# CRISPR AC

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### Advantage 1 – Innovation

#### Advantage 1 is innovation:

#### A huge influx of patents is coming – most recent data and trends from this year

Mischel 4/27 [(Fiona Mischel, Editor-in-Chief of SynBioBeta. She frequently covers sustainability, CRISPR research, food and agriculture technology, and biotech for space travel) “Who Owns CRISPR in 2021? It’s Even More Complicated Than You Think” SynBioBeta, 4/27/2021. https://synbiobeta.com/who-owns-crispr-in-2021-its-even-more-complicated-than-you-think/] BC

Still Want To Patent CRISPR? Here’s What You Need To Know

The biggest challenge for anyone trying to sort out CRISPR patent rights is fully understanding just how many patents there are.

A search in the USPTO revealed 262 patents or patent applications listing CRISPR-Cas9 and over 5,000 general CRISPR patents. And these are only the patent applications for Cas9. This doesn’t include the growing number of patents for other Cas molecules or Cas molecules yet to be discovered. This also doesn’t include patent applications in other big synthetic biology regions like China, Europe, the UK, and Israel.

The competition for CRISPR patents is unlikely to diminish in the future as more companies and academic centers clamber to join the race. The race has become increasingly global with more countries filing for CRISPR patents—new patents are filed at a rate of 200 per month.

What isn’t clear is how these enormous numbers of CRISPR patents will affect the future of science. Will they hamper progress by limiting the commercial use of the technology, or will researchers prevail and make new therapies accessible to everyone? When the dust settles—if it does at all—the hope is that CRISPR technology will be accessible for a wide range of applications at a competitive cost. The power to engineer biology should not be limited to the very few. We are now in the Age of Biology. If we are to build a better future, we cannot leave the fundamental promise of science in the dust.

#### Makes development of genomic medicine impossible – 3 warrants:

#### Patent disputes are imminent – new entities and foreign governments getting involved ensures conflict

Stramiello 18 [(Michael, PhD, an intellectual property litigation associate in Washington, DC. His practice focuses on the life sciences industry) “CRISPR: The New Frontier of Biotechnology Innovation” American Bar Association, Jan/Feb 2018. https://www.americanbar.org/groups/intellectual\_property\_law/publications/landslide/2017-18/january-february/crispr-new-frontier-biotechnology-innovation-digital-feature/] BC

As the UC-Broad interference winds down, CRISPR watchers should not lose sight of the USPTO, where more challenges may wait in the wings. For example, at least one ex parte reexamination against a foundational patent owned by Broad has already been granted (and suspended until the interference concludes). There is also a looming threat of additional interferences, as mentioned in recent USPTO communications19 and acknowledged in the pre-IPO disclosures of all three CRISPR-centric biotechnology companies publicly traded in the United States (i.e., CRISPR Therapeutics AG, Editas Medicine Inc., and Intellia Therapeutics Inc.). Potential dark horses identified in those filings include: (1) Rockefeller University, a joint applicant on certain Broad applications; (2) ToolGen Inc., whose suggestions of interference against Broad are still pending; and (3) Vilnius University, which has its own US patent for use of CRISPR/Cas9 systems and is party to a cross-licensing agreement with one of UC’s licensees. Other entities may also come out of the woodwork with freedom-to-operate strategies that challenge key patents via inter partes review or post-grant review.

Additional CRISPR disputes will happen overseas in 2018—and if patent grants are any indicator, foreign agencies might not simply follow the USPTO’s lead. The European Patent Office’s (EPO’s) Opposition Division (OD) will kick things off on January 16, when it hears oral arguments in oppositions lodged against a foundational patent owned by Broad. Among other things, challengers have attacked the purported novelty of Broad’s claims, a determination that may hinge on whether Broad validly claimed priority to two of its early applications. If it did not, at least seven of Broad’s other opposed patents may be vulnerable too. The OD has already issued a preliminary opinion indicating that it expects the oppositions to succeed.20 While that opinion is nonbinding, European analysts have stressed that it is usually “very difficult” to sway the OD from its preliminary views.21 In any event, Broad will not be the only foundational patent holder fighting to keep its rights alive across the pond in 2018, as the EPO has also granted noteworthy patent rights to UC, Sigma-Aldrich, and Cellectis, thus opening nine-month windows for would-be challengers to file post-grant oppositions. The fight over UC’s patent, which controversially covers use of CRISPR in both prokaryotes and eukaryotes, may be especially heated. It has already withstood over a half dozen third-party observations (including some filed by Broad),22 and at least two groups have now filed post-grant oppositions.23

China, home to the world’s second-busiest CRISPR patent landscape (after the United States), may host similar turf wars in 2018. UC and Broad, among many others, are already on the scene and may be drawing up battle plans. While Broad’s applications remain pending, China’s State Intellectual Property Office announced in June its intention to grant UC a patent covering CRISPR/Cas9 methods and compositions for applications in any environment. One of UC’s key licensees in human therapeutics praised the decision as “further global recognition that [UC and its collaborators] are the pioneers in the application of CRISPR/Cas9 in all cell types.”24 Not missing a beat, Broad issued an ominous reminder that “[i]n China, patents are subject to invalidation proceedings after they are issued.”25

#### IP disputes foreclose research collaboration between universities, which has historically enabled critical scientific breakthroughs

Sherkow 17 [(Jacob, Professor of Law at the College of Law and Affiliate of the Carl R. Woese Institute for Genomic Biology at the University of Illinois, where his research focuses on the legal and ethical implications of advanced biotechnologies, especially as related to intellectual property. He is a leading expert on IP protection for genome-editing technologies, including CRISPR. He is the author of over 60 articles published in both scientific journals and traditional law reviews, including Science, Nature, the Yale Law Journal, and the Stanford Law Review. Since 2018, Sherkow has also been a Permanent Visiting Professor at the Center for Advanced Studies in Biomedical Innovation Law (“CeBIL”) at the University of Copenhagen Faculty of Law) “Patent protection for CRISPR: an ELSI review” Journal of Law and the Biosciences 12/7/2017 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5965580/] BC

One notable aspect of the CRISPR patent dispute is that it is, by and large, a dispute between academic research institutions. It pits lawyers representing the University of California against lawyers representing the Broad Institute of MIT and Harvard.22 To be sure, university rivalries are common.23 But because universities share among themselves a larger mission to create and disseminate knowledge to the public, litigiousness among them has been historically rare.24

