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JOURNAL OF NATURAL PRODUCTS

Editorial

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Gordon M. Cragg, D.Phil., D.Sc. (*h.c.*): A Man for All Natural Products

It is indeed an honor and a pleasure for the four of us to serve as Guest Editors of this issue of the *Journal of Natural Products* dedicated to our great friend and colleague, Dr. Gordon M. Cragg. We wish to express our deep thanks to all contributors to this issue who have submitted the excellent articles that represent all aspects of natural products science. The depth, breadth, and diverse geographical origin of these articles show the true impact Gordon had in the field of natural products research.

Gordon spent his early years in South Africa, where his father was a Methodist minister (with a significant North English and Scots ancestry) and then settled in the area of the Eastern Cape Province. Gordon grew up in the small rural town of Alice in the Eastern Cape Province and attended both school and university in neighboring Grahamstown, where he graduated with an honors B.Sc. in Chemistry from Rhodes University in 1957. Following a short sojourn as a junior lecturer at Rhodes University in 1960, he came to the U.K. for doctoral studies at the University of Oxford, graduating with a D.Phil. in Organic Chemistry in 1963 for studies related to the synthesis and spectroscopy of steroids with Professors E. R. H. Jones and G. D. Meakins. Gordon then migrated in a westerly direction, finishing up at UCLA as a postdoctoral fellow in the laboratory of Professor Ted Geissman, working on the biosynthesis of gibberellins.

It was at this time of his life that his carefree single days came to a sudden halt, as he met, successfully wooed, and became engaged to a UCLA undergraduate, Jacqueline Tuers. In early 1965, Gordon returned to a position with the National Chemical Research Laboratory (NCRL) of the South African Council for Scientific and Industrial Research (CSIR). They were married in North Hollywood in late 1966 and returned to South Africa, and for the past 45 years Jacqui has been a very strong and steadfast supporter for Gordon. He decided to return to academe, and in 1966 he joined the Chemistry Department at the University of South Africa. After a sabbatical year with Professor Bob Pettit at Arizona State University (ASU), he transferred to the University of Cape Town in 1972, where he rose to the rank of Professor in 1979. It was during those years that he became interested in plant natural products (having previously worked extensively on steroidal molecules and written a monograph on the chemistry of organoboranes, and, with Bob Pettit, he published three volumes entitled *Biosynthetic Products for Cancer Chemotherapy*).

In 1979, he and Jacqui accepted an offer from Bob Pettit to return to the United States and work with him at the Cancer Research Institute at ASU. It was during this period of his career that he isolated the compound from a South African tree that is now known as combretastatin,[1,2] and he also made the acquaintance of another of the Guest Editors of this issue, Sheo Singh, who came to work in the Pettit laboratory at the same time there and on whom Gordon had a tremendous impact in shaping his future career. It was during this period that Gordon first met Matt Suffness, who then was the Chief of the NCI's Natural Products Branch (NPB), following on from John Douros. In late 1984, Matt "persuaded" Gordon to leave the very hot and sunny climes of Tempe, Arizona, and move to the "hot, horrible, and humid" environs of Bethesda and Frederick, to enjoy four seasons of weather, sometimes in as many days, as a member of the NPB.

This was the time when Taxol was undergoing its revival due to the pioneering work of Susan Horwitz from a mechanistic aspect and from the work of Drs. Peter Wiernik and Eric Rowinsky from a clinical perspective. This compound permeated the work of NPB and in particular the lives of Gordon and Ken Snader, as they, together with Matt Suffness, had to find adequate supplies of the Pacific yew tree in the United States, a species that was then considered by the U.S. Forest Service to be a "trash tree" during logging operations. At that time, it was estimated that three 6-inch-diameter yew trees were required to provide a course of treatment for one patient. In this same time period, the NPB raw materials collection program was being resuscitated for plants, marine invertebrates, and microbes, so in addition to the pressures generated by the requirement for the yew trees (or a substitute), these programs had to be run concurrently. That the NPB group was successful in the *Taxus* story is now well known, and it was recognized by the NIH Award of Merit in 1991, the first of three NIH Awards of Merit bestowed on Gordon.

In 1989, Gordon was appointed Chief of the NPB, but was not content to rest upon his laurels (perhaps we should substitute *Taxus* needles instead!), as he played a significant role in developing the technical aspects of the National Cooperative Natural Product Drug Discovery Groups, or NCNPDDGs, which were organized by Matt Suffness. They, together with colleagues from NCI, the NIH Fogarty International Center, NSF, and USAID, parlayed this process into the international program known as the ICBGs, or International Cooperative

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Biodiversity Groups. These melded together the concepts of the NCNPDDGs and the involvement of the biodiversity resources of megadiverse countries, with the fundamental precept that there had to be foreign Co-principal Investigators involved, and, in particular, there had to be benefit sharing with the source countries and building of suitable infrastructure, now known as "capacity building", within the source countries.

