

Biochemistry of Peptide Hormones and Neurotransmitters Produced by Lung Cancer

Peptide Hormone Biosynthesis – Recent Developments

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Peptide Hormone Biosynthesis – From Nucleus to Secretory Granule

The biosynthesis of peptide hormones is now recognized to be a highly ordered series of events. These biosynthetic events can frequently be localized to a particular subcellular organelle (Fig. 1). Each organelle will be discussed in turn, to emphasize the sequential nature of the maturation process. There will be frequent references to the synthesis and processing of the corticotropin/endorphin precursor within the pituitary. This multihormone precursor is often referred to as pro-opiomelanocortin (POMC). POMC is an interesting model to study, since many post-translational modifications are manifest within its maturation products. More intriguing is the fact that processing of this multihormone precursor is tissue specific. In the pars distalis or anterior lobe of the pituitary, ACTH, β -lipotropin (β -LPH), and an N-terminal or 16 K fragment are the major biosynthetic products. In the pars intermedia or intermediate lobe processing is more complete, and α -melanotropin (α -MSH), corticotropin-like intermediate lobe peptide (CLIP), γ -LPH, various forms of acetylated endorphin, γ -MSH, and a shortened N-terminal (16K₁₋₄₀) fragment are the major products (Fig. 2). More is known of this system than of many others, primarily because pituitary tissue is relatively easy to maintain in culture and lends itself well to classical pulse/chase biosynthetic experiments. Also the AtT-20 mouse pituitary tumour cell line has been an extremely useful and accurate model for anterior pituitary processing (for extensive reviews on this subject see Eipper and Mains 1980; Chrétien and Seidah 1981).

The study of peptide hormone biosynthesis, whether at the transcriptional level or at the level of post-translational processing, is progressing rapidly on several fronts. It will not be possible to discuss all aspects of this multistep process in detail. Instead, some of the recent developments which are of particular interest in our own laboratory are discussed.

The Nucleus

In eukaryotic organisms gene transcription is a nuclear event. The resulting RNA transcript must be transported to the cytoplasm for translation to take place. Recently it has been shown that conditions that acutely alter ACTH release from the anterior pituitary also have longer term effects upon the levels of POMC mRNA levels in the cytoplasm. For

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elevated blood levels of PTH in patients with renal failure may exert deleterious effects on many systems and as such may participate in the genesis of many of the manifestations of the uremic syndrome 3 Thus the essence of the Massry hypothesis is the notion that PTH may act as a major uremic toxin The search for uremic toxins did not yield successful results In the last three decades many compounds have been implicated as uremic toxins However a cause and effect relationship between these compounds and the manifestations of the uremic syndrome has not been established in most cases Research

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 - The Rise of Digital Reading Recent Developments In Peptide Hormone Assay And Action
 - Advantages of eBooks Over Traditional Books
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 - Exploring Different Genres
 - Considering Fiction vs. Non-Fiction
 - Determining Your Reading Goals
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 - Features to Look for in an eBook Platform
 - User-Friendly Interface
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 - Personalized Recommendations

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 - Interactive Elements Recent Developments In Peptide Hormone Assay And Action
- 8. Staying Engaged with Recent Developments In Peptide Hormone Assay And Action
 - Joining Online Reading Communities
 - Participating in Virtual Book Clubs
 - Following Authors and Publishers Recent Developments In Peptide Hormone Assay And Action
- 9. Balancing eBooks and Physical Books Recent Developments In Peptide Hormone Assay And Action
 - Benefits of a Digital Library
 - Creating a Diverse Reading Collection Recent Developments In Peptide Hormone Assay And Action
- 10. Overcoming Reading Challenges
 - Dealing with Digital Eye Strain
 - Minimizing Distractions
 - Managing Screen Time
- 11. Cultivating a Reading Routine Recent Developments In Peptide Hormone Assay And Action
 - Setting Reading Goals Recent Developments In Peptide Hormone Assay And Action
 - Carving Out Dedicated Reading Time
- 12. Sourcing Reliable Information of Recent Developments In Peptide Hormone Assay And Action
 - Fact-Checking eBook Content of Recent Developments In Peptide Hormone Assay And Action

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- 13. Promoting Lifelong Learning
 - Utilizing eBooks for Skill Development
 - Exploring Educational eBooks
- 14. Embracing eBook Trends
 - Integration of Multimedia Elements
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