

Chimeras

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Chimera

- Greek ki-MEE-ra
- First mentioned in Book VI of the Aeneid
- Lion's head, goat's belly, snake's tail
- Killed by Bellerophon

Fifth Century Arezzo Bronze



Dictionary Definitions

- 1.(often initial capital letter) a mythological, fire-breathing monster, commonly represented with a lion's head, a goat's body, and a serpent's tail.
- 2.any similarly grotesque monster having disparate parts, esp. as depicted in decorative art.
- 3.a horrible or unreal creature of the imagination; a vain or idle fancy: *He is far different from the chimera your fears have made of him.*
- 4.Genetics. an organism composed of two or more genetically distinct tissues, as an organism that is partly male and partly female, or an artificially produced individual having tissues of several species.

Natural Plant Chimeras

- Grafted plants: desirable fruit or blossoms grafted onto hardy root stock;
- Forced mutation by application of colchicine

Natural Animal Chimeras

- Wholphins – whale-dolphin hybrids are found in nature
- Ligers – lion/tiger crossbreed
- Mules – deliberately produced by human mule-breeders
- Dog cross-breeds – cockapoos, labradoodles

Natural Human Chimeras (1)

- Blood chimeras: fraternal twins share part of the same placenta. Each has two blood types. About 8% of fraternal twins are blood chimeras.
- Recent case of a cyclist who was accused of blood doping, defended himself on grounds he was a blood chimera
 - *Science* 24 June 2005:
Vol. 308. no. 5730, p. 1864

Natural Human Chimeras (2)

- Fraternal twins merge in utero. Result is a mosaic of genes from the original embryos.
 - May have eyes of different colors
 - May have both male & female sex organs
 - Recent case of both types of organs arising from in vitro fertilization, implanting multiple embryos
 - The New England Journal of Medicine (1998; 338: 166-169, 194-195)

Some Distinctions

- Hybrid: cross-breeds from two species or breeds; all cells are genetically alike (mules, ligers);
- Mosaics: more than one population of genetically different cells, but all cells of a given type arise from same zygote;
- Chimeras: more than one genetically distinct population of cells that originated from more than one zygote (in plants, often grouped in adjacent tissues)

Some Qualifications

- People with pig heart valves- chimeras?
 - Senator Jesse Helms: "Every time I pass a plate of barbecue, I cry. It might be one of my relatives."
- People with kidney/heart/liver transplants

What's Already Done: Animals

- Mix embryonic black & white mouse cells to get patchwork mice
- Quail cells introduced into chick embryos produced chick-quail chimera
- Mouse-hamster chimeras

What's already done: Humans

- Human DNA introduced into mouse chimeras via embryonic stem cells
- August 2003, Shanghai, human skin cells introduced into rabbit eggs, allowed to develop for several days
- Pigs with human blood
- Sheep with partly-human hearts and livers
- Mice and monkeys with human stem cells in their brains