Contemporaneously with these ideas and programs, Gordon was a prime leader with Dr. Tom Mays, who was then the Director of NCI's Technology Transfer Branch, in the establishment of the NCI's Letter of Collection (LOC), which was first signed with the Malagasy Republic in 1990 and predated the Convention on Biodiversity (CBD) by two or more years. Since the United States has not ratified the CBD, the LOC and agreements based on it have formed the legal basis for the NCI's natural products collection program since the late 1980s. Thus even if an agreement was not signed, but permission was given for collection, the tenets of the agreement will be obeyed by the NCI. One of the present Guest Editors in particular (D.J.N.) can testify to the problems inherent in working with these documents and the restrictions that the U.S. Code places upon NIH scientists. However, due to the foresight of Gordon and Tom, they work. As a result of his commitment to the maintenance of biodiversity by these methods and many others, including the training of new technology transfer fellows at NCI and, at times, other institutes, Gordon received the NIH Award of Merit two more times in his career, for leadership in international collaborative research in biodiversity and natural products drug discovery (2004) and for contributions in developing and teaching NIH technology transfer courses (2004).

As part of his efforts with megadiverse countries, Gordon contributed immensely in aiding the development of recent natural product chemistry programs in Brazil, mainly in the northeast and southeast regions. In Brazil, he helped change the research scenario at the Universidade Federal do Ceará, located in Fortaleza, northeast Brazil. With a perception beyond his time, he organized the signing of a memorandum of understanding between the Federal University of Ceara and the Developmental Therapeutics Program of NCI in 2001. His contribution during the past ten years gave the support for the establishment of a solid program aiming at the discovery and development of new anticancer compounds from Brazilian biodiversity, including plants, marine organisms, and fungi. Furthermore, Gordon played a pivotal role in expanding the objectives of the Biota-FAPESP Program [The Virtual Institute of Biodiversity (www.fapesp.br/biota)] created in 1999, with the focus on biodiversity conservation and sustainable uses (*Science* **2010**, *328*, 1358−1359) in Brazil. This provided a valuable contribution to the creation of a subprogram aimed at zbioprospecting of Brazil's rich biodiversity. This was accomplished by Gordon as a result of his role as an international advisory board member of the program in 2008, which culminated in the production of an excellent document substantiating the role of the board of FAPESP, resulting in the approval of the subprogram Bioprospecta. Today, this is a successful initiative leading to the exploration of potential pharmaceutical, cosmetic, and agrochemical bioproducts in Brazil. He went several times to Brazil (2000, 2001, 2004, and 2008), and Brazilian researchers who have been or are working on natural products have an immense admiration for Gordon. He is renowned as a great scientist who has made, and continues to make, outstanding contributions to worldwide natural products science, particularly in developing countries, encouraging research and collaboration around themes of local, national, and international relevance.

In addition to the NIH awards, Gordon was elected President of the American Society of Pharmacognosy in 1998−1999 and was subsequently elected to honorary membership of the society in 2003. Perhaps the most unusual honor, however, for a natural products chemist was that, in November 2006, he was given the William L. Brown Award for Plant Genetic Resources by the Missouri Botanical Garden. This was presented at a two-day symposium (*Festschritte*) held in his honor, entitled "Realizing Nature's Potential: The Once and Future King of Drug Discovery". In addition to this honor, botanists at the Missouri Botanical Garden named a new Madagascan plant, *Ludia craggiana*, in his honor.[3] In April 2010, Gordon was also awarded an honorary doctorate [D.Sc. (*honoris causa*)] from his alma mater, Rhodes University, in recognition of his enormous contribution to international natural product-based anticancer drug discovery.

At the very end of 2004, having completed just over 20 years of NCI service and occupying the position of Chief of the NPB from late 1989, which equated to the longest tenure of any one person in this position, Gordon retired from full-time employment at the NCI. However, he was not going to be allowed to just "ride off into the sunset", as he was "persuaded" by the then Acting, now Chief of the NPB (D.J.N.) to "re-enlist as an NCI Special Volunteer" associated with the NPB, a totally unpaid position. He has not yet succeeded in severing these connections and is very actively involved with the NPB's efforts and also those of NCCAM, OCCAM, and the ASP, to name just a few of the many calls for his expertise. Gordon has continued to write prolifically, as exemplified by the recent publication of the second edition of *Anticancer Agents from Natural Products*, in which he played the major role of "nudge" to all of the authors and the other editors!

How Gordon is able to "persuade" Jacqui to let him continue his natural product efforts, now seven years after his formal retirement, is something that only they know, but hopefully he will continue, so that his knowledge and expertise will continue to be utilized by all of us.

It is in this vein that the Guest Editors of this special issue salute Gordon Cragg, a true scholar and gentleman. He is a great friend and continues to serve as a mentor to many of his former colleagues.

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