John D. Loike and Moshe D. Tendler

John D. Loike, Ph.D., is the Co-Director of Graduate Studies, Department of Physiology and Cellular Biophysics and Director for Special Projects, Center for Bioethics at Columbia University College of Physicians and Surgeons.

Rabbi Moshe D. Tendler is Professor of Biology and Rabbi Isaac and Bella Tendler Professor of Jewish Medical Ethics at Yeshiva University.

ETHICAL DILEMMAS IN STEM CELL RESEARCH: HUMAN-ANIMAL CHIMERAS

INTRODUCTION

Since Thomson, et al.,\(^1\) reported growing and maintaining human stem cells from embryos,\(^2\) there has been a great deal of discussion concerning ethical issues related to stem cell research. These ethical concerns include: a) human beings “playing God”; b) at what point does an embryo attain human status; c) human therapeutic cloning; d) respecting the procreative potential of the human zygote; e) allocation of limited resources for biomedical research; and f) slippery-slope issues that could emerge from this technology, such as human reproductive cloning. In response to these ethical concerns, many excellent articles have been published that focus on Jewish/halakhic perspectives.\(^3\) This article presents a Torah perspective on an emerging ethical issue in embryonic stem cell research that has not received sufficient attention.

We present the following case that is currently being debated among bioethicists in the United States: What are the ethical considerations in transplanting embryonic human brain stem cells into an animal embryo in an attempt to reconstitute an animal’s brain with human nerve cells? Such an organism, composed of both human and animal cells is called a chimera, a Greek name for a mythical beast that had a lion’s head, goat’s body, and a serpent’s tail. Is it halakhically permissible to create an animal whose brain is composed of human nerve cells? Is such a being really an animal? What if this organism speaks or expresses human-like intelligence? Is it human? As these experiments are now being done in a vari-
ous laboratories around the world, rabbinic authorities will have to face the ethical challenges from this emerging stem cell biotechnology.

There are several halakhic and philosophical concerns regarding the use of stem cells to reconstitute a human brain in an animal fetus. Two primary concerns are the prohibition of kil’ayim, or constancy of speciation, and preservation of human dignity (kavod ha-beriyot).⁴

THE USE OF HUMAN-ANIMAL CHIMERAS
USE IN MEDICINE

Human-animal chimeras or organisms that are composed of a mixture of human and animal tissues have been developed in medical centers around the world for two decades and have led to significant medical applications. One of the first human-mouse chimeras was developed in the 1980s by Dr. Irving Weissman of Stanford University. He transplanted human bone marrow stem cells into a strain of mice that lacked their own immune system. The human stem cells from the bone marrow reconstituted a human immune system in these mice, rendering these mice extremely valuable in studying a variety of human diseases, such as AIDS. Since the virus (HIV) that causes AIDS does not normally infect mouse cells, these human-mouse chimeras serve as an important laboratory model to learn how HIV infects and replicates in human immune cells. Other human-mice chimeras are currently used by biotechnology and drug companies to develop and test potential new therapies for fighting other viruses that affect the immune system and certain hematological (blood born) cancers.⁵ In addition, scientists have been able to repopulate a mouse liver with human liver cells to gain a better understanding of liver development and to examine drug metabolism within human livers.⁶

Chimeras are not only useful in understanding the way the human body works, but they may eventually be used to reproduce human body parts. Esmail Zanjani, of the University of Nevada, is developing a technology that has the potential to create patient-specific organs for transplantation.⁷ Research has shown that about halfway through a sheep’s embryological development, its immune system does not reject any transplantable foreign cell (normally, foreign cells are identified as such by the immune system and are rejected just like other foreign bodily invaders, such as bacteria and viruses). Scientists can therefore transplant human stem cells into a fetus of a sheep thereby incorporating these human cells into various sheep organs and allowing these organs
to contain primarily human cells. This has tremendous potential therapeutic benefit. For example, if a patient requires a liver transplant, physicians could remove the patient’s bone marrow stem cells and inject them into the liver of a sheep fetus. Once born, this sheep would have a liver composed primarily of human cells, meaning that it would be genetically compatible with that patient. The human liver developed in the sheep could be transplanted into that same patient with a minimal danger of organ rejection and without the need to provide anti-rejection drugs that are normally administered for long periods of time. There are still other medical obstacles that must be overcome before this research enters clinical studies. However, if this research leads to the creation of human-sheep chimeras with over 90% of its liver or kidneys composed of human cells, such a therapeutic protocol might alleviate the backlog and difficulty of finding appropriate organ donors.

IS THERE SCIENTIFIC MERIT IN USING CHIMERAS FOR NEUROLOGICAL RESEARCH?

There has not been any significant halakhic debate concerning transplanting human blood stem cells or liver stem cells into mice or sheep. A more challenging concern, is whether it is halakhically permissible and/or proper to transplant precursor human brain stem cells into animal embryos with the intention of allowing human nerve cells to become incorporated into the brain of a mouse or monkey and possibly creating an animal with human-like intelligence. One critical aspect in analyzing halakhic parameters regarding this issue is whether such human-animal chimeras might be useful in developing new medical therapies. Two different research scenarios are presented that could emerge from these experiments and lead to advances in medicine.

- Developing human-animal chimeras with human brain cells might help scientists better understand how the human brain is formed during embryological development. Scientists may use human-animal chimeras to understand how brain size is regulated or how human neural networks or circuits are formed during embryological development. Chimeras provide a novel model system because there are many different kinds of human cells that are found in the embryo or fetus that are necessary for the brain development. Identifying these cells and understanding how these diverse cell types regulate brain development in an animal environment is important in understand-
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ing how the human brain develops normally.

