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chimeras, hybrids and 'cybrids'

By Calum MacKellar

In biotechnology it is now possible to combine elements between organisms of different species. It is also possible to create cloned animals using parts of eggs from one species and nuclear genetic material from another. It is even possible to create novel organisms via interspecies combinations of gametes. Should such procedures ever be permissible between animal species? If so, should we ever combine human beings with animals?

Early in 2007 a UK parliamentary committee met to discuss the technological and ethical issues surrounding any possible mixing together of human and animal species. They sat as a response to proposed legislation which, if enacted, would have banned such work. After effective lobbying from scientists and other associated interest groups, the committee decided in favour of the creation and limited use of human-nonhuman hybrids, chimeras and 'cybrids'. [1]

The interest in mixing species is neither new, nor is it confined to the realms of myth or fiction. True, many ancient cultures told stories and built statues of entities such as human-lion sphinxes and winged horses, but the natural mixing of animals has occurred for centuries. A mule, for example, starts life when a male donkey mates with a female horse (a cross between a female donkey and male horse is less common, and called a hinney). The gametes (sperm and egg) fuse and the resulting embryo develops into a healthy animal. Though normally infertile, there are even occasional reports of mules giving birth. [2]

But in recent years, research has raised a host of new possibilities. In 1984 scientists created the world's first sheep-goat chimera by fusing a sheep embryo and a goat embryo. The resulting 'geep' consisted of goat cells and sheep cells. Externally this combination was obvious, as the skin that grew from the sheep embryo was woolly, while the areas of skin that originated from goat cells bore hair. [3]

The potential power of inter-species combinations became clearer with a series of experiments conducted in the late 1990s. In these, small sections of brains from quail embryos were transplanted into the developing brains of chickens. When they hatched, the resulting chickens exhibited quail-like vocal trills and head bobs, showing that the transplanted parts of the brain were not only incorporated into the brain, but that such mixing of tissues could allow complex behaviours to be transferred between species. [4]

The next step for many scientists is to start combining human and nonhuman cells. The immediate objective is not to generate beings that are fully grown half-humans, but to create a source of stem cells that could potentially be used in research and therapy. Initial requests for permission to perform this work envisage that any embryo created by mixing human and nonhuman cells would not be allowed to develop beyond the 14-day stage.

Political landscape

This push to develop the combining of human and nonhuman cells has come from technological developments since the 1990 legislation. Anxiety about this new possibility can however be seen in a 2001 UK report from the Home Office's Animal Procedures Committee, which recommended that 'No licences should be issued for the production of embryo aggregation chimeras, especially not cross-species chimeras between humans and other animals, nor of hybrids which involve a significant degree of hybridisation between animals of very dissimilar kinds'. [5]

This reluctance to involve human cells and embryos is also found in European documents such as Article 13 of the Council of Europe's European Convention on Human Rights and Biomedicine, which prohibits any action that aims to modify the human genome in a way that will be passed on to future generations. In effect this would ban any genetic technologies applied at a very early embryonic stage of life. European policy makers are clearly anxious about the technology, though the UK government has not so far signed up to this convention.

In his January 2006 State of the Union address, American President George W Bush expressed his position when he slipped in a small but significant comment that announced his intention to ban human-animal hybrids: 'A hopeful society has institutions of science and medicine that do not cut ethical corners, and that recognize the matchless value of every life. Tonight I ask you to pass legislation to prohibit the most egregious abuses of medical research: human cloning in all its forms, creating or implanting embryos for experiments, creating human-animal hybrids, and buying, selling, or patenting human embryos. Human life is a gift from our Creator - and that gift should never be discarded, devalued or put up for sale.' [6]

This *File* will examine what is currently possible, and what is envisioned for the near future. By drawing on Christian principles it will ask whether any form of species mixing is ethically justified, particularly where one of the components is human.

What's been done so far

One complication is that there are various ways of deliberately mixing two species of animal (see box). Each process produces a different outcome and raises different issues.

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Genes from humans in bacteria

At the simplest end, there are the many examples of genes harvested from the human genome and placed inside bacteria. These transgenic bacteria have huge medical and commercial potential. For example, most insulin is now produced from *E. coli* with the insulin gene from a human inserted amongst other genes. These bacteria consequently produce an individual human protein, but are far from bearing any distinctively human characteristics.

