a matter of tort law, and so the case of the robotic diagnosis will be addressed through this lens.

One may think that a new cause of action is needed to deal with robotic diagnoses.[78] The trouble with this view is that robotic diagnostics are actually nothing particularly new. As mentioned above, machine learning techniques have been in existence since at least the 1950s, and statistics as a science has existed for hundreds of years. On this account, modern machine learning is just a more powerful application of statistics aided by powerful computers. A protocol is an output from data that excises human discretion from the medical decision-making process.

Even older than machine learning is the idea of judging the actions of doctors in accord with prevailing standards of care. Indeed, one of the first mentions of medical malpractice comes from the Code of Hammurabi in 2030 BC: "If a physician make[s] a deep incision upon a man with his bronze lancet and cause[s] the man's death, or operate[s] on the eye socket of a man with his bronze lancet

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[78] See Michael Smith, *Dr. Watson Will See You Now* (MedPage Today, Dec. 10, 2016), online at https://www.medpagetoday.com/meetingcoverage/sabcs/61986 (visited Oct. 2,, 2018) (Perma archive unavailable).

and destroy[s] the man's eye, they shall cut off his hand."[79] Here a standard of care was established and the doctor's actions weighed against it. All that is new now is that there are new standards of care being established by machines instead of human inferences.

The threshold question for any good lawyer is: whom do I sue? There are arguably two situations that can exist with a treatment protocol derived from machine learning. In the first, a human doctor weighs the output from the algorithm as one factor in his decision.[80] He is allowed to exercise his own discretion, however. In the second, the healthcare institution requires the removal of human discretion and the rote application of the protocol. The first of these situations is an easier case. There is a rich case law dealing with consulting physicians, i.e. physicians that provide advice to the treating doctor. The general holding is that consulting physicians are not liable to the patient.[81] This would be the situation when a doctor relies on a diagnosis or treatment proposed by an artificially intelligent system. The second case is more difficult because it involves no human discretion. This is what makes black-box medicine "new in the instance."[82]

This begins to look more like a situation of products liability where strict liability is the general standard. This means that for a

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[79] J.M. Powis Smith, *Origin & History of Hebrew Law* 211 (U. Chi. 1931).

[80] Randolph A. Miller, Kenneth F. Schaffner, and Alan Meisel, *Ethical and Legal Issues Related to the Use of Computer Programs in Clinical Medicine*, 102 Annals of Internal Med. 529, 530 (1985).

[81] See, for example, *Corbet v McKinney*, 980 SW2d 166 (Mo Ct App, 1998).

[82] *Pasley v Freeman*, 100 E.R. 450, 456 (1789) (Ashhurst, J.) (". . .where the case is only new in the instance, and the only question is upon the application of a principle recognized in the law to such new case, it will be just as competent to Courts of Justice to apply the principle to any case which may arise two centuries hence as it was two centuries ago; if it were not, we ought to blot out of our law books one fourth part of the cases that are to be found in them.").

product introduced into the stream of commerce a party is liable for any damage caused by the defect in either the manufacture, design, or failure to warn on its products. This liability is assigned without questioning whether the defects were reasonable, but simply as a matter of law. Thus, a plaintiff could make a colorable claim that if an artificially intelligent machine operates in a defective manner, the manufacturer should be liable.

This claim is complicated by the fact that there are two kinds of defects that a machine can have. The first is a defect that could have been rectified beforehand with proper processes. The second is a defect that is inherent in the nature of diagnoses and treatment. The first type of error would occur if, for example, a computer programmer made a typo such that the machine recommended a dose of 1,000 grams instead of 1,000 milligrams. Or if there were some type of error with data input. These can be analogized to situations like the exploding bottle of soda in *Escola v. Coca-Cola Bottling Co*.[83] In both instances, there would be some defect in the manufacture of the product in question before it left the defendant's control. The second type of error are those that are inherent in medicine. For situations where there are known error rates, it would make little sense to hold a machine's owner strictly liable simply because the outcome was not the desired one.