- Human-animal chimeras could be utilized to study human neurological diseases. For example, one could transplant human stem cells from an individual with a genetic predisposition to develop Alzheimer's disease or Huntington's disease into an animal fetus. Then, one could follow the progress of brain development from birth until old age to characterize neural degeneration within an animal model. Such an animal model would answer several important questions including whether these diseases only develop latter in life or whether there are early, detectable changes in the younger brains of these patients. There are also other clinical applications for this type of research. For example, scientists could use specific mice genetically altered to develop Alzheimer's disease to create chimeras that express human brain non-neural cells, such as microglial cells or astrocytes. Work at Columbia University College of Physicians and Surgeons and at other institutions has shown that microglial cells or astrocytes are critical in removing amyloid plaques that normally develop during aging. It is thought that in Alzheimer's patients, these cells are less effective in removing these plaques and respond to the build up of amyloid plaques by releasing chemicals that destroy surrounding neurons. Human-mouse chimeras could provide an animal model to examine whether reengineered human microglia or astrocytes could prevent amyloid plaque build-up, delay onset of the disease, or repair areas of the brain destroyed by Alzheimer's disease. All of these types of experiments are based on the principle that the more humanlike the animal, the better research model it makes for testing drugs and new therapies.

Using human-animal chimeras in neurological research is not an easy choice, even for scientists. There is a real concern that creating human-animal chimeras with human brain cells might trigger the transfer of human behavioral characteristics to an animal. Could transplanting human embryonic stem cells into animal embryos or fetuses create talking chimps or animals that express human-like intelligence?

There is limited scientific evidence that transplanted brain cells from one species into another can indeed transfer behavioral characteristics. In one report, Dr. Evan Balaban at McGill University in Montreal, took small sections of brain from developing quail and transplanted them into the developing brains of chickens. The resulting chicken-quail chimeras exhibited vocal trills and head bobs unique to quail, suggesting that the transplanted parts of the chicken brain contained the neural
circuitry for quail calls. This research offers astonishing evidence that complex behaviors could be transferred across species.10

Currently, scientists are not interested in transferring behavioral characteristics from humans to animals and certainly not from animals to humans. The main objective in developing human-animal chimeras with human brain cells is to examine basic questions in neural development and circuitry and to help cure neurological diseases. While there is scientific merit in using human-animal chimeras to study neurological process, we must question whether there is the danger that this technology may violate halakhic principles, especially if such chimeras express human behavioral traits.

HALAKHIC ISSUES RELATED TO HUMAN-ANIMAL CHIMERAS

You shall keep My statutes. You should not let your cattle mate with a diverse kind; You should not sow thy field with two kinds of seed; neither shall there come upon yourself a garment of two kinds of stuff mingled together.11

*Kil’ayim*, the prohibition of cross-breeding animals, is one halakhic issue that may impact the creation of human-animal chimeras. *Kil’ayim* comes from the root *kaleh*, which means the restraint or withholding of goodness.12 Ramban states that a *bok*, such as *kil’ayim*, is a divine right of the King to instill heavenly awe, *yir’at Shamayim*, onto his people by instituting laws without revealing the reasons for those laws.13

Yet, the Talmud (Pesahim 54a) seems to offer a different explanation. In discussing the origin of cross-breeding animals, R. Yossi teaches that, fire and the mule were not actually created during *bein ha-shemashot* of *Erev Shabbat* of creation. Rather, at that time, God only “thought about” creating them, but delayed doing so until after Shabbat, when “God endowed man with *da’at* (divine wisdom) similar to His, as it were, enabling man to have the insight to create fire and to cross-bred species to create a mule.” *Sefat Emet* explains that these two acts—creating fire and creating a cross-bred species—involves original creativity and that *da’at* reflects this ability to be creative.

If crossbreeding involves creativity, then what is the reason for its prohibition in Jewish law? The reason may relate to a discussion in the Talmud that creating animal *kil’ayim* may result in producing a dangerous species.14 The Talmud explains that the Hebrew word for the wild
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desert mule is yeimim “because they cast fear [eima] upon men.” Thus, Jews are prohibited to engage in kilayim to highlight an inherent danger associated with this technology. Interestingly, non-Jews can engage in kilayim and Jews can benefit from cross-bred species, including the mule. Thus, crossbreeding animals represents a technology that has destructive potential and God delineates the limits of this technology through the prohibition of kilayim.

However, we would like to propose that a chimera and a cross-bred animal are fundamentally different that standard kilayim, from both a biological as well as a halakhic perspective. The Torah describes the prohibition of kilayim as creating hybrid species that result from breeding two different animal species via normal sexual mating. When two different species of animals cross breed then each cell and organ of the resulting offspring contains genetic elements and information from each of the different parent species. Thus, the genetics composition of each cell and organ in the offspring is going to be similar but reflect a combination of the genetic elements of each parent species. The reason that cross bred animals are generally sterile is because their parents have different chromosome numbers or incompatible chromosome homology that interferes with reproductive capacity of the offspring.

In contrast to hybrids, a chimeric animal is created by transplanting embryonic stem cells from one species into the embryo or fetus of another species and allowing those stem cells to develop with the host fetus. Chimeras are then composed of cells from two different species, a cellular mosaic, in which each cell of the chimera contains genetic information of only one of the original species, not a genetic mixture as found in hybrids. Each organ can potentially contain various numbers of cells from either species. Moreover, chimeras would not be necessarily sterile. For example, if human embryonic stem cells are transplanted into the sex organs of a female and male sheep fetus, respectively, then it is theoretically possible that those human-sheep chimeras will be able to produce human sperm and eggs. Allowing these two chimeras to mate might result in human sperm fertilizing human eggs that could generate a viable human being.

