# Charles M. Lapière (1931-2007)

We mourn the loss of our respected colleague and close friend, Charles Lapière, who died on 8 November 2007, in Liège, Belgium.

Charles had a successful career as a dermatologist and cell biologist, with a strong focus on connective tissue research. He was actively involved in founding the European Society for Dermatological Research (ESDR) and the European Tissue Repair Society. He received many honors and awards, including honorary memberships in the ESDR and the Society for Investigative Dermatology. For many years, he was a member of the Editorial Board of the *Journal of Investigative Dermatology* and served as European Editor. This past spring, the University of Cologne honored his achievements with a doctor *honoris causa* degree.

**Charles Lapière at the bench, 2007.**

Charles's interest in physiology and pathology of connective tissue can be traced back to his days as a medical student in the 1950s. At that time, his scientific curiosity focused on the activity of topically applied steroid hormones, and his work led to the now classic concept that androgens and estrogens participate in the pathophysiology of diseases such as acne. This sparked his growing interest in the physiology and pathology of connective tissue, a research field that he investigated enthusiastically for the next 50 years, publishing more than 300 articles and numerous book chapters. Notably, these publications set several milestones with long-standing impact not only on the fields of connective tissue research and dermatology but on many other biomedical research areas as well.

The first milestone was achieved when Charles was in Jerome Gross's biology laboratory at Harvard Medical School. His work there as a young research fellow led to the discovery of animal collagenase and to the characterization of its role in physiology and pathology. This was a major discovery, as documented by hundreds of papers referring to Charles's seminal articles. This breakthrough opened a new field of research, that of metalloproteinases, enzymes that are crucial for development, tissue repair, inflammatory reactions, and tumor invasion, which are now the focus of extensive investigation in basic science and in clinical and industrial laboratories worldwide.

Upon his return to Belgium in 1963, and in parallel with clinical activities in the Department of Internal Medicine at the University of Liège, Charles established a clinical and basic research unit focusing on the metabolism of collagen in skin and bone. In 1970, he was appointed professor and chairman of dermatology at Liège. As a dermatologist and scientist interested in the molecular mechanisms responsible for skin diseases, he became intrigued by dermatosparaxis in cattle, a heritable disorder in which animals suffer from extreme skin fragility. Suspecting that something must be wrong with the collagen in the skin of these animals, Charles and his co-workers analyzed the collagen isolated from skin biopsies from affected calves. Their results led to the discovery of collagen precursors called procollagens and the identification of a molecular defect in the procollagen peptidase in cattle. The enzyme cleaves the aminoterminal procollagen peptides from the precursor molecule. This work led to several important publications, among them the two famous 1971 articles demonstrating the existence of collagen precursors and how they were processed. Apart from being a major advance in the understanding of collagen metabolism, highly appreciated by the worldwide scientific community and stimulating further research in many laboratories, it was the first demonstration of a genetic disease affecting collagen. Later, Charles and his group identified a similar defect based on procollagen peptidase that results in disease in humans, Ehler–Danlos syndrome type VIIC.

In the 1980s, Charles introduced another novel aspect to his research: in 1984 his team was among the first to show that connective tissue, or extracellular matrix, transfers mechanical information to cells and that traction and relaxation forces represent major regulatory elements for cells *in vitro* and *in vivo*. These concepts have contributed greatly to the development of artificial skin and the establishment of *in vitro* models that allow physiological and pharmacological studies under *in vivo*–like conditions. In addition, since 1995 his team has been involved in space biology experiments with NASA in the United States and the European Space Agency, with the goal of better understanding the cellular and molecular mechanisms of microgravity-induced disorders.

Besides his own academic achievements, Charles was a stimulating and generous mentor for junior scientists and

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clinicians. He established an international community of scholars who are now directing research and clinical departments around the world. Among them are Betty Nusgens, who took over Charles's Laboratory of Connective Tissues Biology, and Michel de la Brassinne, who succeeded him as head of dermatology. Gerald Pierard heads the dermatopathology unit at Liège, and Jean-Michel Foidart founded the Laboratory of Tumor and Developmental Biology, which is now headed by Agnes Noel, one of Charles's former students. Hiroshi Shinkai chairs the dermatology department at Chiba University in Japan. I somehow regard myself as one of his scholars—since I took over the chair of dermatology at the University of Cologne, we have developed many fruitful scientific collaborations and enjoyed friendly interactions on many occasions, both scientifically and personally.

Charles was an enthusiastic clinician and scientist par excellence, one who achieved important breakthroughs in cell biology and dermatology. His international view of science resulted in the establishment of lifelong friendships with scientists and clinicians around the globe. His scientific merits are recognized worldwide in the fields of dermatology and connective tissue research. Even in his years as professor emeritus, his enthusiasm continued to take him to the laboratory every day until last October.

Besides his scientific activities, Charles deeply enjoyed life in many ways: he was an excellent tennis player, he loved nature, dogs, hunting, and fly-fishing, and he enjoyed good wines and excellent cooking, which he shared with his friends.

We deeply regret the loss of an incredible original mind and close friend.

***Thomas Krieg***

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