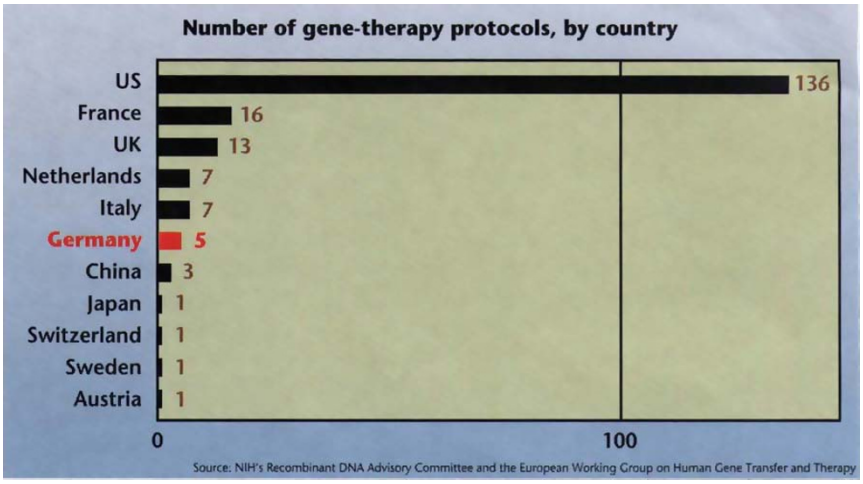
Germany playing "catch-up" in gene therapy



More than five years after the United States took the lead in gene therapy protocols there are signs that Germany is beginning to follow suit, largely due to a recent strong show of government support. The latter follows the establishment of a more favorable climate for such work, brought about in part by the easing of previously restrictive gene laws, resulting in the removal of many bureaucratic hurdles. Coupled with a more gradual change in the public's acceptance of the technology, these two factors have sent a strong signal to both the research and investment communities. This shift has generated considerable German scientific interest in gene therapy research and has led to the beginnings of a fledgling industry based on that research. Even the Green Party, which still warns against the perils of genetic engineering in general, is beginning to tolerate medical applications of the technology.

However, Germany is playing "catch-up." It ranks only fifth among countries in Europe in terms of the number of gene therapy trials approved to date (five trials with a total of 30 patients), well behind France, the UK, the Netherlands, and Italy (see chart). The United States leads the way, however, with an estimated 136 gene therapy protocols approved and some 750 patients enrolled in trials to date.

Although the number of approved trials in Germany is still relatively small, this is likely to change. The German research ministry received a flood of grant applications after it announced in 1993 plans to launch its first gene therapy funding program, totaling DM60 million (US$40 million) over the next six years. The ministry recently revised this figure, and is now planning to spend $17.5 million each year for five years starting in 1997. "Almost everybody who was able to spell the words "gene therapy" jumped on the [band]wagon," says one ministry official. After scientific evaluation had separated the wheat from the chaff, 58 projects out of a total of 312 applications were singled out for support, 36 of which were funded last year, with the remainder slated for funding this year, according to the ministry's Robert Hauer.

In addition to the strong interest from the research community, there are now at least three companies in the country — all founded within the last 20 months — that are in the gene therapy business. The triumvirate of CellGenix (Freiburg), MediGene (Munich) and HepaVec (Berlin) have spun out of academic research centers, such as the Max-Delbrück-Centre for Molecular Medicine in Berlin. All three must now compete with the thirty or so companies in the United States and a smaller force of five European firms (Introgene, Leiden; Q-One, Glasgow; TheraGene, Stockholm; Therexys, London; Transgene, Strasbourg). The German companies were founded primarily with money from private investors, but with additional financial support from government programs set up by the research ministry and the Deutsche Forschungsgemeinschaft, Germany's main source of funding for basic research.

Despite the promising start, without any backing from industry, the German gene therapy newcomers could face a shortage of capital in the longer term. Venture capital is still rare in Germany: Less than one percent of the $700 million raised in venture capital in Germany in 1994 was directed toward biotechnology. "If these companies don't manage to get additional money from the international capital markets or from public offerings, they are unlikely to survive more than three or four years," says Helmut Schühsler of Techno Venture Management in Munich, one of MediGene's several funding sources. Producing genetically modified cells according to GMP (good manufacturing practice) guidelines alone can consume several hundred thousand dollars, says Felicia Rosenthal, head of CellGenix's executive board. CellGenix is focusing on treating cancer patients using cytokine gene therapies and *ex vivo* expanded blood stem-cell transplants.

The newest of the start-ups is HepaVec, which is expected to become operational within the next month, will concentrate solely on *in vivo* gene therapy, according to Michael Strauss, one of its founding members. HepaVec's first targets will be liver cancer, colorectal cancer and familial hypercholesterolemia, and a clinical protocol for patients with the former is expected to begin this summer. Completing the triumvirate is MediGene, which is specializing in the development of adenoassociated gene transfer systems for the treatment of non-Hodgkins lymphoma and cervical cancer.

All of the German companies will have to bring their products to market via the European Medicines Evaluation Agency (EMEA), which was set up a year ago to approve medicines, including gene therapy products, on a centralized, pan-European basis. According to Patricia Brunko, who is responsible for gene therapy regulation within the European Commission: "Everybody who wants to introduce 'living' [cells as medicinal] products into the market will have to knock on EMEA's door." Moreover, the agency's decisions will be binding on all 15 — later 16 (if Norway is included) — members of the European Union, providing Europeans with simultaneous access to gene-based therapies. That won't be any time soon, however, as all of the European trials are still in the very early stages.

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