From a halakhic perspective, creating human-animal chimeras may not constitute a direct violation of crossbreeding. First, the laws of kilayim do not specifically mandate against cross breeding human beings with animals. Second, the Biblical term rivya, used to describe the prohibition of kilayim, suggests that kilayim must involve sexual mating. Hazon Ish, commenting on the Mishnah, explained that the use of artificial
insemination to produce a hybrid animal does not violate the prohibition of *kil‘ayim* because no sexual mating was involved.\(^\text{18}\)

Thus, creating chimeras would not infringe on the laws of *kil‘ayim* for several reasons. First, one could infer from the comments of *Hazon Ish* that creating human-animal chimeras is halakhically equivalent to artificial insemination, especially since no sperm or eggs are used to create these chimeric organisms.\(^\text{19}\) Second, chimeras would not be sterile, whereas a halakhic concern in the prohibition of creating cross bred animals is generating sterile offspring.\(^\text{20}\) Finally, a fundamental principle in halakha described by *Tiferet Tisrael* in his commentary on the Mishnah, is that all actions other than those explicitly prohibited by biblical or rabbinic decrees are categorically permitted.\(^\text{21}\) There is no apparent activity in creating chimeras that is explicitly prohibited by Biblical or rabbinical decrees. This is especially relevant to *kil‘ayim*, as it is a *hok*, for which no reason was provided. Therefore, the laws of *kil‘ayim* cannot be extended analogically to include creating human-animal chimeras.

At first glance, one might think that creating chimeras might be inconsistent with the remarks that Ramban made regarding *kil‘ayim*. Ramban explains that one reason for the prohibition of *kil‘ayim* is that God created all species of the world and instilled within them the power to reproduce so that these species would exist for as long as He wills the world to exist. God ordered that animals should only reproduce with their own species. Therefore, any individual who breeds two dissimilar organisms together adulterates the creation.\(^\text{22}\) In fact, Ramban is not inconsistent with *Hazon Ish* or with the concept that chimeras would not be included in the prohibition of *kil‘ayim*. Ramban’s reasoning regarding the prohibition of *kil‘ayim* applies only to God’s creation, to nature itself. God instilled in the animals the power to reproduce by sexual contact and ordered that they should do so only “after their kind.” But He also gave human beings the power and right to develop technologies to improve the world.\(^\text{23}\) Thus, the use of chimeras would be allowed for medical purposes but not as a means of animal reproduction.

The second halakhic concern regarding human-animal chimeras is the issue of speciation, or how does halakha define *Homo sapiens* as a unique species? In science, there is a great debate how to establish scientific criteria for species classification. The debate is based on the fact that there are limited physical, behavioral, or even genetic characteristics that are specific to a particular species. In addition, scientists have the capacity to alter, via genetic engineering, the physical and behavioral characteristics of plants, animals, and even human beings, making it even more dif-
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ficult to differentiate species. Several scientists view species as merely a convenient linguistic term with limited scientific merit.24

However, in Torah and halakha, identifying a specific species appears to be very important. In Genesis, there is the clear description of how all living organisms were created according to theirмин, species. Noah used his understanding of classifying species to appropriately collect into the ark those specific species of animals that could serve as progenitors of other animal species. In this way, he saved the animal kingdom from destruction by the flood. Moreover, the Torah defines pure (мин таbеr) and impure (мин таме), kosher and non-kosher animals, according to their physical characteristics and often utilizes the term species in the laws of kashrut with respect to birds and insects.25 An intimate understanding of species identity also is necessary to delineate the Biblical and rabbinic laws related to the mitzvot of bikkurim and to the issurim of helev, orla, and kil’ayim.

While the Torah describes essential physical characteristics of various mammals, birds, and fish, the Talmud introduces another characteristic in classifying a mammalian species.26 The Talmud states that the species status of an animal generally depends upon its gestational mother, rather than its own genetic makeup.27 If genetic mutations cause a piglet or donkey-looking animal to be born from a cow, then that piglet or donkey is still kosher, even though it does not have the appropriate physical characteristics of a kosher animal.

Based on the above discussion, what is the halakhic perspective of defining human beings as a species? Studying the Talmud and halakhic responsa yields at least six characteristics that are associated with describing Homo sapiens as a unique species.

An organism formed within, or born from, a human being is the most important and absolute criterion in defining a Homo sapien.28 Hakham Tsvi proposed that any organism born from a human is halakhically human, based on the discussion in the Talmud.29 R. Yshmael explains the verse, “[He] who sheds the blood of ba-adam ba-adam (human within human) shall his blood be shed, for in the image of God made Him a human,”30 that it is a capital offense for a non-Jew to kill a fetus in utero. According to Hakham Tsvi, the Torah uses the phrase “ba-adam ba-adam” to teach an additional principle, that an organism is considered human, only if it was formed within another human being. Thus, killing any organism born from another human is considered murder.31

A second characteristic is derived from Niddah 30b, that states there are three partners in the creation of a human being: man, woman,
and God. It appears from this statement in the Talmud that the creation of a child requires that both man and woman donate biological material. This Talmudic approach is supported by an interesting Midrash Rab-bah, quoted by Mizrahi that states the reason Eve names her first born son, Cain, is because “I have acquired a man with the help of God.” The Midrash continues to explain how Adam was created from the adamah (ground) and Eve from Adam. But in the future, there shall be no man created without woman, no woman created without man, and not both of them without the Shekhina.

