PREFACE

The Twelfth Annual Washington Spring Symposium on Health Sciences attracted over 300 scientists from 20 countries. It was held at the Lisner Auditorium of the George Washington University in Washington, D.C. during June 1-5, 1992. The theme of the meeting was "Growth Factors, Peptides, and Receptors," and speakers emphasized both basic and clinical research in these areas.

The seven plenary sessions emphasized Peptides, Growth Factors, Peptide Receptors, Growth Factor Receptors, Second Messengers, Proliferation, and Clinical Correlations. The chapters in this volume are derived from each of these scientific sessions plus the poster and special sessions.

The Abraham White Distinguished Scientist Award was presented to Dr. Solomon H. Snyder for his numerous contributions to the field of neurochemistry. He presented the keynote address "Nitric Oxide: A Novel Neuronal Messenger." Dr. Snyder discussed the pathway of nitric oxide (NO) synthesis by the enzyme NO synthase. Released NO may be responsible for the neuronal toxicity associated with NMDA, an excitatory amino acid analogue. Dr. Snyder noted that NO may be the first of a new class of transmitters, with carbon monoxide being another candidate.

The Distinguished Public Service Award was presented to Senator Fritz Hollings in recognition of his leadership and outstanding achievements in the United States Senate and for his legislative support for biomedical research and education. In the symposium banquet address, Senator Hollings stressed the need for continued support of research to combat serious diseases such as cancer.

The field of peptide and growth factor research has been active for over three decades. It has been richly endowed with Nobel Laureates including Drs. Rita Levi Montalcini and Stanley Cohen (nerve growth factor isolation), Vincent DuVigneaud and Bruce Merrifield (peptide synthesis), Rosalyn Yalow (peptide radioimmunoassay), Roger Guillemin (TRH isolation), and Andrew Schally (somatostatin isolation). The symposium emphasized that important research contributions have been and continue to be made in peptides, growth factors, and receptors.

In its infancy, the field was concerned with the isolation and sequencing of peptides and growth factors. Radioimmunoassays and bioassays were developed to assay for biologically active peptides and growth factors. Subsequently, receptor binding and second messenger assays were developed to estimate the potency of various peptide and growth factor analogues. This resulted in the definition of both receptor agonists and antagonists. With the advance of molecular biology, genes for the growth factors and peptides were cloned. Agents were defined which alter peptide and growth factor gene expression. More recently, peptide and growth factor receptors have been cloned and receptor subtypes identified.

Peptides and growth factors are synthesized in the form of high-molecular-weight precursor proteins, and thiol proteases as well as enzymes with cathepsin D and subtilisin-

like activity regulate posttranslational processing. The processed peptides and growth factors affect a multitude of biological processes. Endothelin is a potent vasoconstictor, but VIP, in contrast, is a potent vasodilator. FGF, which binds to receptors and can be translocated to the nucleus, causes angiogenesis and wound repair. Transforming growth factor β causes cellular differentiation reducing the growth of many cells. NGF, which binds to receptors and causes neurite outgrowth, increases cholinergic parameters such as choline uptake, acetylcholine synthesis, and choline acetyltransferase activity; cholinergic function is deficient in Alzheimer's disease. It may be possible to deliver growth factors such as NGF to the brain using genetic engineering techniques.

Peptide receptors, such as bombesin/gastrin releasing peptide and CCK, were cloned and found to be linked to G-proteins. The receptors contain approximately 400 amino acids and 7 transmembrane domains. The third cytosolic loop interacts with G-proteins, and bombesin/GRP as well as cholecystokinin cause phosphatidylinositol turnover. The inositol-1,4,5-trisphosphate released elevates cytosolic calcium whereas the diacylglycerol released activates protein kinase C. In contrast, VIP elevates cAMP and somatostatin inhibits the increase in cAMP caused by VIP. Potent receptor antagonists have been synthesized for bombesin/GRP, CCK, and VIP receptors. The EGF receptor is a large 170-kdalton protein which crosses the membrane once and contains a tyrosine kinase. When EGF binds to the extracellular domains, tyrosine kinase activity is stimulated causing phosphorylation of protein substrates and growth. Monoclonal antibodies have been elicited and found to function as EGF receptor antagonists. Also, EGF-toxin conjugates, which may serve as antitumor agents, have been defined.

TGFα, which interacts with the EGF receptor, causes proliferative changes in transgenic mice. EGF receptors are abundant in several cancers including breast, gastric, and non-small-cell lung cancer. Somatostatin receptors are present in several cancers including gastrointestinal, pituitary, medullary thyroid, and small-cell lung cancer. The somatostatin receptor is associated with tyrosine phosphatase activity resulting in the dephosphorylation of protein substrates. Potent somatostatin agonists such as octreotide can be radiolabeled and utilized to image tumors. In the future, knowledge obtained about peptides and growth factors may be important in the development of new cancer therapies.

The Washington Spring Symposium provided an international forum for the exchange of new ideas. This preface highlights only a few of the scientifically significant and exciting research results that were presented. This volume will be of interest to neuroscientists, gastroenterologists, psychiatrists, oncologists, and others interested in acquiring state-of-the-art information about peptides, growth factors, and receptors.

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