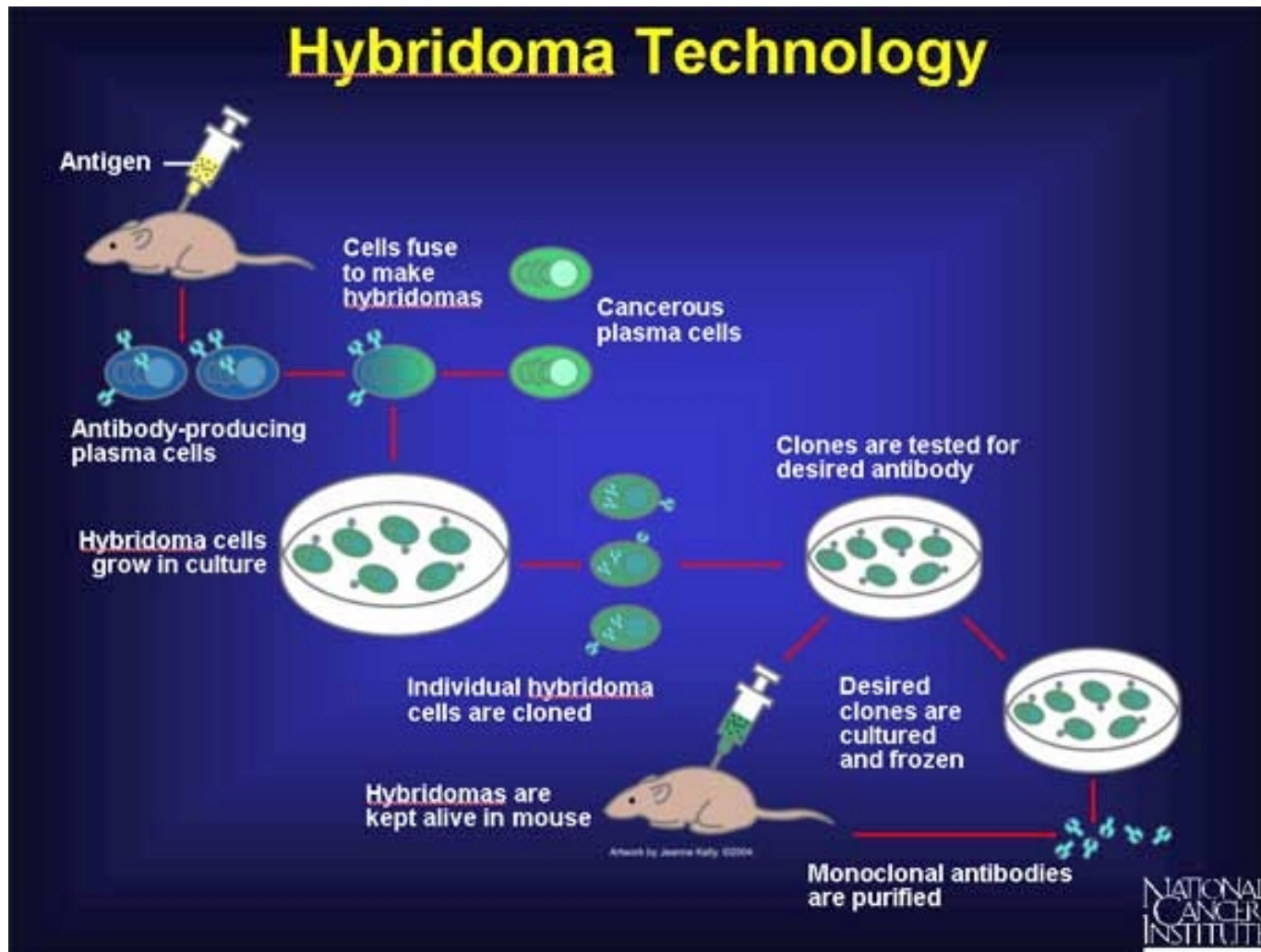
NYU Cancer Institute

- Transgenic Mouse Lab
 - The Transgenic Mouse/ES Cell Chimera (TgESC) Facility provides three basic services: production of transgenic (Tg) mice by zygote injection, **production of embryonic stem (ES) cell chimeras**, and rederivation of mouse strains.
 - ES cell chimeras are produced by injection of ES cells into C57BL/6 blastocysts

Hybridomas

- Antibody-producing cells merged with cancer cells (melanoma)
- Resulting cells are immortal and produce the desired antibody

National Cancer Institute - Hybridomas



Plasma cells from mouse spleen

Human/Mouse Hybridomas

Produce monoclonal antibodies for therapeutic purposes:

- Abciximab, approved for prevention of clotting during surgery;
- Rituximab, approved for treatment of non-Hodgkin's lymphoma;
- Basiliximab, approved for prevention of kidney rejection after transplant;
- Infliximab, approved for Crohn's disease and the treatment of rheumatoid arthritis;
- Trastuzumab (Herceptin), approved for the treatment of metastatic breast cancer.