The other three characteristics that may be criteria for defining human beings as a unique species include: a) capacity to speak complex language, b) ability to differentiate between good and evil (da’at) or expressing free will, and c) their capacity to generate offspring with another human being.

If one accepts that specific criteria are required to identify an organism as a human being, then one must address the issue of whether a human being needs to possess all or just some of above mentioned characteristics. From the Talmudic and halakhic literature, there is support for the position that being born or formed from a woman is a primary criterion. A child born who is sterile, or lacks the capacity to speak, or has little or no mental capabilities, is still considered as a full human being because that child was born from a woman.

Can a human being not born from a woman attain personhood? There is a fascinating discussion in the Talmud that is conventionally interpreted to refer to the status of a creature that had the appearance of a human being but was nonetheless killed by Rav Zeira without violating the prohibition of murder. Several commentators explain that such an organism, termed a golem (an artificial humanoid), created via mystical processes, would not be considered human because it could not speak or exhibit da’at. Some commentators propose that if such a creature were created with the capacity to speak or with the capacity to exhibit da’at, it would be considered human even though it was not born from a human being. However, there is another way of interpreting this discussion in the Talmud that focuses on the statement of Rav Zeira who calls this golem, “min havranya at” (literally translated as “you are the creation of my friend”). The term havranya in the Talmud also denotes kishuf or sorcery. Perhaps Rav Zeira killed this golem because an organism created via sorcery and not being born from a woman is not considered human. Thus, it is an open question as to whether a human-like being created without gestation in a human female is considered to be a halakhic human being.
Hida offers an interesting insight into those characteristics that distinguish human beings from all other organisms in his homiletical translation of the verse, “and man’s superiority over beast is ayin” (the word ayin is literally translated as “nothing”). The word ayin is an acrostic for amira (speech), yedi’a (intellect) and neshama (soul) by which human beings are distinguished from all other life forms. Underlying this view is the principle that human beings express their free will to say no (ayin). In contrast, animals lack free will and operate primarily by instinct.

How do we relate the above-mentioned criteria in defining human beings as a species to our original case of a human-monkey chimera that possesses a reconstituted human brain? This research poses the uncomfortable question about the boundaries between man and animal. First of all, the human-monkey chimera with the reconstituted brain will be born from an animal, thereby lacking an essential criterion for personhood. In addition, a chimera can be created from stem cells obtained from either a man or woman, so that it does not fit the human characteristic that both a man and woman should contribute material to generate a child. What remains challenging from a scientific perspective is whether such a human-monkey chimera will possess the ability to speak, or exhibit da’at, or other human behavioral characteristics. Even if one accepts the notion that an organism, not born from a human being but possessing human-like intelligence, could be classified as a human being, one still must assess from a halakhic perspective, the minimal levels of speech or human mental capacity that may be required to classify such a chimera as human. These are some of the halakhic questions that make this case so interesting.

The capacity of a human-monkey chimera to sexually mate with a human being is another potential criterion of human identity. From a scientific perspective, the answer whether human-animal chimeras can reproduce has not been provided. One could speculate the following hypothetical scenario, based on current scientific research. As discussed above, research has shown that stem cells can be transplanted into sheep or even cow embryos to create human organs in these chimeras. In fact, human embryonic stem cells have been coaxed to become human sperm or eggs. Similarly, it may be soon possible to transplant human stem cells into animal fetuses to alter their sex organs providing them with the capacity to generate human sperm and eggs. What would happen if a male and female human-sheep chimera with transplanted human sperm and eggs were allowed to mate and possibly produce a human offspring? How would halakha classify this offspring,
especially if these offspring could be produced either via sexual mating or IVF procedures?

**JEWISH PHILOSOPHICAL CONCERNS REGARDING CHIMERAS-RESPECTING HUMAN DIGNITY**

In addition to these specific halakhic issues, there are philosophical issues regarding the generation of human-animal chimeras with reconstituted human brain cells that are of concern and that deserve analysis. These related concerns are tampering with the dignity of human beings and with biological order.

Judaism views human dignity as derived from the fact that God created human beings in His image and that humanity emanated from a single individual. In Judaism, human dignity comes from God, and this dignity exists within each human being starting as an embryo and continuing until even after death. The Torah declares that each person is special. God’s creating humankind as a single individual, rather than a group of people teaches the principle that one who saves a single life saves an entire world and one who destroys a single life, destroys an entire world.

These philosophical principles resonate within specific Torah commandments that guarantee human dignity. For example, Judaism directs the physician with an obligation, not merely permission, to heal the sick. In addition, Jews are commanded to bury the dead before the body deteriorates and not to mutilate their corpses.

An excellent litmus test for human dignity’s importance is to ask what happens when human dignity conflicts with other Torah values. The Talmud teaches, “Great is human dignity, “so much so that it overpowers a prohibition of the Torah.” What happens if the value of human dignity conflicts with the value of saving a person’s life? Such an example is presented in Sanhedrin 75a and Yerushalmi Shabbat.

Rav Yehuda said in Rav’s name: A man once conceived a passion for a certain woman and his heart was consumed by his burning desire to the point that his life was endangered [possibly because he was suicidal]. When the doctors were consulted, they said, “His only cure is that she shall submit.” Thereupon the Sages said: “Let him die rather than that she should yield.” Then [said the doctors], “Let her stand without clothes before him.” [The sages answered] “sooner let him die.” “Then,” said the doctors, “let her converse with him from behind a
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fence.” The Sages replied, “Let him die, rather than allowing her to converse with him from behind a fence.” Now R. Yaakov ben Idi and R. Shmuel ben Nahmani related a dispute concerning this case. One said this case involved a married woman; the other sage claimed that the woman was unmarried. Now, if this woman was unmarried, why were the Rabbis so strict? R. Papa said: Because of the disgrace to her family.