Genes from humans in mice

Moving up in scale, there are also many thousands of strains of mice that have had sizable pieces of genetic code that originated from the human genome spliced into their genes. Many of these are used in cancer and pharmaceutical research as experimental animals that mimic human disease. In terms of each specific disease they have distinctly humanised traits, but they are still clearly mice.

Andi – primate with jellyfish gene

In the first two examples a small element of human DNA has been incorporated with a mass of another organism's genes. In the case of Andi, the process was the other way around. Andi was the first primate to have a package of foreign genes inserted into its genome. The genes came from jellyfish and although present in his cells, they did not function particularly well. Andi, however, shows the possibility of introducing new genes into primate cells, and thus that it would potentially be possible to add new genes to human beings. If the gene were merely repairing the function of an organ such as the liver, then most people would probably accept this as a legitimate medical intervention. But what would happen if the gene were expressed in the brain and altered the individual's ability to think, or their innate behaviour?

Cow egg-human clone

In 1999 the US company Advanced Cell Technology Inc announced that it had developed a method for producing primitive human embryonic stem cells by uniting human adult material with a cow egg. [7] This egg had previously had its nucleus removed. The company hopes this method will enable them to produce 'unlimited' supplies of stem cells for research into transplant medicine.

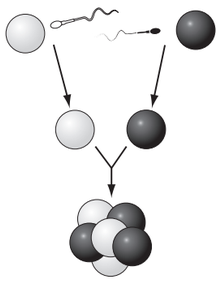
Defining terms

chimera

An organism made up of cells that come from two genetically distinct individuals.

This can occur when embryos from two different species are brought together in early development, and the two sets of cells merge. In a chimera, each set of cells contains components from only one species.

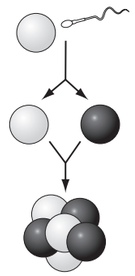
An example of this is the so-called 'geep' that was created by combining two embryos, one from a goat, one from a sheep. It is interesting to note that the geep consequently had four parents.



Artificial chimeras, such as the geep, have four parents

naturally occurring chimera

Not all chimeras have four parents. Human-human chimeras often occur quite naturally. This can happen when two separately fertilised embryos growing side-by-side in the womb merge into one. A variant of this is when a single cell experiences a significant genetic change, such as the loss of a chromosome, but carries on growing. The resulting individual can then be made of a mixture of cells, some with the full genetic complement, and others with a reduced genome. In each of these situations the resulting individual will have just two parents.

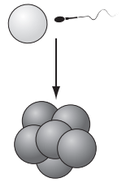


Naturally occurring chimeras have two parents. The chimera occurs as twins fuse.

hybrid

An organism created by combining eggs and sperm cells of different species, so that all of its cells contain a mixture of both components. Human-animal hybrids can potentially be created when:[9,10]

- a human egg is fertilised by nonhuman sperm
- a nonhuman egg is fertilised by human sperm



A hybrid has two parents of different species

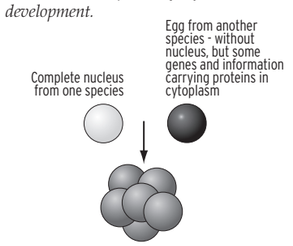
'cybrid' (a cytoplasmic hybrid)

An organism that, like hybrids, has cells that all contain components from two different species. This time, however, the situation is more complex.

A 'cybrid' would be created when nuclear genetic material from one species was placed inside an egg from another species. In the case of a human-nonhuman 'cybrid' this could be human material placed in a nonhuman egg with its nucleus removed, or vice versa.

The result of this is that the new individual would have the full set of nuclear genes from the species that donated the nucleus, but would start with the cytoplasmic composition of the other species.

Although there is the possibility that genes residing in mitochondria (organelles within the cytoplasm containing some genetic material) have the potential of being passed into the new individual, the majority of the genetic inheritance would come from the nucleus donor. However, considerable information stored in proteins and other components of the egg's cytoplasm would also be present, at least in the early embryo, and would most probably influence development.



A 'cybrid' has two unequal 'parents', of two different species. At least one parent (the egg donor) will be female; the other (the cell donor) could be either male or female.

Researchers hope the technique will remove a very important barrier in current research into embryonic stem cell transplantation therapies, namely the need for fresh human eggs of which there is a very limited supply for the creation of cloned embryos. Scientists are eager to obtain these embryos in order to harvest their stem cells for biomedical research.