What's Proposed

- Transgenic animals, incorporating human genes, as sources for organs (liver, heart, kidney, etc.)
 - Wider availability than human “matches”
 - Human genes inhibit rejection factors
- Pigs, sheep raised for organs as well as meat

Some Medical Problems

- Xenozoonoses: animal diseases transmissible to humans
 - Over sixty porcine infectious agents with a potential to cause disease in humans have been identified
- Organ rejection
- Risk of disease from suppressing immune system

Some Philosophical Problems

- How much transplantation can take place before the human is “no longer there?”
- What does it mean to be “human” when parts of you come from sheep or pigs?

Beyond Transplantation

- Manipulation at the genetic and cellular level
- Production of “entities” that are part-human, part-animal (or even part-vegetable) at the cellular level

Where do we stop?

- Soldiers with armadillo-like armor?
- Astronauts engineered for space travel? For life on other planets?
- “Flesh robots” who are just barely capable of
 - Riding a bus
 - Following simple instructions
- And who will
 - Pick vegetables in 120 degree heat?
 - Do hazardous work (mine coal, work around dangerous machines) without safety precautions?
- Superman?

Moral Issues (1)

- Is there a dividing line between human and animal?
 - Should we maintain it if it exists?
 - Do humans stand “outside nature?” To what extent?
- What is the moral status of a human-animal chimera?
 - Slave?
 - Less-than-citizen?
 - Expendable soldier?

Moral Issues (2)

- Allocation of health care resources
 - Xenotransplantation will be very expensive
 - Health care resources are finite
 - Should resources be expended on xenotransplantation when some people cannot obtain even routine medical care?
 - Who pays? Insurance? Taxpayer?

Moral Issues (3)

- Patentability
 - Should life forms be patentable?
 - Should transgenic animals incorporating human genes be patentable?
 - If not, will drug companies pay to develop them?
 - If so, how close to “human” can they be and still be patentable?

Moral Issues (4)

- Is it moral to kill a partly-human chimera?
- Is it moral to create a creature whose moral status we are uncertain about?

Where do we stand?

- National Academy of Sciences Guidelines
- Human Chimera Prohibition Act

National Academy of Sciences

- Permit creation of human-animal hybrids
- Prohibit breeding of the hybrids
- Human embryonic stem cells may be introduced into nonhuman mammals “under circumstances when no other experiment can provide the information needed.”

Action in Congress

- Human Chimera Prohibition Act of 2005
- Introduced by Senator Brownback
- Referred to Committee on Judiciary
- No further action since 2005
- Definitions of what is prohibited are very exhaustive

Legal Definitions

- (1) Human Chimera – The term Human Chimera means
 - (A) a human embryo into which a non-human cell, or any component of a non-human cell, has been introduced;
 - (B) a human embryo that consists of cells derived from more than 1 human embryo, fetus, or born individual;
 - (C) a human egg that has been fertilized by a non-human sperm;

Legal Definitions (2)

- (D) a non-human egg that has been fertilized by a human sperm;
- (E) a human egg into which a non-human nucleus has been introduced;
- (F) a non-human egg into which a human nucleus has been introduced;

Legal Definitions (3)

- (G) a human egg or a non-human egg that otherwise contains haploid sets of chromosomes from both a human and a non-human life form;
- (H) a non-human life form engineered such that human gametes develop within the body of a non-human life form; or
- (I) a non-human life form engineered such that it contains a human brain or a brain derived wholly or predominantly from human neural tissues;

Legal Prohibition

- (a) In general – it shall be unlawful for any person to knowingly, in or otherwise affecting interstate commerce—
 - (1) create or attempt to create a human chimera;
 - (2) transfer or attempt to transfer a human embryo into a non-human womb;
 - (3) transfer or attempt to transfer a non-human embryo into a human womb; or
 - (4) transport or receive for any purpose a human chimera.

Some Problems Ahead

- Some scientists recognize the moral and ethical problems
- Some scientists insist on the autonomy of science
- Some moral questions are as yet unanswered
- There is no legal framework to govern this research

Just remember:

Dr. Frankenstein is alive and well and is probably funded by the National Institutes of Health