

ANNALS OF THE NEW YORK ACADEMY OF SCIENCES

Special Issue: *Regulatory Peptides*

COMMENTARY

Progress in regulatory peptide researchLimei Zhang¹ and Lee E. Eiden²¹Departamento de Fisiología, Facultad de Medicina, Universidad Nacional Autónoma de México (UNAM), Mexico City, Mexico.²Section on Molecular Neuroscience, National Institute of Mental Health Intramural Research Program, National Institutes of Health, Bethesda, Maryland

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The field of regulatory peptide research has developed significant momentum owing to several recent converging trends. Dozens of peptide-based drugs have been approved by the U.S. Food and Drug Administration in the past decade, the majority for the treatment of metabolic disorders, including diabetes. These are the “tip of the spear” for peptide therapeutics, revealing that impediments of delivery, stability, and bioavailability inherent in peptide drugs have in many cases been overcome. While most are orally available, and directed at peripheral targets, pharmaceutical delivery of peptides to the central nervous system through nasal mucosal routes has also seen much progress. Cell-based high-throughput drug discovery methods, the X-ray crystallographic structural definition of G protein-coupled receptors, and deorphanization of peptide-liganded receptors have contributed to the emergence of new targets for pharmacological intervention and accelerated the development of peptide-based as well as nonpeptide congeners for existing ones. Finally, the recognition that peptides act at their receptors, in a cellular context, in conjunction with other peptides and other first messengers, including neurotransmitters, hormones, and autocrine and paracrine factors, has led to an increased appreciation for the combinatorial possibilities of regulatory peptide action, now penetrating to drug design and discovery efforts. The fifteen reviews, reports, and perspectives collected in this special issue of *Annals of the New York Academy of Sciences* provide a snapshot of the frontiers of the field of regulatory peptide research as they expand physiologically, pharmacologically, and therapeutically.

Keywords: regulatory peptide; neurotransmitter; hormone; GPCR; therapeutic

Regulatory peptides include neuropeptide neurotransmitters of the central and sensory, autonomic, and enteric nervous systems; hypophysiotropic hormones of the hypothalamus, paracrine, and incretin peptides of the gut; and classical peptide hormones whose effects are mediated throughout the organism via receptors found in other endocrine tissues and visceral organs. Often, the same peptide found in the gut to regulate intestinal response to food intake is produced in neurons of the brain to subserve behavioral cognates of food intake, such as hunger and satiety. In short, endogenous peptides, usually, but not always, acting at highly diversified G protein-coupled receptors (GPCRs), in multiple, often redundant regulatory networks through-

out the body, provide probes for broad, translationally relevant themes in physiological regulation in both health and disease.

The 22nd International Symposium on Regulatory Peptides (RegPep2018), sponsored by the International Regulatory Peptide Society, featured 138 plenary and specialized oral presentations spanning the physiology and pharmacology of central, peripheral, immune, metabolic, and inflammatory regulatory peptides, and translational advances in targeting regulatory peptides and their receptors to human diseases, including posttraumatic stress disorder (PTSD), cancer, diabetes, depression, anxiety, alcohol and opiate use disorders, inflammatory disorders, and neurodegeneration.

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David Kirk



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