Chapter One

What is Science-based Bioethics?

Introduction

Each year, biotechnology bravely ventures into unexplored scientific territory. The year 2016 was no exception: The number of scientific breakthroughs that emerged during this year is overwhelming with gene editing (CRISPR) technologies, gene drives to eliminate harmful mosquitos, and synthetic DNA topping the list. As will be discussed in Chapter Eight, scientists have developed ingenious methods to edit the DNA code of the human genome in cells, embryos, and human beings. Equally astonishing are the reports of two new synthetic DNA bases that have been synthesized. Applying this synthetic biology technology, scientists have expanded the DNA code from 4 to 6 base pairs (Malyshev et al., 2014). Yet, the real dangers of gene editing, synthetic biology, and the creation of a synthetic human genome remain unknown, raising the question whether humankind is dramatically overstepping innate ethical boundaries.

In May of 2016, a closed door meeting convened to discuss the issue of constructing an entire human genome in a cell line, a project prospectively titled 'HGP-Write: Testing Large Synthetic Genomes in Cells'. As the New York Times reports, the meeting was invite-only and "The nearly 150 attendees were told not to contact the news media or to post on Twitter during the meeting."

In the past year, neuroscience research has led to countless innovations as well. Selected examples include: a) stem cell and genetic technologies to enhance the cognition and learning potential of mice, b) brain rejuvenation of older mice to their youthful plasticity with stem cell technologies, c) artificial intelligence in human-like robots (see https://www.youtube.com/watch?v=W0_DPi0PmF0 for a dramatic video about human-like robots), and d) genetically modified bacteria that can function as biological circuits. Even in the area of human life span, research into telomeres has generated protocols that could increase the human life span by decades. All of these advances in science raise complex bioethical dilemmas that must be addressed by legal, scientific, and ethical scholars.

Four scientific breakthroughs have paved the path for many of the above mentioned biotechnologies. The first of which, reported in 1997 (Wilmut et al., 1997), was cloning a sheep called Dolly. The groundbreaking method utilized nuclear transfer technology to produce a mammal cloned from an adult cell obtained from the mammary gland. Within a year after Dolly was cloned, scientists reported an innovative method to isolate human embryonic stem cells from discarded embryos and to maintain them indefinitely in culture (Thomson et al., 1998). Induced pluripotent cell (iPS) technologies was the third milestone that allowed the transformation of adult fibroblasts into embryonic stem cells without using embryos as a cellular source (Takahashi et al., 2007). The leap in our understanding of the regulation of genetics is the final breakthrough. Together with the mapping of the human genome and our increased awareness of epigenetics and capacity to edit our genes, these technological discoveries have ushered in a new era of human therapeutic and research cloning. If ethically developed, these technologies will allow us to control our own biological and genetic destinies in ways never before imagined.

Every new scientific advancement and discovery generates a plethora of ethical questions and dilemmas. This book is based on the principle that bioethics itself is an amalgam of many different disciplines and skills that must include the underlying science. Once the scientific principles are understood then other bioethical approaches incorporating philosophy, social values, culture, and religion can be integrated with the scientific facts to attempt to resolve these complex, and often contentious, moral issues.

Aims of this Textbook

This book has multiple aims. It presents advancing perspectives on how scientific discoveries elicit bioethical concerns and challenges to all students interested in the future of scientific progress. Readers interested in enhancing the sciences and allied fields or pursuing careers in these fields will be pushing the boundaries of scientific discovery, and will need to deliberate bioethical issues that often arise from scientific experiments. As their professional careers in science and medicine develop, their innovative research and ability to communicate science to the public will stimulate bioethical debate. The cardinal rule in ethics is that good ethics begins with a factual understanding of the underlying science. This book thus provides the essential scientific background and bioethical information that should allow basic scientists, healthcare professionals, clinical researchers, and indeed students, to better comprehend, appreciate, and address the complex bioethical dilemmas that our society confronts now and will confront in the future.

