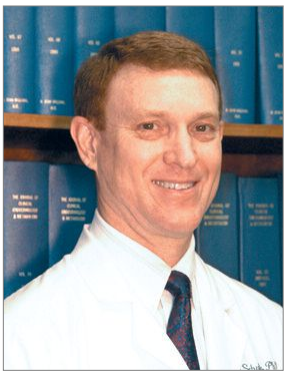
An Interview with **Dr. Gregory S. Schultz**:

A Leader in Wound Healing Research



Dr. Gregory S. Schultz

INTERVIEWED BY Catherine Harley, Associate Editor, *Wound Care Canada*

Gregory S. Schultz, PhD, is a Professor of Obstetrics and Gynecology and a director of the Institute for Wound Research at the University of Florida. His research focuses on the role of growth factors, cytokines and proteases in normal and chronic wound healing in the skin and eye. He has published more than 210 research papers, chapters and review articles, which have been cited more than 5,100 times, and he has over a dozen patents in the area of wound healing. He is funded by grants from the National Institutes of Health and from pharmaceutical companies, and he is a consultant for multiple biotechnology companies. Dr. Schultz is currently the Chair of the Wound Bed Preparation Advisory Board, and he served as president of the Wound Healing Society from 1999–2001.

Q How long have you been involved in wound-related research?

About 20 years.

Q How did you first become involved in wound research?

I began conducting research on growth factors in breast cancer in the early 1980s, but at the urging of clinical colleagues in the departments of Surgery and Ophthalmology, I also started investigating the effects of exogenous growth factors on promoting healing of wounds in the skin and eye. Over the next few years, I increasingly shifted the focus of my research onto the area of wound healing, which has been my primary area for about 20 years.

In 1989, I moved from the Department of Biochemistry at the University of Louisville to the Department of Obstetrics and Gynecology at the University of Florida. In 1992, my colleagues and I established the Institute for Wound Research, which serves to integrate the collaborative research efforts of scientists and clinicians from multiple departments who are interested in various aspects of wound healing.

Q Do you work alone or with a team?

Almost all of my research involves a team approach. My faculty colleagues include surgeons (Dr. David Mozingo, head of the burn unit; Dr. Scott Berceli, vascular surgeon), ophthalmologists (Dr. Sonal Tuli, cornea; Dr. Mark Sherwood, glaucoma), an otolaryngologist (Dr. Pat Antonelli), nurses (Dr. Joyce Stechmiller), basic scientists (Dr. Nasser Chegini, ob/gyn; Dr. Lyle Moldawer, surgery; Dr. Al Lewin, molecular genetics), a biomedical engineer (Dr. Chris Batich) and a veterinarian (Dr. Dennis Brooks). A major strength of the Institute for Wound Research is the broad background of the personnel, which spans molecular biology, biomedical engineering and clinical practice.

Q What types of wound research have you been involved in?

A major focus of my research during the last 10 years was to characterize the molecular and cellular differences between acute, healing wounds and chronic, non-healing wounds. This led to the discovery that chronic wounds have chronically elevated levels of inflammatory cytokines (TNFa, IL-1), which cause levels of proteases (matrix metalloproteases [MMPs] and elastase) to be highly elevated. Although proteases play important roles in normal healing by promoting migration of cells, formation of new blood vessels, removing denatured matrix components and remodeling scar, chronically elevated proteases have "off target" effects resulting in destruction of growth factors, receptors and intact matrix proteins that are essential for healing. This led us to develop therapies that attempt to correct these molecular imbalances, including topical treatment with growth factors and protease inhibitors. This also stimulated the development of the concept of "wound bed preparation," which incorporates molecular and cellular components into an integrated framework for advanced wound-

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*Data on file.

care practices. The most recent areas of my research include development of advanced wound dressing with bound microbicidal polymers and development of diagnostic test strips that can assess the molecular status of acute and chronic wounds.

Q Is it easy to get research projects funded?

