## Genetic repair in mammals

In the 1960's Henry Harris of Oxford University came up with an elaborate scheme for fusing different kinds of cells together. It consisted of putting a particular virus with a particular enzyme on its surface in the presence of two kinds of cells to be fused. The viral enzyme fused the two kinds of cells so that the hybrid cells contained the genetic material and the cytoplasmic material from both.

Using this technique, a team of researchers at Duke University Medical Center, Walter Reed Army Institute of Research and the National Institute of Allergy and Infectious Diseases has managed to correct genetically deficient cells in tissue culture, then return the corrected cells to living mammals, where they function normally. This is the first time that such an achievement has been made. It offers a potential course for correcting a number of human genetic abnormalities.

The researchers are Nelson L. Levy and Ralph Synderman of Duke University, Roger L. Ladda of Walter Reed and Rose Lieberman of the NIAID. They report their findings in the latest PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES.

They corrected a genetic deficiency in a strain of mice that does not make one kind of protein. The protein is the fifth in a series of 11 proteins known as "complement." Complement proteins provide the punch behind antibody reactions. When an antibody recognizes a foreign cell it activates the first protein in the complement series. That protein activates the next protein in the series, and so on. A protein toward the end of the series destroys the foreign cell.

To correct the nonproduction of the fifth complement protein in the mice, the investigators had to first determine which cells in mice usually make the protein. They took various cells from normal mice, cultured the cells, then assayed them to see which made the protein. It turned out to be macrophages from the spleen. They then took spleenic macrophages from the mice deficient in the protein and showed that the macrophages were indeed not able to make the protein. The macrophages, then, were the genetically deficient (protein deficient) cells to deal with.

They set about trying to correct the deficiency in the macrophages. Using Harris's cell-fusion technique, they fused kidney cells from normal mice with the protein-deficient macrophages. The kidney cells did not make the protein that the macrophages lacked, but they did have the chromosome that makes the protein. So when the kidney cells fused with the macrophages, cytoplasmic influences in the deficient macrophages were able to turn on the usually silent chromosome from the kidney cells. Once the chromosome was activated, the hybrid cells started making the protein that the macrophages lacked.

The team took the hybrid cells, now making the desired protein, and injected them into mice lacking the protein. The mice continued to make the protein, and it had all the right properties, including complement activity.

The technique that Harris devised and that the researchers have elaborated "is a potential way to correct human genetic abnormalities," Levy told SCIENCE NEWS. "It could be accomplished in the same way that we did in the mouse, except that in man we would have a problem that we did not have in the mouse, on one hand, and we would lack a problem that we did have in the mouse, on the other."

The problem they didn't have was rejection by the mice that received the hybrid cells. The reason that the mice did not consider the hybrid cells foreign is that the kidney cells incorporated into the hybrid cells came from mice closely related to the recipient mice. If cells from two persons were fused and then injected into one of the persons, the recipient would probably reject the hybrid cells as foreign. This is because the two individuals are not related. There is a way around the problem, though. "What you do," Levy says, "is select out populations of cells that are normal, because they make the right protein, but are compatible with the person to whom you want to give them back." When asked whether such selection would be possible, Levy replied, "Oh yes. In fact, experiments like these have been reported from several laboratories."

The advantage Levy said they would have over their mice experiments is that most human genetic deficiencies (protein deficiencies) are partial rather than absolute. Because the complement protein was new to the recipient mice, they made antibodies against it. But if a protein that an individual is partially deficient in is injected into him, he would probably not make antibodies to it because his body is used to it.

A number of protein-deficiency conditions might be corrected by their technique, Levy believes—hemophilia, immunoglobulin diseases, enzyme deficiencies. Ladda and some investigators at Duke University hope to use the technique to correct some of them. □

## An organic free-radical ferromagnet

Ferromagnetism is a condition in which all of the elemental microscopic magnets in a sample of a given substance line up in the same direction so that there is a large overall field in the substance. Ferromagnetism is the basis of permanent large-scale magnets. As its name, which contains the Latin word for iron, indicates, it is found mainly in certain metals and minerals.

A long-standing ambition of physicists and chemists has been the discovery of a true organic ferromagnet. Up to now they have found some cases in which the elemental magnets of a substance may line up in pairs or in a one-dimensional line, but a substance with the true three-dimensional, long-range order of true ferromagnetism has eluded them. Now it appears that such a truly ferromagnetic organic substance has been found. The report is by M. Saint-Paul and Cl. Veyret of the organic physical chemistry laboratory of the Center for Nuclear Studies at Grenoble, France.

The substance involved is the crystal of the suberate of bi (2,2,6,6-tetramethyl-4-piperidinol-1-oxyl). In metallic or mineral ferromagnetism the elemental magnets that have to be lined up are either atoms or ions; in the organic case the elemental magnets are free radical, molecules with an odd number of electrons. The substance in question contains the nitroxide group, a particular combination of carbon nitrogen and oxygen that lends great stability to molecules that contain it. A whole chemistry of such substances has been developed over the last 15 years, but their physical properties are just beginning to be studied: It appears that the process that causes the elemental magnets to line up may proceed by a direct relation between the nitroxide groups rather than by various intermediaries as occurs in other cases. Calculating the mathematical relation involved will give specialists in theoretical chemistry a fine problem to work out, remarks LA RECHERCHE.

The Curie point for this suberate, the temperature below which ferromagnetism appears spontaneously, is no more than 0.38 degrees K., about a third of a degree above absolute zero. Therefore as LA RECHERCHE remarks, it is hardly a suitable substance for making permanent magnets. However the lowness of the Curie point is something of a benefit to pure scientists studying ferromagnetism since at that level many activities of the crystal that affect magnetism are suppressed so that the study of pure magnetism is facilitated. □