It is important to predict what bioethical issues will emerge from new biotechnologies. The emphasis of this book highlights how understanding the underlying science can assist in resolving bioethical dilemmas. Wherever possible this book also emphasizes the key role that philosophy, cultural values, and religious approaches to bioethics can play and influence how bioethical challenges are resolved. Only then can there be a practical analysis of how to resolve, manage, or defuse the bioethical dilemmas. Rather than simply presenting hypothetical resolutions to bioethical dilemmas, this book discusses current as well as futuristic cases to better enable students to formulate their own practical strategies for identifying and resolving emerging bioethical dilemmas.

Four Specific Objectives of this Book

To promote these aims, this book outlines four specific objectives: (1) to present the scientific basis for new biotechnologies and discuss how these technologies trigger bioethical dilemmas; (2) to highlight situations where bioethical concerns in research may differ from classical concerns of medical ethics; (3) to demonstrate when a historical analysis of ethical controversies arising from earlier biotechnological advances can, at times, provide insights into resolving current bioethical debates; and (4) to present appropriate scientific strategies that can be implemented to resolve, defuse, or manage bioethical disputes.

The first objective of this book assumes an appropriate scientific and ethical mindset to understanding both the potential and the limitations of a new technology. It is important to also recognize that bioethical dilemmas can sometimes arise from factual misinformation. Misconceptions about the underlying science may lead to misunderstandings of the emerging ethical issues that ultimately can generate bioethical shockwaves that reverberate through the government and media, distracting society from the more salient, factual issues. Thus, it is critical to grasp the underlying facts related to the bioethical dilemmas to ensure that discussions are not tainted by imprecise knowledge or scientific bias. In other words, the ability to address bioethical challenges begins with obtaining the most accurate scientific information. As senator Moynihan stated, “Individuals are entitled to their own opinions, but they are not entitled to their own facts”.

There are many misconceptions concerning the sovereignty of genetics in shaping human personality and abilities. Equally important, many students are unfamiliar with the emerging insights that can be obtained from epigenetics. In natural twinning, as one example, each twin experiences his/her individual environment simultaneously. In contrast, if someone is cloned using donor cells from a professional athlete such as Lebron James, there is a preconceived notion of how the clone’s genetic endowment will influence his life’s development. Will the cloned Lebron James also develop into a professional basketball superstar? What impact will the woman’s uterine and hormonal environment have on the clone during fetal development? How much self-motivation and what other environmental contributions will be required to develop this cloned child into a skilled athlete? These questions raise broader bioethical questions such as: Will reproductive cloning challenge human individuality or autonomy? Is it ethical to subject this cloned child to the psychological, physical, or financial pressures arising from knowledge of the successes and failures of his genetic donor, the original Lebron James? Moreover, what other social pressures will shape his environment in order to nurture his presumed athletic ability or future as a superstar basketball player?

The general public tends to underestimate the complexity of the nature and nurture interaction in determining one's biological destiny. In particular, it is now increasingly evident that DNA, although inherited, still responds to environmental pressures (Robinson, 2004). Epigenetic research addresses these issues in understanding how "software" in programming gene regulation is influenced by chemical modifications of DNA base pairs and their associated proteins without altering the base sequences of the genome. Through epigenetic research, we are unraveling how environmental and genetic factors do not necessarily work in opposition; rather, a synergistic and continuous interaction of these factors orchestrates human behavior, aging, and disease (Goldman, 2012; Marx, 2012).

Epigenetics changes of identical twins during their youth generate dramatic changes in their athletic skills or in the diseases that they developed as adults (Aaltonen et al., 2014; Castillo-Fernandez et al., 2014; Rottensteiner et al., 2015). Studies of identical twins in Finland showed that those twins who shared the same sports and other physical activities as youngsters but different exercise habits as adults soon developed quite different bodies and brains. This study highlights the extent to which exercise shapes our health via epigenetics, even in people who have identical genes and nurturing.

In 2016, many scientific reports claimed to have developed reliable blood based assays to predict the onset of diseases such as Alzheimer's disease. This diagnostic blood test identifies men that are more likely to develop Alzheimer's disease when they has been lose their Y sex chromosome. The public often accepts these reports as absolutely accurate even though it will take decades to establish the scientific validity of these technologies.