University-against-university patent disputes, like CRISPR, complicate interinstitutional research agreements on several levels. First, they have the potential to chill formal interinstitutional research collaborations among universities if the institutions cannot agree on intellectual property issues beforehand.25 Universities may simply be unwilling to enter into such agreements in the first instance, or, perhaps more perniciously, discourage their faculty from informally developing such networks.26 While the empirical evidence for such a diminishment in collaborative efforts is slight—difficult to demonstrate, in part, because it requires the proof of opportunities not taken by universities—some recent survey data have found that ‘institutionally mandated [materials transfer agreements] put sand in the wheels of a lively system of intra-disciplinary exchanges of research tools’.27 Aside from this, there is substantial anecdotal evidence of institutional difficulties in creating such agreements.28 It stands to reason that, at least in some instances, these difficulties have ended some collaborations before they could begin. More immediately, this is a current issue with the CRISPR patent dispute given some internal dissention between Doudna and Charpentier's respective institutions concerning the intellectual property involved. Although Doudna and Charpentier filed their joint patent application in 2012, their institutions did not formally assent to a cross-licensing agreement until December 2016.29 If assenting to a cross-licensing agreement for a single piece of technology has proved difficult, it is unclear how the two institutions will deal with one another on future collaborations.

Second, even with some friction between universities over obtaining patents for their researchers’ work, it has been rare for universities to sue one another regarding inventorship—until now. In 2011, for instance, the University of Utah sued the Max-Planck Institute concerning inventorship over a foundational group of patents concerning RNA interference technology.30 And since 2012, Stanford University and the Chinese University of Hong Kong have battled one another over lucrative patent rights to noninvasive prenatal genetic diagnostics.31 That dispute—despite several rounds of appeals—is still ongoing.32 Such patent disputes are costly, high stakes, and high profile. And while the CRISPR patent dispute itself is not a cause of such conflict, it has become emblematic—and potentially prophetic—of the tenor of such disputes today. Avoiding them in the first instance is a sensible institutional priority. But that sometimes comes at the cost of avoiding one's colleagues.33

Third, even apart from the administrative institutional level, patent disputes like these damper the culture of scientific collaboration, clearly something of tremendous import to modern science.34 Putting a price on a loosely defined culture of scientific collaboration is difficult—its loss is difficult to quantify. Nonetheless, many of the most significant breakthroughs of the past century arose in part from a culture of scientific openness and collegiality.35 Abandoning that in favor of inuring patent rights to researchers from a single institution seems, at best, unwise. Relatedly, it may erode scientists’ penchant for honest, if critical assessments, of their own work among collaborators and colleagues. A key piece of evidence used in the U.S. CRISPR patent interference against the University of California was a single one of Doudna's public statements that her collaborators ‘weren’t sure if CRISPR/Cas9 would work in eukaryotes—plant and animal cells’.36 That statement has now echoed throughout laboratories across the USA as a cautionary tale against critical reflections of one's work—at least while patents are pending.37

Lastly, patent conflicts’ hindrance of interinstitutional collaborations may simply be costly. Today, some research benefits from economies of scale, such as where expensive equipment can be shared among institutions.38 The New York Genome Center, for example, is a joint venture among several New York-area research institutions: NYU, Columbia, Cold Spring Harbor Laboratories, to name a few.39 This arrangement allows researchers at these institutions to share a fleet of Illumina X Ten sequencers, the total cost of which—including operations—runs into the millions of US dollars.40 Where research funding is diminishing—as is sadly the case in much of the Anglophone world41—universities may foolishly hesitate to engage in similar cost-saving arrangements in the short-sighted hope of avoiding future patent lawsuits.42 One would hope that the CRISPR patent dispute teaches others that such myopia isn’t warranted.

#### Patent disputes create fears of litigation that deter genome research and investment

Reader 10/10 [(Ruth, writer for Fast Company, covers the intersection of health and technology) “2 women won the Nobel for CRISPR, but the battle for its patent rages on” Fast Company, 10/10/2020 https://www.fastcompany.com/90561762/nobel-prize-jennifer-doudna-emmanuelle-charpentier-crispr-patent-lawsuit] BC

CRISPR’S UNCERTAIN FUTURE

While the Nobel award certainly affixes Doudna and Charpentier’s place in history, the ongoing litigation continues to hang heavy over the development of CRISPR Cas-9’s editing capability. Some scientists feel that with so much public money involved in discoveries such as the ones around CRISPR Cas-9, no one should have a right to the intellectual property. This would keep the science open and allow others to innovate on top of it without the fear of litigation or the sometimes high costs of royalties. Meanwhile, investors, ever aware of the legal landscape, are looking to finance new biotechnology that doesn’t infringe on the existing CRISPR patents.

“We’re mindful that that litigation is going to have an impact on the freedom that our companies have to operate in,” says Paul Conley, a managing director at venture capital firm Paladin Capital Group. “We try to remain agnostic by finding the companies who are using CRISPR machinery—these nucleases—that definitely don’t tread on any of the IP that’s being litigated.”

That litigation hasn’t entirely stopped CRISPR exploration. In fact, a whole industry of apparatuses and chemicals has emerged to facilitate CRISPR gene edits. CRISPR Cas-9 is showing promising results as a treatment for rare diseases such as sickle cell anemia as well as an implement for biomanufacturing. But the litigation may be shifting gene-editing research. Like any technology, CRISPR Cas-9 is not perfect. It’s not as precise as some scientists would like, and it can have unanticipated effects outside of the desired outcome. Scientists who don’t already have a claim to the CRISPR Cas-9 system may be more inclined to seek out other gene-editing opportunities rather than improve Cas-9. Conley says scientists may be wary of pushing the technology ahead.

“It has absolutely put fear in the minds of many scientists who frankly could do great things for society,” says Conley. “They are living in terror of, well, if I go down this road a) am I going to be sued? And b) is there any commercial outlet where I’m going to have trouble raising money, because there’s fear and loathing around the CRISPR component”

Much of the new science surrounding CRISPR Cas-9 has come from scientists with a stake in the intellectual property. Last year, David Liu, a scientist at the Broad Institute and cofounder of gene-editing therapeutics company Editas Medicine, published a way of making more precise edits with fewer unintended effects using a new process called prime editing. One of Doudna’s companies, Scribe Therapeutics, is engineering CRISPR molecules, rather than using the ones found in nature, in order to do away with the natural aspects that get in the way of putting it to good use as a targeted gene editor. The company just raised $20 million and signed a deal with pharmaceutical company Biogen to implement its technology.