This case teaches that there are times when public-policy concerns for the dignity of human kind override competing values of saving human life. 46

In applying the principle of human dignity to our case of a human-animal chimera that has a reconstituted human brain, several factors must be considered. First, Jews are commanded to have children to create families and fulfill the mitsva of pirya veriya, to be fruitful and multiply. Secondly, Halakha demands appropriate sensitivity to those individuals who are mentally and physically challenged and/or disabled.

The motivation for scientists to attempt to create a monkey with a human brain is different from having a child by normal means. In general, chimeras will be created to serve as experimental subjects without the benefits of being born from a woman or being raised by parents as a child. Moreover, if the reconstituted human brain cells in fact impart human-like intelligence in this human-monkey chimera, then it would be a denigration to create a chimera that harbors a human personality within an animal body. From a halakhic perspective, this situation would represent a major affront to human dignity. Rav Tanhuma states that one must never shame or insult another human being, who is created in God’s likeness, for to do so is to shame and insult God. 47

Not only does preserving human dignity impact our case of the human-animal chimera, but it may underscore an ethical issue related to in vitro fertilization (IVF). There are many ethical debates in the USA concerning a reported case of a couple who wanted to use pre-implantation genetic diagnosis (PGD) 48 to select for a hearing impaired child because both partners were hearing impaired. 49 The hearing-impaired couple may want such a child because they believe their experience with hearing impairment would make them qualified to raise such a child, while they would struggle raising a child who had normal hearing function. However, from a halakhic perspective, using any technology that would create or select for a child with a physical or mental handicap would also be an affront to human dignity and would be prohibited. Homilectically, the following verse in the Torah may be appropriate in this context. When Moses refuses to follow God’s directive to lead the children of Israel out of Egypt, God says to him, “Who placed a mouth
TRADITION

in a human being? Or who makes a person mentally challenged, or deaf, or seeing, or blind? Is it not I the Lord?” Moses tells God that his speech impediments make him an inappropriate candidate to serve as the spokesperson in redeeming the children of Israel from Egypt. God’s response is profound; only God has the right to inflict such handicaps on human beings. The first lesson from this story is that the success of Moses’s mission did not depend on his homiletic or rhetorical skills, only on the will of God. The second lesson, relevant to our case, is that human beings are charged with healing illness, not with creating disease or physical handicaps.

NEITHER YOUR HONEY NOR YOUR STING

The second philosophical issue concerning chimeras is human beings tampering with the way God created the world. Chimera research raises the issue of how Judaism views appropriate versus inappropriate human experimentation. While there are different opinions how Jewish philosophers view the role of human beings in the creation process, there is one common element. Human beings are created as a unique species that have certain obligations to improve and preserve the world. For example, Sefer ha-Hinukh, in his discussion of the commandment to circumcise a male child, states that fulfillment of this commandment represents the fulfillment of human potential and affirmation of tselem Elokim (God creating man in His image). The commandment to circumcise teaches us that just as we are commanded to perfect the human form, we are also commanded to perfect the human soul. The fulfillment of this commandment highlights the active role that human beings serve as a partner of the creation process. This partnership, according to Ramban is reflected in the term ve-kivshuha (and conquer it), and charges the human race to acquire scientific knowledge and develop new technologies to better society and the environment. Furthermore, the Torah’s description of human beings as “created in the image of God,” is viewed as a mandate to work as a creative partner with God, such that all activities reflect the very action of the Creator of the universe in improving the world, in conquering illness, and in trying to make the world better for others.

Accepting the view that human beings are partners in creation, leads one to ask whether there are inappropriate human experiments that people should not engage in. The Talmud in Bekhorot relates how students of Rabbi Yishmael dissected the body of a prostitute who had been condemned to death by the king. They examined her body and
found a total of 252 “units” (joints, limbs, etc.). They told R. Yishmael of their findings and he provided an explanation of why this was not inconsistent with his proposal that the human body contains 248 units, but he offered no comment as to propriety of his students’ experiments. Does the silence of the Talmud suggest that it has no moral qualms about scientific experimentation for the advancement of legal or medical determinations, or was the experiment so obviously unethical that the Talmud did not have to discuss that aspect?  

In contrast, the Talmud in *Nidda* 30a-32b, appears to make a moral comment. It presents a controversy between R. Yishmael and the Sages concerning the amount of time it takes for a male or a female human embryo to attain form or structure in utero. R. Yishmael claims that the requisite period is 40 days for a male and 80 days for a female. The Sages claim it takes 40 days for both a male and female embryos. They attempt to disprove R. Yishmael by relating Queen Cleopatra’s experimental data to substantiate their halakhic view. According to the Sages, handmaids of Cleopatra from Alexandria who were condemned to death were subjected to become pregnant and then were killed at specific times to study fetal development. Upon opening their wombs, it was discovered that both males and females develop by 41 days. R. Yishmael rejects the Sages’ argument, stating that one should not aduce proof from fools and he challenges the scientific validity of Cleopatra’s experiment, by showing that it is virtually impossible to validate the time of impregnation and fetal development as described. From this discussion and from *Mo’ed Katan* 17b, we learn that obtaining information by immoral and unethical means is never justified in order to carry out scientific research. In addition, experimental data obtained from research that violates ethical principles cannot be used as proof in halakhic discussions.

