
The 2002 CSBMCB's Merck Frosst Prize Lecture

Dr. Jeffrey L. Wrana

Dr. Wrana obtained his Ph.D. in 1991 from the Department of Biochemistry, University of Toronto under the supervision of Dr. Jaro Sodek, head of the MRC Group in Periodontal Physiology. His graduate work which focussed on understanding how the secreted factor, Transforming Growth Factor-beta, (TGF β) altered cell function produced 15 papers, 5 as first author. He embarked on a post-doctoral fellowship programme with Dr. J. Massague at Memorial Sloan Kettering Cancer Center in New York City. While there, he made major contributions to the identification and characterization of a family of transmembrane serine/threonine kinases as receptors for TGF β superfamily members. During this time he published extensively in top-tier journals (Cell and Nature). This work culminated in his elucidation of the mechanism of Ser/Thr kinase receptor activation (Wrana et al., 1994; Nature, 370, 341-347). This paper, in which he is first author, has been and continues to be extensively cited (around 1,000 citations to date) and is considered a "classic" in the field of signal transduction.

Dr. Wrana started his independent research program in 1995 at the Hospital for Sick Children in Toronto and is currently a Senior Scientist at the Samuel Lunenfeld Research Institute. He has continued to make significant and lasting contributions to the TGF β signalling field in particular and signal transduction pathways in general. When Dr. Wrana started his laboratory, the intracellular mediators of the TGF β pathway were completely unknown and he has made critical contributions to the identification of the Smad signal transduction pathway and towards its functional analysis. To this end, Dr. Wrana identified the first R-Smad (called MADR1 at the time) and went on to show that R-Smads are direct substrates of Ser/Thr kinase receptors. This was the first demonstration of a physiologically relevant substrate of the Ser/Thr kinase class of receptors. He also identified the inhibitory class of Smads



and identified a novel FYVE domain protein that controls Smad subcellular localization. In addition, Dr. Wrana has demonstrated the contribution of Smads in human diseases such as cancer. In his more recent work, Dr. Wrana was instrumental in the identification of the Smurf family of E3 ubiquitin ligases and he has shown that, in addition to transcriptional mediators, Smads also function to control protein turnover.

During his independent career, Dr. Wrana has received several prestigious awards. He is a 'first round' PREA award recipient and has won Scholarship and Investigator awards from the MRC/CIHR. In addition, Dr. Wrana was the first non-American ever to receive the Gertrude B. Elion Award in 1997, which is given to one outstanding young investigator each year by the American Association for Cancer Research (AACR). In 1998, he was also awarded the William E. Rawls prize from the National Cancer Institute of Canada and just last year won the Allan Bruce Robertson young investigator award from the Clinical Research Society of Toronto. Recently Dr. Wrana has been named a Howard Hughes International Research Scholar.