#### Uncertainty about licensing ensures technology is not distributed or developed - smaller firms don’t know where they need to seek approval from

Sterlin 20 [(Ian, JD from the University of Michigan Law School, Executive Editor of the Michigan Technology Law Review) “The CRISPR War Drags On: How the Fight to Patent CRISPR-Cas9 Creates Uncertainty in the Biotechnology Sphere,” Michigan Technology Law Review, 3/2020] JL

On September 10, 2018, the Federal Circuit Court of Appeals (“Federal Circuit”) affirmed the ruling of the United States Patent Trial and Appeals Board (“the Board”) in *Regents of the University of California v. Broad Institute*, finding that there was no interference-in-fact between competing patents that claimed methods of using CRISPR-Cas9 to modify cellular DNA. Rather than settling the patentability issue, however, exhaustive litigation has continued, as both parties seek to protect the results obtained from costly research. Such protracted litigation has created significant uncertainty among members of the scientific, legal, and biotechnology communities as to the exact demarcation of patent ownership and may ultimately reduce the amount of innovation in CRISPR-based technologies and stifle developing industries.

Clustered Regularly Interspaced Short Palindromic Repeats (“CRISPR”) are a family of DNA sequences found naturally in bacteria that, when paired with guiding RNA sequences and CRISPR-associated proteins (Cas), can selectively modify an organism’s genetic material (genome) more effectively and cheaply than comparable gene-editing systems. Since the discovery of CRISPR’s gene-editing capacity by researchers at the University of California, the University of Vienna, and Emmanuelle Charpentier, innovators have applied CRISPR technology in diverse industries, including the medical, industrial, and agricultural sectors. Several thousand CRISPR-related patent applications have already been filed worldwide, with the majority being filed in the United States, China, and Europe.

Researchers at the University of California were the first to (“UC”) demonstrate that isolated CRISPR-Cas9 components could effectively function in an *in vitro* environment. UC subsequently filed a patent application in May 2012 broadly claiming a method to using CRISPR-Cas9 without referencing specific cellular environments. In December 2012, a research team led by Feng Zhang at the Broad Institute filed a patent application directed to a method of using CRISPR-Cas9 in mammal cells. UC unsuccessfully sought to invalidate Dr. Zhang’s patents in an interference proceeding in front of the Board. UC appealed the Board’s ruling to the Federal Circuit, arguing that the Board employed an improperly rigid obviousness test and that it erred in dismissing evidence that other researchers simultaneously applied CRISPR-Cas9 to non-bacterial (eukaryotic).

The Federal Circuit rejected UC’s arguments and affirmed the Board’s finding that substantial evidence indicated there was no reasonable expectation of success a person of ordinary skill in the relevant art (POSITA) could successfully apply CRISPR-Cas9 to eukaryotic genomes. The Federal Circuit approved of the wide range of evidence the Board used to make its determination, including expert testimony, evidence of past failures in the field, simultaneous invention, and statements by members of UC’s research team expressing doubt that CRISPR-Cas9 could be successfully implemented in eukaryotic systems. The Federal Circuit also rejected UC’s contention that evidence of simultaneous evidence alone sufficiently demonstrated an invention’s obviousness. While the fact that six independent research teams successfully applied CRISPR-Cas9 within months of its disclosure by UC was useful evidence in determining obviousness, the weight of such evidence must “be carefully considered in light of all the circumstances.”

It is unclear what the Federal Circuit’s decision means for the non-obviousness standard of CRISPR-related patents. Some observers have praised the ruling as affirming the Board’s comprehensive analysis of available factual evidence while noting that some evidence existed that could support a finding of obviousness. While the Federal Circuit rejected UC’s argument that simultaneous invention alone could not demonstrate a showing of obviousness, it was careful to state that such evidence had not demonstrated “a reasonable expectation of success given the ‘specific context of the art at the time.” This may suggest that evidence of simultaneous invention may gain greater significance in future decisions as advances are made in CRISPR technology. The Federal Circuit further clarified that its ruling determined that the competing sets of patent claims comprised distinct subject matter and did not rule on the validity of either parties’ claims.

The Federal Circuit’s holding has also generated a heated discussion outside of the legal field. Many members of the scientific community have criticized the decision, with some indicating that they believe the Board’s factual determination does not reflect the practices found within the field of molecular biology. The uncertainty resulting from the Federal Circuit’s decision is also reflected in the confusion among third party innovators regarding who they should seek a license from in order to commercially exploit existing CRISPR patents. This confusion is further compounded by the fact that the “surrogate companies” the Broad Institute and UC have created to manage the licensing of their patents grant differing levels of exclusivity when licensing their patents.

Further complicating the determination of patent rights in the foundational CRISPR-Cas9 patent is a lack of uniformity among the various national (and multinational) patent offices. Even before the Federal Circuit’s ruling, China’s State Intellectual Property Office (now renamed National Intellectual Property Administration or CNIPA) granted UC a patent for its CRISPR technology, and the European Patent Office (EPO) granted UC a patent for use CRISPR-Cas9 in both prokaryotic and eukaryotic organisms. The EPO subsequently rescinded a patent grant it had issued to the Broad Institute in 2015, finding that the prior art from UC’s patent demonstrated a lack of novelty for the invention. On January 17, 2020, the EPO’s Board of Appeal dismissed the Broad Institute’s appeal against the rescission, and in February, the Board of Appeal rejected the Broad Institute’s opposition proceeding against UC’s patent. Rather than creating a clear standard within Europe, however, the EPO’s rulings have resulted in greater uncertainty, with both the Broad Institute and UC, as well as other patentholders, having overlapping patent rights that may result in further litigation. In addition, several of the Broad Institute’s EPO patents for CRISPR remain valid and the CNIPA has granted three patents to the Broad Institute for CRISPR technologies.

Perhaps the most worrying development has been the renewal of UC and the Broad Institute’s legal battle in the United States. In June 2019, the Board filed documents to commence interference proceedings between the Broad Institute and UC’s patents that will address the question of priority. These new interference proceedings, which will examine who first invented the use of CRISPR-Cas9 in eukaryotic organisms, have already begun with both parties accusing the other of engaging in questionable legal conduct. Although some observers are optimistic that the new interference proceedings may induce the parties to reach a settlement, it is equally possible that the proceedings may result in a protracted legal battle and another appeal to the Federal Circuit. The protracted legal battles surrounding the UC and the Broad Institute’s CRISPR patents have created significant uncertainty as to the final determination of ownership and patentability. What is certain, however, is the need for greater clarity in patent rights in order to make researchers feel secure in developing further technological innovations using CRISPR-.