Another reason for not holding the protocol-generating artificial intelligence system strictly liable for outcomes, as opposed to inputs, is that it would discourage healthcare providers from moving to these systems, even if the outcomes were better for patients in aggregate. Although protocols have been demonstrated to be

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[83] *Escola v Coca-Cola Bottling Co.*, 150 P.2d 436, 437-38 (Cal. 1944).

superior to discretion in many situations, the error rates are not zero.[84]

Professor Price has made his own suggestion for assigning liability to healthcare providers. He proposes a risk-based, spectrum standard of care, where the law looks at where the recommendation of the black-box deviates from previously-known correlations and treatments.[85] The spectrum he gives us is instructive. On one end stands non-risky black-box treatments, like prescribing low-side effect drugs like aspirin or monitoring. On the other end is a black-box suggestion to give thalidomide to a pregnant woman. In the middle could fall taking higher doses of a powerful drug for a novel indication.[86]

Professor Price notes that there are problems with this standard. One of the most important of these he notes, but understates, is that this standard will incentivize providers to be "too cautious, avoiding beneficial interventions out of concern for potential risk-based liability."[87] He notes that this is a problem of all novel treatments, generally, however. There is some empirical research to support the idea that juries are more sympathetic to the use of diagnostic aids.[88]

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[84] See Richard Epstein, *Intuition, Custom, and Protocol: How to Make Sound Decisions with Limited Knowledge*, 2 N.Y.U J. L. & Liberty 1, 21 (2006); William G. Baxt, *Use of an Artificial Neural Network for the Diagnosis of Myocardial Infarction*, 115 Annals of Internal Medicine 843, 843 (1991).

[85] See W. Nicholson Price II, *Medical Malpractice and Black-Box Medicine* *10 (University of Michigan Public Law Research Paper No. 536, 2018) online at https://ssrn.com/abstract=2910417 (visited Oct. 2, 2018) (Perma archive unavailable).

[86] See id. at *9-10.

[87] Id. at *10.

[88] See Hal R. Arks, Victoria R. Shaffer, and Mitchell A. Medow, *The Influence of a Physician's Use of a Diagnostic Decision Aid on the Malpractice Verdicts of Mock Jurors*, 28 Medical Decision Making 201, 204–05 (2008).

If it is indeed the case that our human understanding of disease is less than that of a black-box, then perhaps our entire approach to medicine needs to be rethought. The proposed benefits of this system are immense and not using new standards can also lead to liability.[89] But the risks of the system are also immense.[90] It would be unwise, however, to think solely about the risks and weigh them against an ideal state that does not exist.[91]

The trouble with Professor Price's risk-based system is not that it is incorrect, but that it focuses on the wrong question. It is not what decision is made, but who is making that decision. At least on one account of the modern, industrial market economy, its power is in the channeling of decentralized knowledge in a socially beneficial manner.[92] A top-down approach to the economy much like to medicine can be disastrous. What ought to be encouraged is individual patients, in consultation with their doctors and advocates, making their own determinations of their risk profiles. Courts and legislatures can provide guiderails and set the general rules of the game. Again, as mentioned above, what is key here is ensuring informed consent. This is regulating the fairness of the procedure, but not of the outcome.[93] How the aggregated preferences of society

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[89] See, e.g., *Boswer v Craig Ranch Emergency Hospital*, No. 05-14-00501-CV, 2015 WL 3946371, *4–5 (Tex. App. 2015) (using old medical textbooks can constitute a "failure to promulgate policies and procedures regarding the standard of care").

[90] See, e.g., *The Terminator* (Pacific Western Productions 1984).

[91] The Nirvana Fallacy. See Harold Demsetz, *Information and Efficiency: Another Viewpoint*, 12 J. L. & Econ. 1, 1-2 (1969).

[92] See generally F.A. Hayek, *The Use of Knowledge in Society*, 35 Am. Econ. Rev. 519 (1945).

[93] See Robert Nozick, *Anarchy, State, and Utopia* 150—52 (Basic Books 1974) (describing entitlement theory).

shake out is not for healthy academics to say, because their preferences may differ from those with terminal diseases.[94]

CONCLUSION

This article was intended to provide a survey of some particular medical innovations that hold a great deal of therapeutic potential. It was not intended to provide an exhaustive account or claim to resolve any outstanding debates but rather to explore them and show that they do fit nicely into existing frameworks. In certain instances, it is the frameworks themselves that should be reconsidered, not because of the innovations, but because of problems with current policy, such as an inappropriate understanding of risk.

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[94] See, e.g., Richard Posner, *Do We Need More Regulation of Mortgages to Protect Consumers?* (Becker-Posner Blog, Aug. 30, 2009), online at http://www.becker-posner-blog.com/2009/08/do-we-need-more-regulation-of-mortgages-to-protect-consumers--posner.html (visited Oct. 2, 2018) (Perma archive unavailable) ("You are 'irrational' only from the perspective of low-discount-rate persons, such as Professor Bar-Gill, who has two doctorates, two masters degrees, and a total of 13 years of education after high school.").