Rabbit-human hybrid embryos

In August 2003, Hui Zhen Sheng of Shanghai Second Medical University, China, announced that rabbit-human 'cybrid' embryos had been created. Researchers fused adult human material with rabbit eggs stripped of their chromosomes and created rabbit-human hybrid embryos which developed to approximately the 100-cell stage, about four days of development. Moreover, the scientists claimed to derive from these embryos stem cells similar to conventional human embryonic stem cells.

Historic attempts at human-ape

There are well-documented reports that a few scientists in the mid-1920s made serious attempts to create a half-human, half-chimpanzee. One of the Soviet Union's top scientists, Professor Ilya Ivanov, tried to impregnate female chimpanzees with human sperm in Africa in order to create a human-chimpanzee hybrid (a humanzee). These experiments were unsuccessful, but at the time many colleagues believed it was probably feasible.[8]

Genetic barriers – a helpful concept?

It may be said that any form of mixing violates natural boundaries – it breaks the species barrier. To pursue this, however, we need to understand the strengths and weaknesses of the concept of species boundaries. Although it is rare for species to interbreed, the 'barrier' is in reality difficult to define.

First, if each species has a clearly defined genome, then mixing species means mixing up two distinct genomes. But with the human genome, things are not that clear. To start with, around half the genes in human cells create proteins that keep cells alive and growing. These genes are found in many different living organisms where they vary only slightly, if at all, from the versions found in humans. This is why people quote figures such as 'humans are 50% banana'. It is therefore difficult to describe these so-called 'housekeeper' genes as belonging to any particular species.

Secondly, the human genome carries many genes that have no known function in humans, but are known to have specific roles in other animals. The human genome, for example, carries the entire gene sequence for the mouse tail; the cells simply miss the switch to turn it on. [11] Some people therefore argue that adding more mouse genes to a human cell would not be doing anything new, though of course there would be the intention of introducing a new structure or function. In addition, retroviruses constantly carry new genetic material across species into chromosomes. A careful analysis of any organism shows that these viruses have been frequent visitors throughout generations.

Another, more intriguing, view of human beings sees us as communities of organisms. Each of us carries around 100 trillion micro-organisms that live primarily on our skin and in our guts. One paper estimates that humans carry more than 500 different species of micro-organism, and that together this means we carry 100 times as many genes as are found in our 'own' cells. [12]

A further argument used against mixing individuals is that it will violate their genetic uniqueness. That, again, is not as clear as it might seem, because same-species chimeras are probably quite frequent in nature. Some will occur when two embryos fuse as they grow in the womb (see box), but other 'microchimeras' are created when cells from the fetus and placenta break off during pregnancy and birth and enter the mother's blood stream. Colonies of these cells may persist for decades, and on occasions these cells have found their way across the placentas in future pregnancies and become part of the makeup of the bodies of subsequent siblings. Some estimates claim that up to 50% of women who have been pregnant will be chimeric. [13]

Arguments from 'nature'

From all these points, it is difficult to argue against hybrids or chimeras on a purely genetic basis. The issue then becomes less the actual composition of individual people's genomes, but how that composition came into being. Does the simple fact that something occurs in nature give us permission to do the same in the laboratory, and extend it further?

We need to be careful of falling into the trap of assuming that if something occurs in 'nature' then it must be good. Nature presents plenty of examples of actions that seem undesirable, ranging from disease to earthquakes. Similarly, medicine is a discipline that aims to fight off the worst effects of natural actions – if nature really shows us the way, then medicine should be confined to helping people who have physical injuries.

Undermining human dignity

Some people worry that to produce creatures that blur the boundaries between humans and animals could threaten to undermine the concept of human dignity since it is a dignity specifically reserved to humankind.[14] Moreover, other commentators suggest that we should prevent future ethical dilemmas by forbidding anyone from trying to create an animal that may to some extent exhibit human capacities.[15]

Biblical views of humanity

One way to address the ethical issues incurred by creating human-animal mixtures is to see in what way the resulting creatures would show diminution of features commonly held by Christians to be important characteristics of human beings.