#### CRISPR solves disease, but continued innovation is key

Thorne 20 [(Lucy, PhD, received a BSc. in Biochemistry from University of Leeds and a Ph.D. in Biological Sciences from University of Liverpool in the UK. She is currently working as a freelance consultant in Cambridge, UK writing CRISPR-related content for Biocompare.) “CRISPR-Cas Gene Editing: A New Weapon against Infectious Disease” Biocompare, 1/14/2020. https://www.biocompare.com/Editorial-Articles/559757-CRISPR-Cas-Gene-Editing-A-New-Weapon-against-Infectious-Disease/] BC

Infectious disease is a common cause of death worldwide, but the rise of antibiotic-resistant bacterial strains and lack of effective antiviral treatments means a potential future risk of increased mortality and global economic burden due to untreatable infections. This article discusses how CRISPR-Cas gene-editing technology is helping in the fight against increasingly resistant bacterial infections and rapidly mutating viruses—from facilitating a better understand of host-pathogen interactions and improving diagnosis, to potentially providing a new way to treat infectious disease.

The CRISPR revolution

The CRISPR locus (short for clustered regularly interspersed short palindromic repeats) was first discovered in E.coli in 1987 and found to be the basis of a bacterial adaptive immune system, providing prokaryotes with protection against foreign genetic material.1 The CRISPR-Cas system has since been repurposed into a powerful but relatively simple programmable gene-editing technology. A short single-guide RNA molecule (sgRNA) guides the Cas9 endonuclease to the target site, where a double-strand break is introduced. This activates intrinsic cellular DNA repair pathways, either the non-homologous end joining (NHEJ) pathway that results in a disabling deletion of the target gene, or homologous repair (HR) that allows the integration of a donor sequence at the target locus. As well as gene knockout and targeted changes to the genetic sequence, gene expression can be regulated. Other modifications at the target site are also possible with the use of a catalytically inactive version of Cas9 (dCas9)—the expanded CRISPR toolkit also includes modulation of gene expression (CRISPRi and CRISPRa) and base editing.

Since the first CRISPR gene-editing experiments were demonstrated in 2012, the CRISPR-Cas9 technology has exploded into the biological sciences and been rapidly adopted by the scientific community. CRISPR has already shown promise in the prevention of malaria, tuberculosis, and herpes simplex virus.2 Below, we highlight a few ways in which CRISPR has been recently applied to improving our understanding, treatment, and ongoing diagnosis of infectious disease.

Functional genomics with CRISPR to determine new antimicrobial targets

There is currently a distinct lack of new antibiotics and antiviral drugs making it to the clinic. Understanding host-pathogen mechanisms that govern how microbes induce pathogenesis is crucial for identifying new targets for rapid drug discovery and vaccine development. Soon after its debut, CRISPR-Cas9 was applied to functional genomic screening. Using a pooled sgRNA library workflow, CRISPR-Cas9 was successfully used at scale to enable high-throughput, genome-wide loss of function studies. CRISPR-Cas9 genome-wide screening has since been employed in a variety of pathogens to determine the molecular pathways that drive pathogenesis. These include identifying how the α-hemolysin virulence factor S.aureus causes cytotoxicity and genes involved in host-cell dependencies from Zika virus.3,4

CRISPR-Cas9 as a next-generation diagnostic for antimicrobial-resistance genes

Since the discovery of penicillin in 1928, antibiotics have been the main treatment against bacterial infections, reducing mortality and significantly improving life expectancy the world over. But the ability of microbes to rapidly mutate and share genetic information, as well as the overprescription of antibiotics, has led to the emergence of superbugs—strains that are resistant to existing treatments. According to the UN, antibiotic resistance is thought to cause around 700,000 deaths per year, which could rise to 10 million by 2050.

Determining whether genes responsible for antimicrobial resistance (AMR) are present is crucial when formulating an optimal treatment strategy to limit the spread of drug resistance. Unfortunately, real-time metagenomic analysis is hampered by the low abundance of resistant pathogens against a high background. Recent work from the Crawford lab at the University of California, San Francisco used CRISPR to develop a novel NGS-targeted enrichment system called FLASH (finding low abundance sequences by hybridization), which they use as a diagnostic.5 By using sgRNA to guide Cas9 to AMR genes, those sequences are cleaved ready for next-generation sequencing. FLASH enables amplification of AMR targets and high levels of multiplexing and was shown to successfully identify AMR genes in patient samples, including those infected with pneumonia-causing bacteria and Plasmodium falciparum, the malaria parasite.

Selectively controlling the microbiome

The human microbiome is a complex ecosystem of species that all play a role in health —but treatment with broad-spectrum antibiotics to destroy pathogens also kills the “good” bacteria, upsetting the delicate balance and the positive symbiotic relationships that help control pathogens. This blunt instrument also provides a selective pressure that can lead to the further development of antibiotic-resistant strains.

In a recent Nature Communications paper, Hamilton et al used CRISPR-Cas9 to selectively target and kill Salmonella enterica but leave other bacteria species in a co-culture unharmed.6 Their work utilizes a conjugative plasmid to put the delivery machinery together with the necessary Cas9 molecules in a cis-conjugative system to selectively target essential genes in S. enterica cells and destroy them. The authors also suggest their new delivery system could be beneficial in controlling microbial imbalances on biofilms with potential applications in medicine, healthcare, and industrial processes—for example in treating Clostridium difficile, a hospital-acquired infection that is placing an increasing economic burden on healthcare systems worldwide.

CRISPR: as nature intended?

In nature, CRISPR is an endogenous bacterial system used to protect from foreign genetic material, so it makes sense that it is now being used in medicine against the bacteria themselves to fight infectious disease. And not only bacteria—recent work from the Broad Institute used the Cas13 protein from the CRISPR system to selectively target and destroy single-stranded RNA viruses, including Influenza A, significantly and rapidly reducing viral load and infectiousness.7

The programmable nature of the CRISPR gene-editing system means that as microbes continue to evolve and mutate, the CRISPR machinery can be quickly altered to destroy the new target as an antimicrobial drug, or detect it as a diagnostic. Work will now move onto demonstrate that these CRISPR-based antimicrobial applications can work in the clinic and help combat the growing specter of antimicrobial resistance and infectious disease.

#### Disease causes extinction -- climate change and genomic mutation irreversibly alter ecosystem equilibrium which leads to the emergence of new pathogens

Supriya 4/19 [(Lakshmi Ph.D., worked as part of the R&D group in diverse industries starting with semiconductor packaging at Intel, Arizona, where she developed a new elastomeric thermal solution, which has now been commercialized and is used in the core i3 and i5 processors. From there she went on to work at two startups, one managing the microfluidics chip manufacturing lab at a biotechnology company and the other developing polymer formulations for oil extraction from oil sands. She also worked at Saint Gobain North America, developing various material solutions for photovoltaics and processing techniques and new applications for fluoropolymers. Most recently, she managed the Indian R&D team of Enthone (now part of MacDermid) developing electroplating technologies for precious metals. She has been a freelance science journalist and science writer since 2016 and has written for publications such as The Wire, Science, and New Scientist.) “Humans versus viruses - Can we avoid extinction in near future?” News Medical, 4/19/2021. <https://www.news-medical.net/news/20210419/Humans-versus-viruses-Can-we-avoid-extinction-in-near-future.aspx>] BC

Expert argues that human-caused changes to the environment can lead to the emergence of pathogens, not only from outside but also from our own microbiome, which can pave the way for large-scale destruction of humans and even our extinction.

