Germline gene therapy 'must be spared excessive regulation'

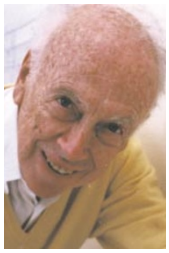
[LOS ANGELES] Germline gene therapy is likely to become a reality within 20 years and should be welcomed, a high-level panel of scientists and other experts said at a meeting in the United States last week. They warned, however, that the procedure could suffer from excessive regulation at either national or international levels.

Any international attempt to regulate germline engineering would be "a complete disaster", said James Watson, the co-discoverer of the structure of DNA, who is the president of Cold Spring Harbor Laboratory on Long Island, New York.

Scientists should proceed unhindered towards germline engineering, he told a symposium called 'Engineering the Human Germ Line', organized by the University of California, Los Angeles. He added: "If there is a terrible misuse and people are dying, then we can pass regulation."

Most of the ten experts on the panel stressed that attempts at germline gene therapy must be preceded by extensive work in animals and human cell lines to develop techniques that would be safe and effective in human embryos. Possible dangers include harmful and unpredictable interactions between inserted or modified genes and others in the recipient genome, causing, for instance, cancer.

But the panellists almost unanimously argued that, once these concerns have been addressed, the potential for curing human disease presented by the incipient technology is so great that it should be implemented — regardless of concern that its use might lead to an ethical morass, and perhaps even to practices such as eugenics.



MIKE BLENKINSOP

Watson: research should go ahead.

Leroy Hood, chair of molecular biotechnology at the University of Washington, said: "We are using exactly the same kinds of technologies that evolution [does]." John Fletcher, a bioethicist at the University of Virginia, said that references to the germ line as a Rubicon not to be crossed, and as being "sanctified", had been virtually enshrined in public policy. "I think [this symposium] tended to dispute that premise."

In contrast to Europe (see panel), whose governments have already indicated that they will take a firm stand on the new technology, the United States has no law that would prohibit germline manipulation for whatever purpose, provided experiments passed safety and efficacy muster with the Food and Drug Administration. Privately funded research towards germline gene therapy using human embryos is also legal in the United States.

But the Recombinant DNA Advisory Committee (RAC) of the National Institutes of Health — which provides a public forum for discussion of the ethical issues involved in gene therapy — has so far refused to consider germline gene therapy proposals. This may change. The RAC is updating its guidelines, which were written in 1990.

"This will be an opportunity for the committee to revisit" the germline gene therapy issue, says the RAC's director, Claudia Mickelson, who is the biosafety officer at the Massachusetts Institute of Technology. Mickelson says the RAC needs to make explicit the conditions under which it would consider such proposals, or to explain why it refuses to do so. She believes that the ethical issues involved need serious examination before such work proceeds.

A lone voice on the panel called for a sharp line to be drawn between germline therapy for enhancement and to fight disease. This call came from French Anderson, a professor of biochemistry and paediatrics at the University of Southern California School of Medicine, who pioneered human somatic gene therapy in 1991.

Anderson argued that, because the possible harmful effects of manipulating the germ line are unknown, researchers have a duty "to use this powerful technology [only] for the treatment of disease and not for any other purpose". He proposed that before germline therapy to fight disease proceeds in humans, long-term experience with somatic gene therapy in hundreds of patients must be accumulated over at least another decade; reliable, reproducible and safe procedures must be demonstrated in primates; and social awareness and approval must be gained.

Presenters at the symposium made it clear that the technology to conduct germline manipulations is rapidly approaching. For instance, human artificial chromosomes, that ultimately could carry hundreds of genes, are expected soon to be in use in somatic-cell gene therapy. And their use is expected to be made markedly easier by the advent of DNA chips.

The panellists said that germline therapy should be technically easier than somatic gene therapy, which in a decade of attempts has produced poor results. Because germline therapy aims at making changes in a single cell, the zygote, the procedure is "actually much simpler" said Mario Capecchi, a professor of biology and genetics at the University of Utah, who produced "knockout" mice by inactivating single genes.

But the panel's scientists conceded that the time to germline therapy is at least a decade off. "It's going to take a long time to work out the bugs," said Capecchi. **Meredith Wadman**

European states outlaw permanent changes

[LOS ANGELES] Gene therapy in humans has so far been attempted only in somatic cells, where genetic changes introduced in an individual die with that person. By contrast, germline gene therapy (see above) – which would be carried out on newly fertilized human zygotes – would introduce changes not only in every cell of the infant born of such manipulations but also in the genes passed to that baby's progeny. (Some of the scientists at the symposium said, however, that simple methods could keep changes in the recipient from becoming permanent.)

The potential for eliminating disease with such methods is tantalizing. For example, single-base changes in the DNA sequence cause devastating ailments such as Tay–Sachs disease. Such relatively simple targets would be prime candidates for early attempts at germ-line therapy. Complex diseases involving many genes would require much more research and are likely to be targeted farther into the future.

But critics are concerned about the potential for abuse of the technology to 'enhance' healthy individuals, by, for instance, manipulating intelligence, emotional stability, longevity or physical appearance. They present the spectre of a booming market in 'designer' babies, made to the specifications of parents hungry for success and superiority in their offspring.

Such concern, in part, informed a bioethics convention produced by the Council of Europe last year that has since gathered signatures from 22 European states. This convention says that genetic manipulation may be undertaken for purposes of prevention, diagnosis or therapy – but only if does not aim to introduce a permanent modification in the genome. **M. W.**