Funding for NIH research grants has decreased in real dollars the last few years, so that only about 15 per cent of grant applications in the area of wound healing are now being funded. Support from pharmaceutical companies, biotech companies and device companies for clinical trials remains relatively stable.

Q Could you walk me through a typical day in the life of a researcher?

My typical day is a combination of traditional academic duties such as lecturing in graduate student (PhD, MS) or professional student (MD, DDM) courses, meeting with students and residents to review results and design new experiments, performing my own lab bench experiments, attending research seminars, and serving on university or college committees (promotion and tenure committee, graduate or medical student admission committees). Other major, never-ending tasks are writing scientific manuscripts and grant applications.

Q What are some of the biggest challenges you experience in the research setting?

A major challenge is trying to stay aware of new developments in multiple fields that have a bearing on my areas of research. The rate of discovery in areas of basic science, engineering and clinical medicine is very rapid. Another challenge is assessing and selecting which pathways of research are likely to produce the most important results. Ideas are cheap; selecting the best idea is hard.

Q What is the most exciting research project you have worked on related to wounds?

That is a hard question to answer because I always get excited initiating a new project. However, if I had to choose one project, I would choose the project to assess if topical application of growth factor would promote healing of skin wounds. These studies were the first clinical studies assessing the effect of a recombinant human growth factor (epidermal growth factor, rhEGF) on the healing of skin wounds. The results, which were published in 1989 in the *New England Journal of Medicine*, clearly showed that rhEGF significantly accelerated healing of paired, partial-thickness wounds (skin-graft donor sites) in patients. These studies opened the field of adjuvant growth-factor therapies and eventually led to recombinant human platelet-derived growth factor for the treatment of chronic diabetic foot ulcers.

Q How has wound research changed since you have been involved?

Research has become more molecular-based and involves more "high-tech" approaches drawing on multiple disciplines such as biomaterials, gene therapy with viral vectors, and microarray platforms.

Q Do you have a collaboration with the clinical community?

Yes, I work closely with my clinical colleagues in the departments of Ob/Gyn, Surgery, Nursing and Ophthalmology on special problems of wound healing in their disciplines. Fortunately, wound healing in the skin, eye, and peritoneal cavity are very similar at the molecular level. In other words, skin cells, eye cells and peritoneal mesothelial cells all "read" the same biochemistry text book, and molecular regulation of wound healing is very similar in these different tissues.

Q Do you ever get the opportunity to see your research impacting clinical wound care?

Yes. The first example was the translation of basic research on growth factors into a topical treatment for chronic wounds. More recently, our research on cytokines and proteases in chronic wounds has led to a clinical trial of a topical protease inhibitor (doxycycline) and the marketing of dressings that contain collagen, which acts as a "trap" for proteases in wound fluid and preserves endogenous growth factors in wounds.

Q How do you store your research information?

All primary laboratory data are stored in research notebooks, a policy that is mandated by the National Institutes of Health. In addition, data are always backed up in computer files.

Q What are the most important tools you have to work with?

As a biochemist and molecular biologist, much of my basic research utilizes typical recombinant DNA techniques to genetically engineer pieces of DNA that enable us to develop gene-specific interventions in wound cells. As research progresses, projects tend to move from test tubes to cell culture systems, to animal models, to clinical trials.

Q Have you had a mentor who made a difference for you in your field of research?

I owe much to my post-doctoral mentor, Dr. James Jamieson at Yale University, and to my many clinical colleagues, including Dr. Marty Robson and Dr. Richard Eiferman, who patiently taught me enough clinical knowledge to envision how I might apply growth factors, proteases and inhibitors to improve healing.

Q What does the future hold for wound research?

The future of wound healing will be very exciting! New approaches will include high-tech viral-vectored gene therapy to stimulate healing of chronic wounds or to prevent excessive scarring and fibrosis. Other advances will be more low-tech, such as low-cost dressings with bound microbicidal polymers that will prevent wounds from becoming infected. A rapid, bedside diagnostic test strip that measures multiple molecular markers will be developed, which will enable wound-care providers to optimize therapy for individual patients.