Whenever there is a change in any system, it will cause other changes to reach a balance or equilibrium, generally at a point different from the original balance. Although this principle was originally posited by the French chemist Henry Le Chatelier for chemical reactions, this theory can be applied to almost anything else.

In an essay published on the online server Preprints\*, Eleftherios P. Diamandis of the University of Toronto and the Mount Sinai Hospital, Toronto, argues that changes caused by humans, to the climate, and everything around us will lead to changes that may have a dramatic impact on human life. Because our ecosystems are so complex, we don’t know how our actions will affect us in the long run, so humans generally disregard them.

Changing our environment

Everything around us is changing, from living organisms to the climate, water, and soil. Some estimates say about half the organisms that existed 50 years ago have already become extinct, and about 80% of the species may become extinct in the future.

As the debate on global warming continues, according to data, the last six years have been the warmest on record. Global warming is melting ice, and sea levels have been increasing. The changing climate is causing more and more wildfires, which are leading to other related damage. At the same time, increased flooding is causing large-scale devastation.

One question that arises is how much environmental damage have humans already done? A recent study compared the natural biomass on Earth to the mass produced by humans and found humans produce a mass equal to their weight every week. This human-made mass is mainly for buildings, roads, and plastic products.

In the early 1900s, human-made mass was about 3% of the global biomass. Today both are about equal. Projections say by 2040, the human-made mass will be triple that of Earth’s biomass. But, slowing down human activity that causes such production may be difficult, given it is considered part of our growth as a civilization.

Emerging pathogens

Although we are made up of human cells, we have almost ten times that of bacteria just in our guts and more on our skin. These microbes not only affect locally but also affect the entire body. There is a balance between the good and bad bacteria, and any change in the environment may cause this balance to shift, especially on the skin, the consequences of which are unknown.

Although most bacteria on and inside of us are harmless, gut bacteria can also have viruses. If viruses don’t kill the bacteria immediately, they can incorporate into the bacterial genome and stay latent for a long time until reactivation by environmental factors, when they can become pathogenic. They can also escape from the gut and enter other organs or the bloodstream. Bacteria can then use these viruses to kill other bacteria or help them evolve to more virulent strains.

An example of the evolution of pathogens is the cause of the current pandemic, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Several mutations are now known that make the virus more infectious and resistant to immune responses, and strengthening its to enter cells via surface receptors.

The brain

There is evidence that the SARS-CoV-2 can also affect the brain. The virus may enter the brain via the olfactory tract or through the angiotensin-converting enzyme 2 (ACE2) pathway. Viruses can also affect our senses, such as a loss of smell and taste, and there could be other so far unkown neurological effects. The loss of smell seen in COVID-19 could be a new viral syndrome specific to this disease.

Many books and movies have described pandemics caused by pathogens that wipe out large populations and cause severe diseases. In the essay, the author provides a hypothetical scenario where a gut bacteria suddenly starts producing viral proteins. Some virions spread through the body and get transmitted through the human population. After a few months, the virus started causing blindness, and within a year, large populations lost their vision.

Pandemics can cause other diseases that can threaten humanity’s entire existence. The COVID-19 pandemic brought this possibility to the forefront. If we continue disturbing the equilibrium between us and the environment, we don’t know what the consequences may be and the next pandemic could lead us to extinction.

### Advantage 2 – WTO credibility

#### Advantage 2 is WTO cred:

#### New EU trade restrictions on CRISPR contradicts WTO agreements which makes future disputes inevitable

Menz et al. 20 [(Dr. Jochen Menz, of Julius Kühn-Institut, Federal Research Centre for Cultivated Plants) Modrzejewski (Dominik PhD, Julius Kühn-Institut, Institute for Biosafety in Plant Biotechnology) Hartung (Frank, Julius Kühn-Institut, Institute for Biosafety in Plant Biotechnology) Wilhelm (Ralf, Kühn-Institut, Institute for Biosafety in Plant Biotechnology) Sprink (Thorben, Julius Kühn-Institut, Institute for Biosafety in Plant Biotechnology) “Genome Edited Crops Touch the Market: A View on the Global Development and Regulatory Environment” Front Plant Sci, 10/9/2020. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7581933/] BC

WTO: Committee on Sanitary and Phytosanitary Measures

In November 2018, the delegations of Australia, Argentina, Brazil, Canada, the Dominican Republic, Guatemala, Honduras, Paraguay, the United States of America, and Uruguay signed the international statement on agricultural applications of precision biotechnology in the WTO Committee on Sanitary and Phytosanitary Measures (CSPM). The delegations agreed to engage for the exploration of science based opportunities for regulatory frameworks and the avoidance of trade barriers for products derived from genome editing (Commitee on Sanitary and Phytosanitary Measures, 2018). In their declaration the states affirmed that cultivars derived from genome editing should be regulated similar to conventional cultivars due to their high similarity. Deregulation of genome editing techniques offers new opportunities for SMEs and national research institutions. Thus, a harmonization at national and international level should be ensured to exploit the full potential of genome editing. Furthermore, within the CSPM the United States with support from Argentina and Paraguay raised specific trade concerns (STC 452) about restrictions from the European Union resulting from the implementation of the CJEU Ruling in Commitee on Sanitary and Phytosanitary Measures (2019). The implementation would lead to unjustified barriers to trade in products of genome editing. It stifles the agricultural research and innovation necessary to prevent hunger and malnutrition in the coming decades, while ensuring environmental sustainability of agricultural activities. Without any changes in European legislation the issue stays unresolved.

#### EU-WTO conflict causes WTO collapse – it’s the glue that holds the organization together in an international arena characterized by US and China trade disputes

Horton and Hopewell 8/3 [(Ben, Communications Manager; Project Lead, Common Futures Conversations) (Dr Kristen, Associate Professor, and Canada Research Chair in Global Policy, University of British Columbia) “Lessons from Trump’s assault on the World Trade Organization”, Chatham House 8/3/2021 https://www.chathamhouse.org/2021/08/lessons-trumps-assault-world-trade-organization] BC

The main reason behind the EU’s success in taking a leadership role is its willingness to put forward a concrete solution, however temporary, to the appellate body crisis. Ultimately, the MPIA is a stop-gap measure – akin to triage or battlefield medicine – but it is respected as a means of salvaging the trading system and preventing the United States from destroying the WTO’s foundational rules and principles. More broadly, the EU holds a lot of credibility as a long-standing champion of multilateralism. If trade tensions between the United States and China continue to escalate, perhaps the EU is best placed to act.