There are many other examples in the Talmud and Midrash that address issues of limitations on scientific experimentation. For example, the Midrash comments on the following verse from Kohelet: “Advantage of the earth is supreme in all its things—even the king is indebted to the field.” The verse is quite difficult to translate and yet R. Shimon ben Halalfa, who according to the Midrash was a scientific researcher (*oskan*), believed this verse suggested that God created all creatures with an innate capacity to survive. To examine the meaning of this verse, he performed the following experiment on a *dukhisat*, or hoopoe bird that had just laid eggs. He saw that the bird’s nest lodged in a sycamore trunk in his garden and he nailed a wooden board over the trunk to prevent the mother bird from reaching the nest. The bird
responded to the situation by collecting a certain herb and placing it directly on the nails. This herb dissolved the nails, allowing the mother bird access to the nest and fledglings. Rav Shimon said, “It is well that I conceal this herb, lest thieves go and use this herb to destroy creation.” Like modern times, Rav Shimon was concerned with issues of bioterrorism and felt it better not to publish then jeopardize security.

That same Midrash presents another story of a man coming from Babylon who saw two birds fighting. After one bird killed the other, it went and brought the dead bird a certain herb that it placed on the bird’s dead body and revived the dead bird. The man then stated that it is well to take this herb that revives the dead to the land of Israel. On the way, he was able to revive a dead fox by placing this herb on its carcass. Further along the way, he placed the herb on a dead lion and revived it as well. However, the revived lion sprang and devoured the man. The lesson is obvious; sometimes technology poses a real danger to social order and should not be pursued. Thus, safety is a major concern in the Torah. “When you build a new house, you shall make a fence for your roof, so that you should not bring blood upon your house, if any man falls from there.”60 The Sages interpreted this verse as a general command to maintain a high level of personal safety.61 The act of building the new house itself is not forbidden; we are only commanded that reasonable safety measures be incorporated into the finished product.

A final example comes from Pesahim 56a, that describes how Hazal praised King Hezekiah when he hid the “Book of Cures.” There are various theories concerning the nature of this book. According to Rambam, this was a book of poisons and antidotes, rather than a medical guidebook or book of cures. It is inconceivable according to Rambam, that a tsadik like King Hezekiah would withhold life-saving information. Rambam believes the King hid the book because it contained scientific information about medications that were medically unproven or that could be destructive.62

These examples underscore the Jewish view that scientists must evaluate and considers medical and social risks associated with any technology. Application of new technology is not a simple matter and not all technology should be introduced to society. Technology that can lead to social upheaval and destruction should not be pursued. This is precisely the lesson highlighted in a Midrash, commenting on the following verse from Kohelet. “Consider the work of God; for who can make that straight, which He made twisted?”63 Alsheikh states that this
verse refers to Adam. Could Adam ever repeal the punishment of death brought about by his mutiny in eating from the Tree of Knowledge? The Midrash states, “When the Holy One, blessed be He, created the first human, He took him and led him around all the trees of the Garden of Eden, and said to him, ‘Behold My works, how beautiful and commendable they are! All that I have created; I created for your sake. Pay heed that you don’t corrupt and destroy my universe; for if you corrupt it there is no one to repair it after you.’ Human beings must always consider whether a new technology will improve society and the environment or harm society and the environment.

How do we relate these philosophical concerns to the case of attempting to reconstitute a human brain in an animal embryo or fetus? Conceptually, there is a difference between reconstituting a human blood system in an animal as compared to reconstituting a human brain in animals. The blood of a human being imparts life but does not define his/her human behavioral or personality characteristics. Therefore, creating human mouse chimeras with human immune system or creating human-animal chimeras for research in organ transplantation are appropriate scientific experiments because they have clear medical research applications with few halakhic concerns. In contrast, generating chimeras by transplanting human brain stem cells in an attempt to reconstitute a brain in an animal may impart human behavioral characteristics such as speech or da’at and might be an affront to human dignity. Such research activities might be viewed as crossing the limits of human creativity even if it may eventually have therapeutic potential.

A PROPOSAL FOR A HALAKHIC RESPONSE TO GENERATING CHIMERAS FOR RESEARCH PURPOSES

From a philosophical and halakhic perspective, what should be the Jewish response to human-animal chimeras for medical research? Interestingly, the issue of reconstituting human brain cells in animals has been, and is being, addressed by the National Academy of Sciences. The National Academy of Sciences is a self-elected group of scientists that advises the United States government, and whose recommendations are non-binding, but are taken quite seriously in both the scientific and governmental sectors. The landmark report by the National Academy of Sciences published in April 2005, lists more than 30 major guidelines some of which are consistent with a halakhic approach.

Using their guidelines as a springboard, we recommend that:
TRADITION

- Human brain stem cells may be transplanted into adult animals to examine new therapeutic approaches to treat neurological diseases or spinal cord injuries.

- Creating human-mouse chimeras with a reconstituted human blood system or human-sheep chimeras with human livers or kidneys would be appropriate research endeavors.

- Transplanting human stem cells into the sex organs of animals should be prohibited because of the remote possibility that an animal containing eggs composed of human gametes could mate with another animal bearing human sperm. Thus, chimeras carrying human stem cells should never be allowed to mate or reproduce.

- For the time being, human embryonic stem cells should not be injected into the embryos or fetuses of nonhuman primates. Similarly, no animal embryonic brain stem cells that could theoretically impact human intelligence should be injected into human embryos for implantation. However, brain stem cells that differentiate into non-nerve cells, such as astrocytes or microglial cells and are not involved in behavior or intelligence, may be used to generate human-animal chimeras to study diseases such as Alzheimer’s disease.

