EB2005 SYMPOSIUM INTRODUCTION

Diagnosis and Treatment Utilizing Natriuretic Peptides

One of the missions of the American Federation for Medical Research (AFMR) is to facilitate translational research. With that objective, AFMR is proud to continue to sponsor the "Bench to Bedside Symposia" at the annual Experimental Biology (EB) meeting. More details on how to apply for holding a symposium for future EB meetings are provided at <www.afmr.org>.

The symposium "Diagnosis and Treatment Utilizing Natriuretic Peptides," sponsored by the AFMR, was held at the 2005 EB meeting in San Diego, California, on April 4, 2005. This symposium was cosponsored by Quest Diagnostics, Inc. The session's content is summarized in the four articles that follow, each authored by one of the speakers at the symposium. Dr. Adolfo J. deBold (Ottawa Heart Institute, Ottawa, ON), who discovered the first of the natriuretic peptides (ie, atrial natriuretic factor, also termed atrial natriuretic peptide), reviewed what regulates natriuretic peptide production by the heart. Dr. John Burnett Jr (Mayo Clinic, Rochester, MN) reviewed natriuretic peptides as treatment modalities of congestive heart failure. Dr. Walter H. Hörl (University of Vienna, Vienna, Austria) reviewed natriuretic peptides as treatment modalities of acute and chronic kidney disease and the effects of hemodialysis on the circulating levels of natriuretic peptides. Lastly, Dr. David Vesely (University of South Florida Cardiac Hormone Center, Tampa, FL) presented data on the basic science and potential clinical application of the newest property of some of the natriuretic peptides, that is, their potential as anticancer agents.

The following articles discuss the molecular biology, animal experiments, and human investigations that have led to one of the natriuretic peptides to be used clinically to treat congestive heart failure. Further, their potential to move from the bench and animal experiments to the bedside to treat renal failure and cancer is outlined for the reader.

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EB2005 SYMPOSIUM

Atrial Natriuretic Peptides: Anticancer Agents

David L. Vesely

ABSTRACT

Atrial natriuretic peptides (ANPs) consist of a family of six peptide hormones that are synthesized by three different genes and then stored as three different prohormones. Within the 126–amino acid ANP prohormone are four peptide hormones: long-acting natriuretic peptide (LANP), vessel dilator, kaliuretic peptide, and ANP, whose main known biologic properties are blood pressure regulation and maintenance of plasma volume. The newest discovered property of these peptide hormones is their anticancer effects. Vessel dilator, LANP, kaliuretic peptide, and ANP decrease the number of human pancreatic adenocarcinoma cells in culture by 65%, 47%, 37%, and 34%, respectively, within 24 hours at their 1 μM concentrations. Similar results have been found with breast adenocarcinomas, squamous cell lung cancer, and small cell lung cancer cells, each associated with an 83% or greater inhibition of deoxyribonucleic acid (DNA) synthesis by these four peptide hormones. Brain natriuretic peptide has no effects even when increased 100-fold (ie, 100 μM). C-type natriuretic peptide has no effects when increased 10-fold, but when increased 100-fold, it decreases 39% of the cancer cells. At this higher 100 μM concentration, vessel dilator kills 92% of the cancer cells within 24 hours. The four peptide hormones synthesized by the ANP gene given subcutaneously via osmotic pumps in athymic mice with human

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