Despite the stated goal of this book's first objective - to present the scientific basis for new biotechnologies and discuss how these technologies trigger bioethical dilemmas - there is the realization that scientific discoveries are developing and changing at such a rapid rate that it is impossible to write a comprehensive book that will remain up to date with all of the given emergent observations and discoveries. Chapter Nine has been completely re-written to focus on CRISPR and synthetic biology rather than classical genetics.

The second objective of this book focuses on differences between research bioethics and medical ethics. Bioethics is generally perceived as an all-encompassing discipline that includes medical ethics, neuroethics, genethics, environmental ethics, and research ethics. Research ethics is an emerging new discipline as the study of ethical practice and the dilemmas that arise with the acquisition of scientific knowledge and the development of new biotechnologies that impact biological species and the environment. A critical component of research bioethics, is the need to translate all research done in vitro or in vivo into human applications. Practically, the often and unanswered question is as follows: When is it ethically appropriate to engage in the first human clinical trialto explore the efficacy of a new procedure or therapy? In contrast, medical ethics focuses on issues already available in the clinic, such as physician-assisted suicide and abortion that immediately and directly impact the patient or the patient-healthcare professional relationship. These conceptual differences may lead to the formulation of unique guidelines for each discipline.

While the concepts of this book focus on research-oriented bioethics, many questions and issues extend far beyond the research laboratory. Stem cell research is a good example that raises broader questions pertaining to the definition of human life, such as identifying the stage of embryological development at which human status or personhood is said to be attained. Another question is appropriate here: How does genomics confer species identity? Similarly, introducing human embryonic stem cells into laboratory animals to create chimeras enables scientists to better investigate how cells differentiate to become specialized cells. Research published in 2014-2015 has shown that introducing specific human genes into mice or reconstituting human astrocytes (non-neural supportive cells of the brain) into mice embryos dramatically improve learning behaviors and intelligence of these animals. Is it ethical to transplant human stem cells into mouse or chimp embryo in an attempt to reconstitute a human brain into an animal? In this way, the capacity to transplant human stem cells into animals and possibility animal genes into humans challenge the classical definition of species. Moreover, the unique status of personhood that was historically limited only to human beings is being applied to other non-human primates. Research showing human-like behaviors in non-human primates have triggered new laws that grant certain monkeys the status of personhood.

The third objective of this book is to demonstrate how the historical analysis of ethical controversies arising from earlier biotechnological advances can, at times, provide insights useful for resolving current bioethical debates. As an example, bioethical concerns about when human personhood begins in fetal development were raised in 1978 after Louise Brown became the first of more than five million “test tube” babies produced by in vitro fertilization (IVF). The success IVF has dampened the original ethical debates first raised in 1978. In contrast, the current bioethical concerns in defining human life in stem cell research often neglects IVF as a historical precedent. One could predict that if stem cell technologies prove to emerge as a successful treatment of diseases, such as diabetes or Alzheimer’s disease, the ethical concerns surrounding this technology may also become less relevant.

One historical lesson from IVF is that once a technology is shown to be effective in treating a medical condition (infertility), the public becomes less concerned about possible bioethical questions inherent in these technologies. This historical example also illustrates that as the technology is enhanced, what the public deems unacceptable shifts over time. This is a subtle societal process which also may dull awareness of serious ethical pitfalls, particularly if the new technology confers high benefits and value to society**.**