Why did we not see a stronger response from China towards US policy on the WTO under Trump?

When Trump came to power, China tried to present itself as a country that was going to step in and play a leadership role – as a champion of globalization and the liberal trading order. But that’s not what we’ve seen at the WTO. China has certainly been an important partner in the MPIA initiative led by the EU, but very much as a follower of the EU’s lead. China doesn’t seem to have either the will or the ability to play the same kind of role as the EU in advancing system-preserving initiatives.

I think there are a couple of reasons for this. The first is that China lacks credibility as a defender of the rules-based trading system because of its own use of protectionist trade policies, and its attempts to weaponize trade as an instrument of economic coercion. We saw this, for instance, when China blocked imports from Canada, and also imprisoned two Canadian citizens, in retaliation for Canada’s participation in the Huawei extradition trial. Second, there is a widespread sense amongst WTO member states that China’s commitment to the rules-based trading system is really only partial and that China will violate the rules when it is in its interest to do so. As a result, Chinese efforts to assume leadership at the WTO have been greeted by a lot of distrust and suspicion.

What has this episode revealed about the strength of multilateral institutions such as the WTO, in the face of spoiling tactics from major powers?

The WTO is unique amongst international institutions because it has a powerful enforcement mechanism – the dispute settlement system. However, the fundamental vulnerability is that if powerful states like the US and others won’t participate in the system and be bound by its rules, they quickly risk becoming irrelevant. And that’s the situation we’re in right now with the appellate body crisis, where, without a functioning mechanism to ensure that WTO rules are enforced, the entire system of global trade rules risk collapsing. Ironically, the United States has been the leader of the liberal trading order for the past 70 years, but since Trump, it has become its leading saboteur.

What are the implications of a permanent collapse of the international trading system?

The very real danger from such a breakdown is a return to what we saw in the 1930s. In response to the outbreak of the Great Depression, you had countries imposing trade barriers, blocking imports from other state, and a general escalation of tit-for-tat protectionism. This response wound up not only exacerbating the effects of the depression itself but has also been credited by some as paving the way for the outbreak of the second world war. The reason why institutions like the WTO were created in the first place was to prevent a recurrence of the 1930s protectionist trade spiral. The danger now – if those rules become meaningless and unenforceable – is the institutional foundations of postwar economic prosperity could unravel, throwing us back into economic chaos and potentially political disorder.

**Economic decline causes global nuclear war**

**Tønnesson 15** [(Stein, Research Professor, Peace Research Institute Oslo; Leader of East Asia Peace program, Uppsala University) “Deterrence, interdependence and Sino–US peace,” International Area Studies Review, Vol. 18, No. 3, p. 297-311, 2015] SJDI

Several **recent works** on China and Sino–US relations **have made** substantial **contributions to the current understanding of how and under what circumstances** a combination of **nuclear deterrence and economic interdependence may reduce the risk of war between major powers**. At least four conclusions can be drawn from the review above: first, those who say that **interdependence may both inhibit and drive conflict** are right. **Interdependence raises the cost of conflict** for all sides **but** **asymmetrical or unbalanced dependencies and negative trade expectations** may **generate tensions leading to trade wars among inter-dependent states that** in turn **increase the risk of military conflict** (Copeland, 2015: 1, 14, 437; Roach, 2014). The risk may increase if one of the interdependent countries is governed by an inward-looking socio-economic coalition (Solingen, 2015); second, the risk of war between China and the US should not just be analysed bilaterally but include their allies and partners. Third party countries could drag China or the US into confrontation; third, in this context it is of some comfort that the three main economic powers in Northeast Asia (China, Japan and South Korea) are all deeply integrated economically through production networks within a global system of trade and finance (Ravenhill, 2014; Yoshimatsu, 2014: 576); and fourth, **decisions for war** and peace **are taken by very few people, who act on the basis of their future expectations**. International relations theory must be supplemented by foreign policy analysis in order to assess the value attributed by national decision-makers to economic development and their assessments of risks and opportunities. **If leaders** on either side of the Atlantic **begin to seriously fear or anticipate their own nation’s** decline then they **may blame** this on **external dependence, appeal to anti-foreign sentiments, contemplate the use of force to gain** respect or **credibility, adopt protectionist policies, and** ultimately **refuse to be deterred by** either **nuclear arms or prospects of socioeconomic calamities. Such a dangerous shift could happen abruptly**, i.e. under the instigation of actions by a third party – or against a third party.

Yet as long as there is both nuclear deterrence and interdependence, the tensions **in East Asia** are unlikely to escalate to war. As Chan (2013) says, all states in the region are aware that they cannot count on support from either China or the US if they make provocative moves. The greatest risk is not that a territorial dispute leads to war under present circumstances but that changes in the world economy alter those circumstances in ways that render inter-state peace more **precarious**. If China and the US fail to rebalance their financial and trading relations (Roach, 2014) then a trade war could result, interrupting transnational production networks, provoking social distress, and exacerbating nationalist emotions. **This could have unforeseen consequences in the field of security, with nuclear deterrence remaining the only factor to protect the world from Armageddon, and unreliably so**. **Deterrence could lose its credibility**: one of the two **great powers might gamble that the other yield in a cyber-war or conventional** limited **war**, or third party countries might engage in conflict with each other, with a view to obliging Washington or Beijing to intervene.

#### Nuclear war causes extinction – famine and climate change

Starr 15 [(Steven, Director of the University of Missouri’s Clinical Laboratory Science Program and a senior scientist at the Physicians for Social Responsibility) “Nuclear War, Nuclear Winter, and Human Extinction,” Federation of American Scientists, 10/14/2015] DD  
While it is impossible to precisely predict all the human impacts that would result from a nuclear winter, it is relatively simple to predict those which would be most profound. That is, a nuclear winter would cause most humans and large animals to die from nuclear famine in a mass extinction event similar to the one that wiped out the dinosaurs.

Following the detonation (in conflict) of US and/or Russian launch-ready strategic nuclear weapons, nuclear firestorms would burn simultaneously over a total land surface area of many thousands or tens of thousands of square miles. These mass fires, many of which would rage over large cities and industrial areas, would release many tens of millions of tons of black carbon soot and smoke (up to 180 million tons, according to peer-reviewed studies), which would rise rapidly above cloud level and into the stratosphere. [For an explanation of the calculation of smoke emissions, see Atmospheric effects & societal consequences of regional scale nuclear conflicts.]

