

Interview with Paul J. Hastings

PRESIDENT AND CHIEF EXECUTIVE OFFICER, ONCOMED PHARMACEUTICALS

PAUL J. HASTINGS has more than 20 years' experience in the biotechnology and pharmaceutical industries. Before joining OncoMed, he held leading positions in a number of companies, including QLT, Chiron, Genzyme and F. Hoffmann-La Roche. In addition to these roles, he is actively involved in the development of the biotechnology industry and serves on the board of the Bay Area Biotechnology Association as well the Biotechnology Industry Organization (BIO) and served as a director on the board of Canada's BC Biotech Association. Mr. Hastings received a Bachelor of Science degree in Pharmacy from the University of Rhode Island.



In June 2006, MorphoSys announced an agreement with the US biotechnology company OncoMed Pharmaceuticals. OncoMed is a young start-up company that focuses on a relatively new and exciting approach to cancer therapy – targeting a recently appreciated subset of tumor cells known as cancer stem cells. Research by OncoMed’s scientists shows that substances such as fully human antibodies, which attack and kill cancer stem cells, could improve therapy for a variety of cancers, such as breast, lung or colon cancer.

MORPHOSYS Mr. Hastings, can you explain what cancer stem cells are and the role you believe they play in carcinogenesis?

PAUL HASTINGS Cancer stem cells were recently identified as a small subset of tumor cells that are uniquely responsible for the growth and proliferation of tumors. They show properties that are typical of stem cells, such as self-renewal and the potential to differentiate. In marked contrast, the bulk of the cells that comprise the tumor are more differentiated cells that no longer possess self-renewal potential. As such, cancer stem cells may be responsible for both extensive tumor growth and for enabling the tumor to spread through the body by forming metastases. They are therefore the central element in a new theory of carcinogenesis.

MORPHOSYS How does the cancer stem cell concept alter our perspective on the development of cancer therapeutics?

PAUL HASTINGS The standard dogma has been that a tumor is simply a collection of mutant cells that divide endlessly. Taking cancer stem cells into consideration completely alters our understanding of tumor development. Instead of being just a group of degenerate cells, a tumor is more of a dis-regulated “organ,” comprised of cancer stem cells and specialized tumor cells that have arisen from these stem cells. Standard therapies often fail to eliminate cancer stem cells, which have a number of properties that render them selectively resistant to radiation and chemotherapy. This makes them extremely dangerous and could explain why although tumors often initially disappear after chemotherapy, they tend to come back later. A therapeutic approach that is targeted specifically to cancer stem cells could therefore have a better chance of success.

MORPHOSYS Who developed the basic principle underlying this approach, and who is leading the research at OncoMed?

PAUL HASTINGS The founder of OncoMed, Michael Clarke, with his team from the University of Michigan, was the first to demonstrate the existence of cancer stem cells within solid tumors, such as breast cancer. This discovery and previous work done by researchers at the University of Toronto demonstrating a fundamental role for cancer stem cells in leukemia laid the foundations for the cancer stem cell field. OncoMed was founded with the aim of translating this seminal scientific advance into a medical application and commercial use.

Dr. John Lewicki leads our research and development team at OncoMed. John came to us from the biotechnology company Scios Inc., where he managed research for a number of years. At Scios, he was closely involved in the discovery of the drug Natrecor™ for congestive heart failure. Dr. Austin Gurney and Dr. Tim Hoey work with him. Tim identified oncogenes as Director of Tumor Biology at Tularik/Amgen and developed drugs to target those genes. Austin came to OncoMed with 12 years' experience at Genentech, where his team discovered and patented numerous growth factors and cytokines involved in control of cell growth and behavior, several of which have entered clinical development. All in all, we have a highly experienced team.

MORPHOSYS What is OncoMed's strategy for attacking these cancer stem cells and what role do antibodies play in this?

PAUL HASTINGS We are focused on developing antibodies as therapeutic agents that selectively target cancer stem cells. Antibodies have been among the most successful and innovative anti-cancer drugs in recent years. Products such as Avastin®, Herceptin® and Rituxan® have greatly improved the treatment of certain types of cancer and generate annual sales of over € 5 billion.

MORPHOSYS Why have you decided to use MorphoSys's HuCAL technology as the source for your antibodies?

PAUL HASTINGS We have already developed an extensive collection of antibodies using traditional mouse hybridoma technology. However, as a company focused on developing antibody-based therapeutics, we feel it is vital to utilize the best available antibody technologies. In particular, the ability to develop humanized or fully human antibodies as therapeutic candidates is very important. We looked at all the systems on the market and decided to use HuCAL technology as we believe the targeted, optimized approach that is HuCAL best serves our needs.

MORPHOSYS The subject of stem cells has provoked lively ethical debate in recent years. How is your work connected to this debate?

PAUL HASTINGS Cancer stem cells are not to be confused with embryonic stem cells. Embryonic stem cells are normal, healthy stem cells that give rise to a variety of tissues and organs. The harvesting and scientific application of these cells takes center stage in the stem cell discussion. Cancer stem cells, on the other hand, occur within cancer patients as a population of tumor cells with the capacity for self renewal, but they can only turn into more tumor cells. As such, they can be considered as "evil" or "bad" stem cells, and there are no ethical arguments against fighting them.

MORPHOSYS The approach has not yet been clinically validated. What makes you so confident that it will eventually lead to new cancer therapies?

PAUL HASTINGS Of course there is no guarantee of success, as with all new scientific advances. However, it is becoming increasingly clear, as evidenced by the avalanche of publications in top scientific journals, that cancer stem cells underlie many if not all cancers. Recent work highlights their role in such major diseases as breast, colon and brain tumors as well as leukemia. We are committed to demonstrating the value of targeting these cancer stem cells and believe that this approach will provide real benefit to patients.

MORPHOSYS Thank you very much for the interview, Mr. Hastings.