In addition, there are times when history can offer insights into conflict resolution and management. We have seen that the original motivation for biotechnological development often differs from its eventual application. The history of cloning Dolly is an excellent example. A biotechnology company, PLL, in collaboration with the Roslin Institute, cloned Dolly for commercial purposes — to develop technology for the production of biological pharmaceuticals in animal milk at a cost significantly lower than conventional production methods. This application required the development of a procedure in the laboratory to genetically modify mammary epithelial cells to encode the production of a specific drug. Once these cells were appropriately modified in the laboratory, a procedure had to be developed to generate an animal that expressed these genetically modified mammary epithelial cells. Nuclear transfer technology using adult cells offered a viable solution to generate these types of genetically modified animals, and is the primary reason why Dolly was cloned. It was no coincidence that the term cloning never was found in their original report that appeared in Nature (Wilmut et al., 1997). Nonetheless, this publication triggered an intense bioethical debate regarding the use of cloning for human reproduction and for embryonic stem cell research. Applying historical analysis to this example, one might conclude that animal cloning may be ethical for commercial use including the development of cheaper and more efficient drugs; applying this limited technology to today's human reproduction, however, remains unethical since reproductive cloning is currently not allowed in most societies today.

However, the tide against human reproductive cloning is changing. In 1997, Gallop poll surveys showed that less than 5% of those surveyed in the United States favored cloning technologies. In 2015, the number of people who find cloning technologies ethical has risen to greater than 15%, presumably because new medical applications of human cloning (i.e. somatic cell nuclear transfer) have been implemented to treat a variety of conditions in reproductive medicine, such as mitochondrial replacement therapy.

Historical analysis also reveals that the rapid pace of biomedical research has seriously challenged society's ability to make informed and reasoned choices about whether and how to proceed with its development and use (Frankel and Chapman, 2001). Traditionally we have proceeded in a "catch-up" or "reactive" mode, scrambling to match our moral values and social and legal policies to scientific advances. Potential breakthrough technologies such as gene transfer take decades to develop, yet choices must be made immediately regarding research directions to take and treatments to investigate.

Any historical analysis should include the role of government policy and regulation in biomedical research. The United States government policy on bioethical issues is often shaped by the moral beliefs of both those in power and the public. The belief that conception is the beginning of human life led to restrictions on the use of Federal funds to support human embryonic stem cell research, initiated by President William Clinton in 1995**.** While many criticize this federal policy, there may be a silver lining in how our government has attempted to deal with the contentious bioethical issues associated with human embryonic stem cell technology. Surprisingly and generally unappreciated is that president Bush's ban on the use of federal funds to support human embryonic stem cell research created a void that stimulated many non-federally funded research efforts that ultimately helped extend and deepen the partnership between the fields of bioethics and biomedical research. New funding streams were created with private and state funds leading to important advances (such as iPS and transdifferention technologies) that spawned new ethical debate. In 2009, President Obama instructed the National Institutes of Health to issue new guidelines for federally supported human embryonic stem cell research to better coincide with the public's belief that stem cell research has the promise to yield dramatic new therapies (Daley, 2012).

While biomedical scientists are primarily driven by the challenge to understand biological processes or the need to create new cures and treatments for major diseases, bioethical issues have begun to play a greater role in defining the landscape of biomedical research, especially in stem cell science. This is but one example that highlights the role of government in shaping the direction of biomedical research.

The book's fourth objective is to introduce science-based strategies as a method for resolving, defusing, or managing bioethical concerns. Bioethical management is a three-step process. First, the facts must be determined. Then the issues and the stakeholders must be identified. Finally proposed strategies for resolution must be created. Determining the facts implies understanding the relevant science and identifying the underlying religious, cultural, legal, or political concerns related to the dilemma. The stakeholders could be patients, companies, or governments. Finally, developing strategies to help manage or resolve bioethical dilemmas involves an integrated approach.

Classically, philosophical paradigms and traditional ethical approaches have been useful in many situations. Ethical values, however, may be relative, never absolute, and often evolving. Today, we are witnessing a paradigm shift in applied bioethics where science-based strategies have begun to offer new integrated approaches to augment the classical philosophically-based strategies. To illustrate this point, if someone believes that an embryo attains human status at conception, no amount of scientific, philosophical, or ethical discourse can sway that individual to support embryonic stem cell research because stem cells are currently derived from a conceived embryo that must be destroyed in the process of deriving stem cells. However, as scientists develop novel methods to generate stem cells, such as reprogramming a normal adult-differentiated cell into a stem cell (Wilmut et al., 2007), research utilizing these stem cells should be less ethically charged than research using the cells of donated embryos. This book will highlight several traditional ethical approaches to help resolve issues and will illuminate how new scientific research approaches offer technological alternatives that could alleviate ethical aporias.