Image of God

A critical feature all Christians agree on is that God created human beings to be in his image and likeness.[16] There is less agreement on the exact meaning of those terms, but most Christians agree it at least implies that humans are in some sense special and distinct from other parts of creation.

Of all created beings, humans are the only ones God talks to directly and with whom he has a special relationship. God also expects humans to respond to him and to relate to each other. It comes as no surprise to Christians that almost all cultures encourage some recognition and worship of the divine, differentiate people from other animals, and expect individual members of their societies to respect each other.

Taken together, all this causes Christians to see human beings as more than clever apes. This is not because they may have physically identifiable superior features, but because God has created them in his image and given human beings added dignity by becoming fully man in the person of Jesus Christ.[17]

Kinds

In the opening chapter of Genesis,[18] and subsequently,[19] there are repeated references to living things being made in different 'kinds'. Within Christianity there is debate about the meaning of this term, but one possibility is the idea that God intended a world in which animals could exist and adapt within each kind, but intended no interbreeding between kinds.

It would thus be acceptable to try mixing animals within a kind, such as generating different breeds of dogs, but not to try mixing between different kinds. The problem here would be drawing up a list of biological features that would allow division of species into distinct 'kinds'.[20]

Therefore, in the biblical perspective, species integrity is ultimately defined by God, rather than by physical features. The fusion of human and nonhuman genomes may therefore be perceived as running counter to the sacredness of human life and humanity created in the image of God.[21]

Historicity

Throughout the Bible, there is a constant emphasis on the importance of historical roots and genealogies. The Old Testament, in particular, is in many ways the story of the history of a community, with that story often recorded at a very personal level. The New Testament then endorses that significance by repeatedly drawing on the genealogies of Christ.[22]

Many forms of biotechnological intervention around the start of life destroy those senses of ancestry, parentage and identity for the resulting individual, and this is a key problem. If ever a person came into existence after a cell had been taken from a male donor and fused with a cow egg, the resulting child would (most probably) look and behave like any other human, but that person's parentage would be controversial in the extreme. There is a world of difference between genetically altering an existing human being who has come about through the fusion of human sperm and egg and bringing a 'human' being into existence by other means.

Relationship

In a similar way the notion of relationship, and in particular relationship within families, is a key aspect of biblical thought. Any technique that encourages the creation of human life outside a family unit is therefore not giving the new person the best start in life. It is also creating communities where children live in less than ideal families, which in turn is likely to create less stable societies. God's design is that children should be the fruit of marriage – a public, lifelong, committed, sexual relationship between a man and a woman.[23]

'Restoring the masterpiece'

John Wyatt[24] has used the analogy that human beings made in the image of God are 'flawed masterpieces'. We have a Christian duty to correct flaws in the masterpiece to restore it as much as possible to God's intention, but we have no mandate to cross boundaries to create something new. While some cross-species manipulations, like inserting human genes into bacteria to create human insulin, are clearly aimed at treating lost function and 'restoring the masterpiece', other manipulations such as creating 'cybrids' involve crossing an ethical boundary to create something new.

Abuse of human embryos

Quite apart from the specific question of mixing species, many Christians will also be troubled by the fact that much of the research will involve using or creating semi-human embryos for research.

In 2007 many people are celebrating the bicentenary of the British abolition of slavery. It is therefore interesting to note that the basic argument for maintaining slavery was that it was good for our economy. Similarly many of the arguments used to defend the development of human-animal embryonic combinations are based around the benefit to the economy. There is even the acknowledgement that by being one of the few countries in the world to give free permission for research in this area we can gain global dominance. For many Christians, using large numbers of human embryos for commercial benefit is just as abhorrent as slavery. Even if the claimed end of treating illness is good, the end does not justify the means.[25]

Conclusion

The word 'science' derives from the Latin *scientia*, knowledge, and science is rightly concerned with 'the systematic study of the nature and behaviour of the material and physical universe, based on observation, experiment and measurement'. However, questions like whether to create human-nonhuman embryonic combinations require more than knowledge, they require wisdom. Wisdom is knowledge tempered by judgment. Science cannot just pursue the acquisition of knowledge without any consideration of the means involved; it must operate within ethical boundaries.

Christians are pro-science, but look for ways of conducting science within an ethically justifiable framework. If the world's scientific community decided not to pursue this particular direction of research, then new avenues would almost certainly open up and lead to alternative modes of finding cures and treatments.

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