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Foot-and-Mouth Disease Vaccines

The AAAS–Newcomb Cleveland Prize for 1981–1982 has been awarded to a group of researchers whose report appeared in the 4 December 1981 issue of *Science*.* The report described the preparation of a vaccine and its successful use in an important viral disease of animals.

Foot-and-mouth disease (FMD) is a highly contagious, severely debilitating infection to which some 32 species of cloven-hoofed animals, including cattle, swine, sheep, and goats, are susceptible. The causative agent is a picornavirus which can withstand comparatively adverse conditions and remain infective for substantial periods. For the time being the disease has been eradicated in a number of countries, including the United States. However, it is endemic in large parts of the world.

The U.S. Department of Agriculture maintains a center for research on FMD at Plum Island off the shore of Long Island. In the 1950's and 1960's a team led by Howard Bachrach succeeded in isolating the virus and growing it in tissue culture. Later a vaccine containing killed virus was produced. Forms of the vaccine are still used. The product is not entirely safe. Half of the recent outbreaks of FMD in Europe are traceable to the vaccine or to escape of virus from research centers. In addition, the vaccine is relatively unstable and it does not confer long-lasting immunity. An important discovery by the Plum Island group was that VP_3, one of the four proteins that coat the viral RNA, is an effective antigen in producing immunity to the virus. This knowledge led to application of recombinant DNA techniques in producing the new vaccine.

The viral RNA contains about 8000 bases. The portion coding for VP_3 is near the center of the genome. DNA complementary to a 2000-base segment of RNA was produced and spliced into a plasmid of a special mutant of *Escherichia coli* at Genentech. Later, information about the terminal amino acids of the VP_3 protein was used to identify the segment of DNA that coded for it, and this was then introduced into a plasmid. *Escherichia coli* containing these plasmids produced an insoluble moiety that included the desired protein. Yields were excellent. The protein is stable: it can withstand a temperature of 100°C. A purified product contained a sequence of about 211 amino acids. Two injections of 250 micrograms of this protein in an oil adjuvant produced a good antibody response in cattle and swine and protection against a challenge dose of virus. The vaccine is completely safe.

Since there are many strains of FMD viruses, a comprehensive vaccine against all of them will not be available immediately. But much has been learned about the viruses. The amino acids near both the carboxyl and amino ends of the VP_3 protein seem to be conserved. However, the sequences of the amino acids of VP_3 of various virus strains differ by as many as 36 residues. It is probable that an effective comprehensive vaccine will need to include as many as 15 different proteins or polypeptides. However, it should be relatively easy to produce them by applying what is now known. Some eight major companies are seeking to create commercial products. Prospects seem good that within this decade FMD will come under more effective control worldwide.

Two diverse streams of knowledge came together to make this achievement possible. Long-term support for basic research on FMD by the Department of Agriculture provided a necessary foundation for the application of recombinant DNA. In turn, the commitment of the National Institutes of Health to long-term support of basic research led to the unexpected recombinant DNA technology. The award of the AAAS–Newcomb Cleveland Prize recognizes only one of the many important benefits for humanity that come from enlightened support of science.

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