- Human brain stem cells may only be transplanted into animal embryos within a test tube environment and only examined under laboratory conditions, before behavioral characteristics develop. At no time should these human-animal chimeric pre-implanted embryos be transferred into a pseudo-pregnant animal for fetal development.

SUMMARY

In summary, there are halakhic challenges in transplanting human embryonic brain cells or precursor brain cells into an animal fetus. The two most troubling issues of these types of human-animal chimeras are whether these chimeras attain human status within the definition of human beings as a unique species and whether they present represent an affront to human dignity.

In the Aleinu prayer we say, “Le-taken olam be-malkbut Shakai,” to correct the world within the Kingdom of Shakai. Even though the authors of this prayer were not referring to scientific experimentation, there is a striking tangential lesson that can be applied to the ethical
dilemmas of transplanting human brain cells into animal embryos. Shakai, as one name of God, means yesb dai, He who creates limits.\textsuperscript{1} While human beings are charged with exploring and bettering our natural world, humankind does not possess the carte blanche right to engage in any scientific experiment that we desire. Human beings have the right to create in God’s image, recognizing that there are limits within the Kingdom of Shakai.

NOTES

2. A human embryo is a term used to describe a period of time from the fertilization of the egg until about eight weeks when the major organs begin form. A human fetus is a term used to describe the last 30 weeks of human gestation from initial organ development until birth.
4. The halakhic issue of animal suffering through medical stem cell research is not as significant as the above two concerns because this technology has great potential to alleviate human suffering and could serve a real human need. Rabbis permit causing pain to animals to benefit a real human need (see the comments of R. Moshe Iserles to \textit{Shulhan Arukh}, Even ha-Ezer 5:14).
10. Jonathan Marks, \textit{What Is Means To Be 98% Chimpanzee: Apes, People, and
TRADITION

_Their Genes_ (Berkeley: University of California Press, 2002).
12. In II Kings 17:4, _a beit keleb is a jail, a place of deprivation._ Rabbeinu Bahya explains that the root of _kil'ayim_ is withholding something (see Psalms 40:12).
14. _Hullin_ 7b. 
15. Genesis 36:24. One explanation of this verse is that Anah discovered the mule, whereas Rashi seems to imply that he developed the cross-breeding technology to create mules.
16. A human being is allowed to plough [the field] and to pull [a wagon] with any of the beasts. See _Bava Kama_ 54b and Mishnah _Kil'ayim_ 8:6.
18. This is consistent with the statement in _Kil'ayim_ 8:1 that it is permissible to raise and maintain animal _kil'ayim_, but it is prohibited to mate them. _Bava Metzitsa_ 91a explains that the mating prohibition applies only to manually bringing two different species together for sexual mating. It is permitted to place the two species together in the same pen even though they may mate. However, the _Hazon Ish_ states that cross-pollination in plants is definitely forbidden and thus, the halakha of _kil'ayim_ in plants differs from that in animals.
19. R. Shlomo Auerbach writes, “Whereas (genetic engineering) in animals … does not involve any prohibition of interbreeding, since the mixing is done only by means of the transfer of ‘material’ from one species into another species of animal ( _Minhat Shelomo_ 2, 97:27).
20. From Leviticus 24:22, the rabbis understood the phrase to prohibit castrating cattle, or any other sort of animal including human beings ( _Sifra Emor_ no. 121). The prohibition of sterilizing animals is related to the Divine directive for all creatures to be fruitful and multiply. By creating sterile animals one is preventing animals from this directive.
21. R. Yisrael Lifshutz, “Anything which we have no reason to prohibit is permitted, without having to find a reason for its permissibility. For the Torah does not mention every permissible thing, but rather only those things which are forbidden” [ _Tiferet Yisrael, Yadayim_ 4:3.] 
25. _Hullin_ 63.
26. _Bekhorot_ 5b.
27. _Kol ha-yote min ha-tahor tahor_ _Bekhorot_ 5b.
29. _Sanhedrin_ 57b.
32. *Mizrachi* quotes this Midrash in his commentary to Genesis 4:1.
33. Ibid., and Genesis 4:1.
35. Ibid., and see Genesis 4:22. “And the Lord God said: ‘Behold, the man is become as one of us, to know good and evil; and now, lest he put forth his hand, and take also of the tree of life, and eat, and live for ever.’”
36. Ibid., 34.
37. Ibid.
38. *Sanhedrin* 65b states that “Rava created a gavra and sent it before Rav Zeira. Rav Zeira spoke to it and it did not respond. Rav Zeira said, “You are a creation of one of my colleagues (and because it lacked the capacity to speak, it was a being lacking a neshama)-return to your dust.” Rav Hanina and Rav Oshaya would sit together every Erev Shabbat and delve into the Sefer Tittira. A 3-year old calf was created for them and they ate it.”
40. Ecclesiastes 3:19.
42. See note 3 above, for discussions concerning what stage of an embryo constitutes human life.
43. Mishnah *Sanhedrin* 4:5.
44. *Berakhot* 19b: “Come and hear: ‘Great is human dignity, since it overrides a negative precept of the Torah.’ Why should it? Let us apply the rule, ‘There is no wisdom nor understanding nor counsel against the Lord?’ [This verse was applied earlier in the text to illustrate that Divine honor takes precedence over human honor and so one cannot desecrate God’s commandments publicly.] Rav b. Shaba explained the dictum in the presence of R. Kahana to refer to the negative precept of ‘thou shall not deviate’ [Deut. 17:11; that is, the rule that human dignity takes precedence relates only to Rabbinic and not Torah precepts] . . . but where a person’s dignity is concerned, the Rabbis permitted [such deviation].” In this classic text (using the Soncino translation), the Rabbis rule that their own decrees—in contradistinction to Biblical precepts—may be superseded by considerations of human dignity. The parallel text in the Jerusalem Talmud presents the opinion of R. Zeira, that even Torah commandments are temporarily overridden where they conflict with human dignity (*Yerushalmi* Kil’ayim 9:1). The *Yerushalmi* seems to consent to R. Zeira’s opinion, citing it in another context to demonstrate that a Torah obligation may indeed be set aside for the sake of human dignity (*Yerushalmi* Nazir 7:1; *Yerushalmi* Berakhot 3:1). The *Yerushalmi*’s seemingly more expansive application of the principle is nonetheless limited to cases in which the dignity of the public (*kavod ha-rabbim*) is threatened— as in cases of public
nudity or burial of the dead; the Bavlī’s more restrictive application of the principle, on the other hand, is specifically singular (kevodo) and universal (kevod ha-briyot), and clearly applies to the dignity of each individual person. However, the priority of human dignity is not unlimited. According to all authorities, one may not transgress a negative, Biblical command in a non-monetary matter where it clashes with human dignity; one may not murder or even wear ‘mixed species’ (linen and wool together) in order to avoid violations to human dignity. See also Shabbat 81b and 94b, Megila 3b, and Eruvin 41b.