The scientists who completed the most recent peer-reviewed studies on nuclear winter discovered that the sunlight would heat the smoke, producing a self-lofting effect that would not only aid the rise of the smoke into the stratosphere (above cloud level, where it could not be rained out), but act to keep the smoke in the stratosphere for 10 years or more. The longevity of the smoke layer would act to greatly increase the severity of its effects upon the biosphere.

Once in the stratosphere, the smoke (predicted to be produced by a range of strategic nuclear wars) would rapidly engulf the Earth and form a dense stratospheric smoke layer. The smoke from a war fought with strategic nuclear weapons would quickly prevent up to 70% of sunlight from reaching the surface of the Northern Hemisphere and 35% of sunlight from reaching the surface of the Southern Hemisphere. Such an enormous loss of warming sunlight would produce Ice Age weather conditions on Earth in a matter of weeks. For a period of 1-3 years following the war, temperatures would fall below freezing every day in the central agricultural zones of North America and Eurasia. [For an explanation of nuclear winter, see Nuclear winter revisited with a modern climate model and current nuclear arsenals: Still catastrophic consequences.]

Nuclear winter would cause average global surface temperatures to become colder than they were at the height of the last Ice Age. Such extreme cold would eliminate growing seasons for many years, probably for a decade or longer. Can you imagine a winter that lasts for ten years?

The results of such a scenario are obvious. Temperatures would be much too cold to grow food, and they would remain this way long enough to cause most humans and animals to starve to death.

Global nuclear famine would ensue in a setting in which the infrastructure of the combatant nations has been totally destroyed, resulting in massive amounts of chemical and radioactive toxins being released into the biosphere. We don’t need a sophisticated study to tell us that no food and Ice Age temperatures for a decade would kill most people and animals on the planet.  Would the few remaining survivors be able to survive in a radioactive, toxic environment?

### Solvency

#### Plan: Member nations of the World Trade Organization should reduce IP protections for Clustered Regularly Interspaced Short Palindromic Repeats.

#### CRISPR is segment of DNA that uses proteins to modify other strands of DNA

Lexico ND [(Lexico dictionary) <https://www.lexico.com/en/definition/crispr>] BC

CRISPR

NOUN

1 Biochemistry

A segment of DNA containing short repetitions of base sequences, involved in the defense mechanisms of prokaryotic organisms to viruses.

CRISPR sequences encode RNAs that can recognize specific target sequences in a genome, at which base pairs can be cut or added. They act in a complex with a specific protein that functions like a pair of molecular scissors, with which they are used as a tool in genetic engineering

1.1A genetic engineering tool that uses a CRISPR sequence of DNA and its associated protein to edit the base pairs of a gene.

#### And it is a drug that treats diseases and cures illnesses

Sfera 2/24 [(Dan, entrepreneur. Clinical Trials) “CRISPR Therapeutics creates gene-based medicines”, Real Dan Sfera, 2/24/2021. <https://therealdansfera.medium.com/crispr-therapeutics-creates-gene-based-medicines-25a66c674998>] BC

Gene-Editing Genius

CRISPR (clustered regularly interspaced short palindromic repeats) has been making news about research and investment. Scientists learned that CRISPR, a naturally occurring gene-editing function of bacteria, has potential for treating genetic diseases. Now a number of companies are using gene-editing to try to cure illnesses caused by errors on a single gene. They include sickle cell disease, hemophilia and cystic fibrosis.

Swiss-based CRISPR Therapeutics, a biopharmaceutical company attempting to create transformative gene-based medicines for serious diseases, “has produced results that could not only make it a winner in single-gene disorders, but position it to tackle much more complex — and profitable — diseases in the years ahead,” according to Jason Hawthorne of The Motley Fool (https://www.fool.com/investing/2020/12/15/where-will-crispr-therapeutics-be-in-10-years/). CRISPR Therapeutics, a gene-editing company, attempts to develop gene-based medicines for serious diseases using its proprietary CRISPR/Cas9 platform. CRISPR/Cas9 is a gene-editing technology that allows for precise, directed changes to genomic DNA. The company has a wholly-owned U.S. subsidiary, CRISPR Therapeutics, Inc., and R&D operations based in Cambridge, Massachusetts, and business offices in London, United Kingdom.

CRISPR’s CTX001 is a potential drug to treat sickle cell disease and beta-thalassemia, disorders that affect the oxygen-carrying cells in the blood. After harvesting a patient’s own cells from his or her own bone marrow, medical professionals use CTX001 to edit the gene responsible for red blood cell production and infuse the cells back into the body. In 2015, CRISPR entered into a partnership with Vertex Pharmaceuticals to develop a number of treatments using this technology, receiving cash, equity and future royalties, while Vertex obtained the rights to market the treatments to be developed.

### Framing

**The standard is maximizing expected wellbeing**

**First, pleasure and pain are intrinsically valuable. People consistently regard pleasure and pain as good reasons for action, despite the fact that pleasure doesn’t seem to be instrumentally valuable for anything.**

**Moen 16** [Ole Martin Moen, Research Fellow in Philosophy at University of Oslo “An Argument for Hedonism” Journal of Value Inquiry (Springer), 50 (2) 2016: 267–281] SJDI

Let us start by observing, empirically, that a widely shared judgment about intrinsic value and disvalue is that pleasure is intrinsically valuable and pain is intrinsically disvaluable. On virtually any proposed list of intrinsic values and disvalues (we will look at some of them below), pleasure is included among the intrinsic values and pain among the intrinsic disvalues**.** This inclusion makes intuitive sense, moreover, for there is something undeniably good about the way pleasure feels and something undeniably bad about the way pain feels, and neither the goodness of pleasure nor the badness of pain seems to be exhausted by the further effects that these experiences might have. “Pleasure” and “pain” are here understood inclusively, as encompassing anything hedonically positive and anything hedonically negative.2 The special value statuses of pleasure and pain are manifested in how we treat these experiences in our everyday reasoning about values**.** If you tell me that you are heading for the convenience store, I might ask: “What for?” This is a reasonable question, for when you go to the convenience store you usually do so, not merely for the sake of going to the convenience store, but for the sake of achieving something further that you deem to be valuable**.** You might answer, for example: “To buy soda.” This answer makes sense, for soda is a nice thing and you can get it at the convenience store. I might further inquire, however: “What is buying the soda good for?” This further question can also be a reasonable one, for it need not be obvious why you want the soda. You might answer: “Well, I want it for the pleasure of drinking it.” If I then proceed by asking “But what is the pleasure of drinking the soda good for?” the discussion is likely to reach an awkward end. The reason is that the pleasure is not good for anything further; it is simply that for which going to the convenience store and buying the soda is good.3 As Aristotle observes**:** “We never ask [a man] what his end is in being pleased, because we assume that pleasure is choice worthy in itself.”4 Presumably, a similar story can be told in the case of pains, for if someone says “This is painful!” we never respond by asking: “And why is that a problem?” We take for granted that if something is painful, we have a sufficient explanation of why it is bad. If we are onto something in our everyday reasoning about values, it seems that pleasure and pain are both places where we reach the end of the line in matters of value.

