innovate to live, live to innovate

2 Further Our Discovery...

Driven at first by innate curiosity and the never-ending "What ifs?," Genentech scientists' penchant to innovate is made more urgent by a sincere desire to benefit patients.

What is the key to discovery? For Genentech, as the company moves into the 21st century, it is focusing on its areas of expertise and asking the right questions. And, with the benefits of modern technology, asking — and getting answers to — the right questions very quickly. This is the essence of SPDI (pronounced *speedy*), Genentech's Secreted Protein Discovery Initiative.

SPDI builds on Genentech's world-class expertise in cloning and expressing genes that encode proteins. It also focuses on identifying the minority of proteins that are secreted by cells. These are the proteins most likely to be of therapeutic interest. SPDI uses computers and the new technologies of bioinformatics to search large databases of information to find secreted proteins. Genentech is cloning, expressing and purifying thousands of these secreted proteins using recombinant DNA technology.

SPDI next uses dozens of biological screens to sift through the purified proteins to find those of potential therapeutic interest. The biological screens were carefully selected by Genentech scientists with many different areas of expertise to identify proteins with therapeutic potential. These screens very quickly ask the question of thousands of proteins, "Might this protein show activity in this area?" and very quickly give an answer, "Yes" or "No." The "Yeses" are then subjected to more thorough screening and testing to identify the most promising therapeutic candidates.

For example, some screens seek to identify proteins that may cause new blood vessels to grow — a process called angiogenesis. These screens have already identified some promising candidates for treating cardiovascular disease, where the growth of new blood vessels to bypass clogged arteries would be desirable. By creating antibodies to such proteins, Genentech has also identified promising potential cancer therapies, where blocking new blood supplies to growing tumors would be desirable.

Genentech scientist William Wood, Ph.D., and computer specialist Kathryn Woods are involved in testing the hundreds of proteins being investigated through Genentech's Secreted Protein Discovery Initiative (SPDI).

Another set of screens, available to Genentech through a partnership with the National Cancer Institute, identifies proteins that cause a process called apoptosis — the biologically programmed death of cells. These screens have identified proteins that may be useful as cancer therapies, where programming the death of tumor cells would be desirable.

A third screen identifies genes rather than proteins — specifically genes that are amplified (exist in multiple copies) in certain cancers. Just as the HER2 gene's amplification in breast cancer led to the development of Herceptin to treat metastatic breast cancer, knowledge of genes amplified in other cancers could lead to specific antibodies to treat these cancers. One gene that has so far been identified, to which Genentech is now developing antibodies, is amplified in colon and lung cancers.

The beauty of SPDI is that, because of its speed, all the screens that Genentech employs can practically be applied to all the proteins to which it has access. Therefore, certain proteins may show activity in certain unexpected areas that might never have been identified with more traditional research techniques. And Genentech scientists with vastly different areas of focus and expertise are all finding uses for SPDI that expedite and enhance their research projects. As always, based on their experience and insight, Genentech scientists are deciding what questions to ask. With SPDI, they are getting useful answers faster than ever.

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