45. Sanhedrin 75a and Terushalmi Shabbat chapter 14.
47. Bava Metsi’a 58b interprets the verse, “Do not oppress (tonu) one another, but fear your God” (Leviticus 25:17) as referring to verbal wrongs – inflicting pain through public embarrassment, insults, or other demeaning speech. The Mishnah uses this verse and the one in Exodus 22:20 (“for you shall neither wrong a stranger, nor oppress him”) to support the prohibition of shaming another person. The Talmud teaches that shaming is akin to murder, the equivalent of shedding blood, an irreparable wrong more serious than a monetary wrong because it injures another’s very personhood rather than his replaceable property.
48. Pre-implantation genetic diagnosis (PGD) is a form of prenatal diagnosis performed on early embryos prior to implantation in the uterus and initiation of pregnancy. PGD testing can help physicians select embryos that are either likely to be unaffected with a specific genetic disease or are more likely to result in a successful pregnancy after IVF. PGD can also be used to select the sex of a child.
49. http://www.nytimes.com/2006/12/05/health/05essa.html?ei=5087%0A&em=
50. Exodus 4:11.
51. Sefer Ha- Hinnukh, no. 2.
52. Genesis 1:26 and 1:28.
55. Hizkuni (R. Hizkiya ben Manoach, France, mid-thirteenth century), extends the God-human partnership even further and interprets the verse (Genesis 9:6), “Whoever sheds the blood of man—through man shall his blood be shed, for in the image of God He made man,” as the explanation of man’s right to judge his fellow man. Hizkuni teaches that God, the Judge of all, created man in His own image and thus bestowed upon him the capacity, the right, and the responsibility to judge and punish, even by capital punishment, the crimes of his fellow man.
56. Bekhorot 45a.
58. “It was taught: R. Yishmael stated, Scripture prescribed uncleanness and cleanness with respect to a male [40 day old fetus] and it also prescribed.
uncleanness and cleanness with respect to a female [80 day old fetus], as in the case of the former his fashioning period corresponds to his unclean and clean periods so also in the case of the latter her fashioning period corresponds to her unclean and clean periods. They (Sages) replied: The duration of the fashioning period cannot be derived from that of uncleanness. Furthermore, they (Sages) said to R. Yishmael: A story is told of Cleopatra the queen of Alexandria that when her handmaids were sentenced to death by royal decree they were subjected to a test and it was found that both [a male and a female fetus] were fully fashioned on the forty-first day. He (R. Ishmael) replied: I bring you proof from the Torah and you bring proof from some fools! But what was his ‘proof’ from the Torah? If it was the argument, ‘Scripture prescribed uncleanness and cleanness with respect to a male and it also prescribed uncleanness and cleanness with respect to a female etc,’ have they not already replied, ‘The duration of the fashioning period cannot be derived from that of uncleanness?’—The Scriptural text says, “she bear,” thus doubling the ante-natal period in the case of a female. But why [should the test spoken of by the Rabbis be described as] ‘proof from some fools?’—It might be suggested that the conception of the female preceded that of the male by forty days. And the Rabbis?—The women were made to drink a scattering drug And R. Yishmael?—Some constitution is insusceptible to a drug. Then said R. Yishmael to them: A story is told of Cleopatra the Grecian queen that when her handmaids were sentenced to death under a government order they were subjected to a test and it was found that a male embryo was fully fashioned on the forty-first day and a female embryo on the eighty-first day. They replied: No one adduces proof from fools. What is the reason?—It is possible that the handmaid with the female delayed [intercourse] for forty days and that it was only then that conception occurred. And R. Yishmael?—The women were placed in the charge of a warden. And the Rabbis?—There is no guardian against immorality and the warden himself might have intercourse with them. But is it not possible that if a surgical operation had been performed on the forty-first day the female embryo also might have been found in a fully-fashioned condition like the male?—Abaye replied: They were equal as far as these distinguishing marks were concerned. [In the Mishnah it stated that the Sages, however, maintain that both the fashioning of the male and the fashioning of the female, etc] (This translation was adapted from the Soncino translation.)

59. Ecclesiastes 5:8.
60. Deuteronomy 22:8.
61. Ketubbot 41b.
63. Ecclesiastes 7:13.
65. Resh Lakish (Hagiga 12a) states “Sheb-dai [Who/Enough!]”—the One who had enough power to say to the ocean enough, when it was about to swallow up the world.