

Professor Stephen Hanessian

A Tribute



Dedicated to Prof. Stephen Hanessian on the occasion of his 84th anniversary

The Scientist and the Mentor

Stephen Hanessian was born in Alexandria, Egypt and was awarded his PhD in 1960 from Ohio State under the guidance of Prof. M. L. Wolfrom with whom he demonstrated some of the very first examples of chelation-controlled diastereoselective additions of organometallic reagents to carbonyl groups. After some time in industry as a medicinal chemist at Parke-Davis, Steve embraced a most productive career in academia at the SH where he is a distinguished Professor. During his tenure, Steve has had a tremendous impact in a variety of fields ranging from carbohydrate and supramolecular chemistry to total synthesis and medicinal chemistry. Since 2000, Steve has also been an adjunct Professor at UC Irvine where he has focused on teaching and training in medicinal chemistry and pharmaceutical sciences. For over fifty years, Steve has also been an inspirational mentor to hundreds of graduate students and post docs. In particular, he has trained people who are now in academia or industry and who have gone on to become experts in their fields. Thus, Drs Compain, Guindon, Vilchis Reyes, Moitessier and Roy, all contributors to this special issue, have made significant contributions to the fields of carbohydrates, nucleotides and aminoglycosides. Mauduit has made valuable contributions in catalysis, Vidal in total synthesis, Guindon and Del Valle in asymmetric synthesis, Petrini and Mauduit in organic chemistry methodology, Guindon, Moitessier and Mascitti in medicinal chemistry and Moitessier in computational chemistry. This special issue contains selected examples of research conducted by members and friends from the Hanessian group research family as well as mini reviews on topics of interest in the field of medicinal chemistry.

The Innovator

At a time when the scientific community is trying more than ever to harness the potential and promise of Artificial Intelligence, one cannot talk about Steve without mentioning his visionary and powerful Chiron approach, one of his major achievements which has influenced the fields of *in silico* and experimental organic chemistry and is the way many of us carry out synthesis today. With this approach, enantiopure natural substances such as amino acids and sugars can be exploited to synthesize complex natural products. His group completed a number of challenging total syntheses using this unique strategy. Among these are the first total syntheses of Avermecting B1a, Ionomocyn and Bafilomycin A1 to name a few.

In the 1980's, Steve also discovered the potential of *trans*-1,2-diaminocyclohexane as a C_2 -symmetric motif in asymmetric processes exploited nowadays in several asymmetric synthetic transformations. Asymmetric methods developed in his lab for the discovery of enzyme inhibitors, have also contributed to the development of drugs such as renin inhibitors for hypertension (Novartis, Basel, Switzerland), BACE 1 inhibitors for Alzheimer's disease (Novartis, Basel), thrombin inhibitors for stroke and embolism (AstraZeneca, Mölndal, Sweden), neuraminidase inhibitors for influenza (Abbott Laboratories), β -lactam inhibitors for infections (Glaxo, Verona, Italy) and aminoglycoside antibiotics for bacterial infections (Ionis, formerly Isis Pharmaceuticals, Achaogen Inc.). The antidiabetic drug saxagliptin features a 4,5-methanoproline nitrile amide as a means to flatten the pyrrolidine ring and was originally reported by Hanessian.

While a renown expert in medicinal chemistry and organic synthesis, he also made outstanding contributions to supramolecular chemistry. In the mid-1990's, he discovered that chiral *trans*-1,2-diaminocyclohexanes are exquisite partners for diols in forming helical supramolecular structures and more recently reported the discovery and characterization of unprecedented tubular structures when this chiron was coupled with tripeptides.

The Family Man

Steve is fostering a culture of scientific excellence and teamwork between group members, illustrating the importance of these invaluable qualities to him at both the professional and personal level. As such the Hanessian group spirit has always been very special, akin to a research family. As illustrations, Raphael Hensienne, a new member of Steve's lab and Philippe Compain's (postdoctoral fellow 1997-98) have co-authored an article in this special issue; Miguel Angel Vilchis Reyes (postdoctoral fellow 2011-15) and Oscar Saavedra (postdoctoral fellow 1997-2000), two alumni, are also co-authoring a manuscript and so are Moitessier (postdoctoral fellow, 1998-2000) and Mascitti (PhD, 1999-2003). Beyond science, Steve is an intellectually gifted individual (he speaks many languages fluently) and an artist. The interplay between science and art is always present in Steve's mind and apparent in the elegance of his work, particularly in the area of total synthesis.

With over 550 publications, nearly 50 patents and a long list of transformational achievements and awards (including the Ernest Guenther Award of the American Chemical Society in Natural Products Chemistry and the IUPAC-Richter Prize in Medicinal Chemistry), Steve is one of the most influential and gifted chemists of all time.

Thank you, Steve, for your many contributions to chemistry, science, and society. We look forward to many more contributions from you and the Hanessian research family.

Nicolas Moitessier, postdoctoral fellow 1998-2000

McGill University

Montreal Canada

Vincent Mascitti, PhD student 1999-2003

Pfizer