Political and financial considerations are also important factors in managing or resolving bioethical concerns. If new biotechnologies are restricted or banned by the federal government, there is a risk that persons with medical needs may be deprived of the future medical discoveries that could emerge from the prohibited research attempts. On the other hand, there are the doomsday scenarios, be they real or imagined, which create pressures to restrict or block basic biomedical research. As a case in point, the technology for creating synthetic biological organisms has the possibility of creating safer vectors for gene transfer in therapeutic protocols, but with "dual use" could also be applied to generate new pathogens that might trigger massive epidemics or serve as blueprints for future weapons of bioterror (Hunter, 2012; Keim, 2012). Risk-benefit analysis, treatment alternatives, and financial resource management all therefore are important considerations when deciding to fund or pursue a new direction in biomedical research.

The public, as taxpayers funding the scientific research community, has a right, perhaps even an obligation, to help shape the course of scientific research and could be playing a larger role in deciding which research is funded. While some within the scientific community fear that engaging the public in research funding decisions could be ineffective, lay leaders are, nonetheless, taking a more empowered role in funding biomedical research. Many foundations in the research-charity sector engage lay leaders (trustees) who are non-scientists to help shape and direct the research funded by these charitable organizations without hindering scientific advancement.

It is critical that scientists, physicians, and the professional scientific research community take responsibility to ensure that the science behind any technology is accurately presented and that the ethical concerns are identified and mapped. With that in mind, this book is designed so that each new technology will span two sections and sometimes two chapters. The first section focuses on a comprehensive survey of the science underlying a new biotechnology. The second section examines the ethical, religious, legal, and social challenges that are precipitated from the technology. In addition, the second section will attempt to explore various ethical approaches to try to resolve the resultant bioethical dilemmas. This integrated format is designed to help the readers of this book explore, express, and formulate their own ideas. Each section will include case studies for students to think about creatively and to allow them to formulate concrete and practical ways to resolve these controversial bioethical concerns.

In the supplementary section of this book, we include a brief description of how to write an op ed bioethical article. It is important that scientists present complex biotechnologies and bioethics to the general public as part of their social responsibility to educate the public about the benefits and risks of new biotechnologies. We encourage our readers who may be or become experts in various scientific disciplines to express their views to the public.

Several important areas (such as animal experimentation, environmental concerns, evolution, and religion) will not be addressed in detail, as they are beyond the scope of this book. Other topics such as research freedom, research responsibility and accountability, conflicts of interest, and scarcity of financial resources will be incorporated, appropriately, into several of the chapter topics.

Conclusions

In summary, bioethics and science intersect and interact at various levels. The potential to understand basic principles in biology as well as the clinical impact of many of these biotechnologies often remains to be established as the resultant bioethical issues are further identified and debated. The resolution of bioethical dilemmas is a complicated process for several reasons. First, simple solutions to bioethical issues may be difficult to obtain because critical facts are not always available at the time when there is a need for practical decisions. Second, decisions in both science and bioethics have to be acted upon immediately in order to forge ahead in a timely fashion even when the facts are incomplete. Third, sometimes issues arise that generate a clash of ethical principles such as beneficence and autonomy. Grappling which bioethical principles will take precedence and must be addressed. These compounding factors related to bioethics may restrict one's capacity to resolve a dilemma but may allow one to develop ways to manage a bioethical conundrum.

This book proposes that both bioethics and science should exist in a mutually beneficial and symbiotic relationship motivated by a common goal to acquire knowledge purely for its own sake and for its potential for needed therapeutic applications. This is the new mission in bioethics: to provide an integrated, multidisciplinary analysis to enable our future scientists, health care providers, lawyers, and politicians to manage and resolve the many significant emerging bioethical issues.

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