بسم الله الرحمن الرحيم

شبكة المعلومـــــات الجامعية

التوثيق الالكتروني والميكروفيلم

شبكة المعلومات الجامعية

جامعة عين شمس

التوثيق الالكتروني والميكروفيلم

﴿ قـــســـم ﴾

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها
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لم ترد بالأصـــل

ADRENOMEDULLIN-NITRIC OXIDE INTERACTIONS IN NORMAL AND CHRONIC RENAL FAILURE RATS.

THESIS

Submitted to the Faculty of Medicine,

Alexandria University,

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By

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بسم الله الرحمن الرحيم

وما أوتيتم من العلم إلا قليلا

صدق الله العظيم

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Dedicated to

The memory of my mother.
My family, my husband,
my brother Ali,
my children, NADA and Abdel Rahman.

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INTRODUCTION

Introduction

Adrenomedullin:

Adrenomedullin (ADM) is a newly discovered 52-amino acid regulatory peptide. It was discovered when a group of scientists in Japan were screening a panel of peptides extracted from a pheochromocytoma. Because it was first isolated from the adrenal medulla it was termed adrenomedullin. [1]

The first paper on adrenomedullin, published in April 1993, described not only the purification of this peptide, but also its action on blood pressure, and the development of specific (radioimmunoassay) RIA to measure circulating adrenomedullin [2]. Three months later the gene encoding human adrenomedullin was sequenced [3], followed by rat gene in September [4]. Within two years plasma ADM had been measured in a wide range of clinical conditions [5].

ADM has been shown to influence a variety of physiological systems, acting both peripherally and centrally to regulate blood volume [2,6], hormone secretion [7] and the autonomic nervous system [8]

Structure and synthesis of adrenomedullin:

Human ADM is 52-amino acid peptide with a single disulfide bridge between residue 16 and 21 and with an amidated tyrosine at the carboxy terminus [2]. In its c-terminal portion (amino-acid residues 16-52) ADM has 27% similarity to calcitonin gene-related peptide (CGRP) [2], and has therefore been added to the calcitonin / CGRP/ amylin peptide family [2]. Rat adrenomedullin has 50 amino acids, with two deletions and six substitutions compared with the human peptide [4]. Porcine adrenomedullin is nearly identical to the human peptide, with only a single substitution (Gly for Asn) at position forty [9]. The sequence for

both canine [10] and bovine [11] ADM have also been elucidated. A comparison of the amino acid sequences of ADM from different species is shown in Fig (1).

Molecular biology of adrenomedullin:

Ishimitsu et al. [12], have reported on the human genomic DNA fragment, which encodes the ADM gene. The DNA fragment was isolated from a human liver genomic library and was found to consist of four exons and three introns (Fig 2). Southern blot studies indicate that the ADM gene is situated in a single locus on chromosome 11. Kitamura et al [2] isolated the human cDNA clone encoding ADM precursor. The precursor for ADM preproadrenomedullin (PAMP) is 185 amino acids in length [2]. The precursor for rat ADM is also 185 amino acid residues in length and, as in human, it included a 21-residue putative signal peptide at its amino terminus [4].