Nobel goes to discoverers of 'split genes'

London. 'Split genes' have taken the 1993 Nobel prize for physiology or medicine. The prize has been awarded jointly to Richard J. Roberts, who now works at New England Biolabs, and Philip A. Sharp of the Massachusetts Institute of Technology.

At a meeting held at Cold Spring Harbor in June 1977, both reported independently that a single adenovirus messenger RNA molecule corresponded to four distinct regions of the DNA encoding it.

Up to that meeting, the general consensus was that genes were continuous stretches of DNA which served as direct templates for messenger RNA molecules, and that these molecules were themselves templates for protein synthesis. Belief in this model was understandable, as all studies of prokaryotic organisms had supported that theory.

But Sharp and Roberts showed that, at least in the adenovirus, things were not always so straightforward. Following the disclosure of their results, many other scientists soon reported that the interruption of coding sequences was found in other genes, and indeed that a discontinuous gene structure is the most common structure found in eukaryotes.

Pierre Chambon, of the Institute of Biological Chemistry in Strasbourg, was one of those who reported similar organizations of another gene, namely that for chicken ovalbumin. "There was no question that Phil Sharp would win the Nobel prize some day," says Chambon.

Chambon claims that Sharp "deserved the award on more than one account, not only for the 1977 discovery, but also for his later work". But he also stressed that, in the case of both Roberts and Sharp, the work was that of a team, and expressed regret that a Nobel prize cannot recognize this fact.

David Baltimore, at the Rockefeller University in New York, whose Nobel prize-winning discovery of reverse transcriptase also broke with the "central dogma" on the relationship between DNA, RNA and proteins, said that the award of the prize was long overdue.

"Everything that's happened in molecular biology since has depended on their discovery of split processing of mRNA," says Baltimore. "It has become a central focus of everybody's thinking on the field."

Sharp in particular has been a "notable contributor" for his broad contributions to the characterization of splicing intermediates of mRNAs, of transcription control, and of both basal and specific transcription machinery.

There was more praise from Walter Gilbert of Harvard University, who shared the 1980 Nobel Prize in Chemistry with Frederick Sanger and Paul Berg for his work on DNA sequencing. Gilbert says he remembers vividly the dramatic reports delivered at the Cold Spring Harbor meeting. "The discovery of RNA splicing was radically new," he says. "There was a paradigm shift when Roberts and Sharp showed that the structure of genes was not what was expected."

Gilbert says that the basic discovery would have emerged for all to see with the advance of various techniques, such as nucleotide sequencing. But Roberts and Sharp had realised what was happening before anyone else. Other groups, he points out, had been looking at gene structures, but had failed to understand them; Roberts and Sharp made their discovery by 'seeing' the splicing of RNA through electron microscopy.

Following the discovery, Gilbert himself began to pursue the evolutionary implications of the finding that genes are discontinuous. It is now widely believed that this exon/intron structure of genes may drive evolution by allowing new proteins to be made by reshuffling different coding regions of the DNA. There are many examples where alternate splicing of one precursor RNA can lead to the production of many different proteins.

Sir David Weatherall, regius professor of medicine at the University of Oxford, whose work has focused on the molecular pathology of human diseases — particularly of thalassaemias, some of which are due to defects in splicing of the globin genes — puts the work in its medical perspective.

"The basic biology is fascinating", says Weatherall. "But in terms of the molecular level underlying disease it has opened up a whole new area, not just in understanding the basic mechanism but also the variations of genetic disease."

Sharp himself describes the award as recognition of a "real discontinuity in science, to which many people contributed". He points out that soon after his and Roberts's announcement there were a "whole slew" of other papers that described spliced genes. "We were just lucky to be able to be at the beginning of the process", he says.

Like Chambon, Sharp also stressed that both his and Roberts's work was that of teams, and that all the members of their respective teams made significant contributions to the discovery. **Kimberly Carr**

France urged to change ethics rule

Paris. The French national bioethics advisory committee this week recommended reform of laws on medical confidentiality, data protection, and free and informed consent, to bring regulations in these areas closer in line with the needs of psychology research.

The committee was convened earlier this year after the government had suspended a study on the cognitive traits of half-brothers and half-sisters born by artificial insemination from anonymous donors (see *Nature* **361**, 481; 1993). This followed allegations in the French press that the researchers had used confidential medical data in the study, and had not provided sufficient details of the experiments when asking the parents of the children for their consent.

Biological experiments on humans and clinical trials are tightly regulated in France under a 1988 law. But the ethics committee says that the legislature has failed to consider the particular issues raised by behavioural studies on humans. For example, it says the legal requirement that subjects give free and informed consent is inappropriate to some psychology experiments, as prior knowledge of the objectives can modify a subject's response.

The committee reaffirms that subjects must give their free and informed consent to all experiments. But it recommends that the law be changed to let behavioural researchers hide some experimental objectives from a subject in the interests of the experiment when requesting consent, on condition that they inform subjects of this.

Subjects would also be told that they could withdraw from the study any time, and that they would be given a complete "debriefing" on the full objectives and results of the study on its completion. If the subjects could be identified from the data collected, the researcher would also have to ask their consent for subsequent use of such data. Furthermore, the committee recommends that the need to hide information from subjects be approved beforehand by new bodies called "Consultative Committees for the Protection of Persons in Behavioural Research". These would be modelled on the committees that now approve clinical trial protocols.

The committees would also evaluate the "scientific pertinence of the research", and check that "the liberty, dignity and safety of subjects" is protected. Researchers would inform subjects before experiments that the committee had approved all hidden objectives.

The ethics committee also recommends that physicians should be allowed to share medical secrets with psychology researchers. At present it is illegal for physicians to tell anyone except another doctor about a patient, and then only if the information is used for therapeutic purposes.

Declan Butler