SAMUEL LUNENFELD RESEARCH INSTITUTE
MOUNT SINAI HOSPITAL
600 University Avenue, Toronto, Canada M5G 1X5
Fax (416) 586-8857
Tel. (416) 586-8273

September 25, 1997.

Dr. Carlo M. Croce,
Chairperson, Selection Committee,
AACR-Pezcoller International Award for Cancer Research,
c/o American Association for Cancer Research, Inc.,
Public Ledger Building, Suite 826,
150 South Independence Mall West,
Philadelphia, PA 19106-3483, U.S.A.

Dear ~~Dr. Croce~~ Carlo:

I am pleased to nominate Dr. Tony Pawson for The 1998 AACR-Pezcoller International Award for his discovery of SH2 domains, for demonstrating their role in mediating protein-protein interactions, and for the important insights that this research has provided on cancer.

Dr. Tony Pawson's work has revolutionized our understanding of signal transduction, and the molecular mechanisms by which cells respond to external cues. His pioneering work on protein modules that control intracellular signalling downstream of tyrosine kinases has been instrumental in elucidating the language through which cells communicate. His work has the broadest implications for understanding both the normal process of cell signalling, and the breakdowns in signalling that underlie cancer. In addition, his work has suggested new strategies for the design of novel cancer chemotherapeutic agents.

In 1986, Dr. Pawson identified a 100 amino acid sequence, conserved amongst non-receptor tyrosine kinases (such as Src, Fps and Abl), that he termed the Src homology region 2 (SH2). The SH2 sequence of cytoplasmic tyrosine kinases is located immediately N-terminal to their kinase domains. Dr. Pawson showed that the SH2 sequence is not required for kinase activity per se, but is important for oncogenic transformation by these cytoplasmic tyrosine kinases, for their phosphorylation of specific substrates, and for regulation of their kinase activities. In this landmark paper, he proposed that "the noncatalytic (SH2) domain may direct specific interactions of the enzymatic region with cellular components that regulate or mediate tyrosine kinase function". This assertion has been fully substantiated over the last decade.

The discovery of SH2 domains and elucidation of their role in mediating protein-protein interactions provided a molecular basis for understanding how tyrosine phosphorylation might alter cellular circuitry. In addition, Dr. Pawson's research immediately provided an understanding of how oncogenes like *crk*, which contains an SH2 but not a kinase domain, subverts the cell's signalling apparatus to induce oncogenic transformation.

.../2