**Moreover, *only* pleasure and pain are intrinsically valuable. All other values can be explained with reference to pleasure; Occam’s razor requires us to treat these as instrumentally valuable.**

**Moen 16** [Ole Martin Moen, Research Fellow in Philosophy at University of Oslo “An Argument for Hedonism” Journal of Value Inquiry (Springer), 50 (2) 2016: 267–281] SJDI

I think several things should be said in response to Moore’s challenge to hedonists. First, **I do not think the burden of proof lies on hedonists to explain why the additional values are not intrinsic values. If someone claims that X is intrinsically valuable, this is a substantive, positive claim, and it lies on him or her to explain why we should believe that X is in fact intrinsically valuable.** Possibly, this could be done through thought experiments analogous to those employed in the previous section. Second, **there is something peculiar about the list of additional intrinsic values** that counts in hedonism’s favor**: the listed values have a strong tendency to be well explained as things that help promote pleasure and avert pain.** To go through Frankena’s list, life and consciousness are necessary presuppositions for pleasure; activity, health, and strength bring about pleasure; and happiness, beatitude, and contentment are regarded by Frankena himself as “pleasures and satisfactions.” The same is arguably true of beauty, harmony, and “proportion in objects contemplated,” and also of affection, friendship, harmony, and proportion in life, experiences of achievement, adventure and novelty, self-expression, good reputation, honor and esteem. Other things on Frankena’s list, such as understanding, **wisdom, freedom, peace, and security, although they are perhaps not themselves pleasurable, are important means to achieve a happy life, and as such, they are things that hedonists would value highly.** **Morally good dispositions and virtues, cooperation, and just distribution of goods and evils, moreover, are things that, on a collective level, contribute a happy society, and thus the traits that would be promoted and cultivated if this were something sought after.** To a very large extent, the intrinsic values suggested by pluralists tend to be hedonic instrumental values. Indeed, pluralists’ suggested intrinsic values all point toward pleasure, for while the other values are reasonably explainable as a means toward pleasure, pleasure itself is not reasonably explainable as a means toward the other values. Some have noticed this. Moore himself, for example, writes that though his pluralistic theory of intrinsic value is opposed to hedonism, its application would, in practice, look very much like hedonism’s: “Hedonists,” he writes “do, in general, recommend a course of conduct which is very similar to that which I should recommend.”24 Ross writes that “[i]t is quite certain that by promoting virtue and knowledge we shall inevitably produce much more pleasant consciousness. These are, by general agreement, among the surest sources of happiness for their possessors.”25 Roger Crisp observes that “those goods cited by non-hedonists are goods we often, indeed usually, enjoy.”26 What Moore and Ross do not seem to notice is that their observations give rise to two reasons to reject pluralism and endorse hedonism. The first reason is that if **the suggested non-hedonic intrinsic values are potentially explainable by appeal to just pleasure and pain** (which, following my argument in the previous chapter, we should accept as intrinsically valuable and disvaluable), **then—by appeal to Occam’s razor—we have at least a pro tanto reason to resist the introduction of any further intrinsic values and disvalues. It is ontologically more costly to posit a plurality of intrinsic values and disvalues, so in case all values admit of explanation by reference to a single intrinsic value and a single intrinsic disvalue, we have reason to reject more complicated accounts.** **The fact that suggested non-hedonic intrinsic values tend to be hedonistic instrumental values does not, however, count in favor of hedonism solely in virtue of being most elegantly explained by hedonism; it also does so in virtue of creating an explanatory challenge for pluralists.** The challenge can be phrased as the following question: **If the non-hedonic values suggested by pluralists are truly intrinsic values in their own right, then why do they tend to point toward pleasure and away from pain?**27

**Moral uncertainty means preventing extinction should be our highest priority.  
Bostrom 12** [Nick Bostrom. Faculty of Philosophy & Oxford Martin School University of Oxford. “Existential Risk Prevention as Global Priority.” Global Policy (2012)]  
These reflections on **moral uncertainty suggest** an alternative, complementary way of looking at existential risk; they also suggest a new way of thinking about the ideal of sustainability. Let me elaborate.¶ **Our present understanding of axiology might** well **be confused.**

**We may not** nowknow — at least not in concrete detail — what outcomes would count as a big win for humanity; we might not even yet **be able to imagine the best ends** of our journey. **If we are** indeedprofoundly **uncertain** about our ultimate aims,then we should recognize that **there is a great** option **value in preserving** — and ideally improving — **our ability to recognize value and** to **steer the future accordingly. Ensuring** that **there will be a future** version of **humanity** with great powers and a propensity to use them wisely **is** plausibly **the best way** available to us **to increase the probability that the future will contain** a lot of **value.** To do this, we must prevent any existential catastrophe.

**Reducing the risk of extinction is always priority number one.   
Bostrom 12** [Faculty of Philosophy and Oxford Martin School, University of Oxford.], Existential Risk Prevention as Global Priority.  Forthcoming book (Global Policy). MP. http://www.existenti...org/concept.pdfEven if we use the most conservative of these estimates, which entirely ignores the   possibility of space colonization and software minds, **we find that the expected loss of an existential   catastrophe is greater than the value of 10^16 human lives**.  **This implies that the expected value of   reducing existential risk by a mere one millionth of one percentage point is at least a hundred times the   value of a million human lives.**  The more technologically comprehensive estimate of 10  54 humanbrain-emulation subjective life-years (or 10  52  lives of ordinary length) makes the same point even   more starkly.  Even if we give this allegedly lower bound on the cumulative output potential of a   technologically mature civilization a mere 1% chance of being correct, we find that the expected   value of reducing existential risk by a mere one billionth of one billionth of one percentage point is worth   a hundred billion times as much as a billion human lives. **One might consequently argue that even the tiniest reduction of existential risk has an   expected value greater than that of the definite provision of any ordinary good, such as the direct   benefit of saving 1 billion lives.**  And, further, that the absolute value of the indirect effect of saving 1  billion lives on the total cumulative amount of existential riskâ€”positive or negativeâ€”is almost   certainly larger than the positive value of the direct benefit of such an action.