

2nd International Conference on

CANCER BIOLOGY, THERAPEUTICS AND DRUG DISCOVERY AND DELIVERY

&

10th Annual Congress on

BIOMARKERS, CLINICAL RESEARCH & THERAPEUTICS

October 03-04, 2018 | Los Angeles, USA

Biomedical potentials of calcitonin gene-related peptide (CGRP) antagonist in the control of prostate cancer and its bone metastasis in adult males: A review

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Calcitonin gene-related peptide (CGRP) is a 37 amino acid regulatory neuropeptide derived from alternative splicing of the calcitonin/CGRP gene. It is primarily localized to C and A-delta sensory fibers which display wide innervations throughout the body. It has been suggested that CGRP, as well as its antagonist, have wide potential as the therapy for treating many diseases depending on the biochemical pathway mobilized by each of them. Nevertheless, limited progress has hitherto been made in these areas. The development of CGRP antagonists has remarkably shown that CGRP antagonists have great potential in the management of pain. Receptors for calcitonin family including calcitonin, CGRP and Amylin, adrenomedullin (AM) are formed by two separate proteins, a seven transmembrane domain G protein-coupled receptor and a receptor activity modifying protein (RAMP). The calcitonin family and their receptors have a wide range of physiological and pathological functions of which the promotions of tumorigenesis across many different cancer types stand out. For many years, the calcitonin-calcitonin receptor axis has been shown to be important in many malignant diseases. Activation of the calcitonin gene-related peptide and its receptors axis stimulates invasion, angiogenesis, chemoresistance and metastasis in many cancer cell lines including prostate cancer cells. Calcitonin gene-related peptide receptors have been often linked with prostate cancer specifically as the number of cells expressing calcitonin and calcitonin gene-related peptide increases with prostate cancer progression with the bone being the most affected by the associated metastasis. Calcitonin peptide family can promote prostate cancer cell growth via adenylyl cyclase and calcium/phospholipid pathways and can also increase invasion of cells in vitro. Calcitonin peptide is not only upregulated in cancer cells but also promotes angiogenesis in hypoxic conditions and prevents apoptosis whilst also suppressing the immune system thus aggravating the progression of the carcinogenesis and consequent metastasis. Cell migration as a process in tumor metastasis is dependent and regulated by intracellular calcium levels induced by transient receptor potential (TRP) channels. The channels have been found to promote the progression of prostate cancer towards a more aggressive phenotype by stimulating migration and invasion in cells. Most calcitonin peptide family stimulates the TRP voltage 2 channel and indirectly promotes tumor progression and metastasis. Many different neuropeptides including CGRP is expressed in the prostate gland in both autonomic and sensory nerves and in neuroendocrine cells. Neuroendocrine cells are known to differentiate more frequently in prostate cancer compared with many other cancer cells and correlates with tumor progression. It has long been known that CGRP can increase invasion and migration capacity of prostate cancer cells by up to 30-40 % in vitro and that serum levels correlate with prostate cancer progression in human patients. The role of CGRP receptors in promoting prostate cancer and its metastasis to the bone is emerging clearly and rapidly too. The presence of CGRP and its secretory sensory and autonomic neurons in prostate cancer models indicates that secretion of CGRP can also influence the bone microenvironment negatively in this regards. It is thus believed that tumor-associated factors like CGRP can trigger the promotion of pathological sprouting of sensory neurons by increasing nerve growth factor (NGF) expression more particularly within the bone microenvironment. Considering the significant roles played by calcitonin peptide family and more specifically CGRP in aggravating the progression of prostate cancer and its metastasis to bone, CGRP receptor antagonist either as non-peptide small molecules, monoclonal antibodies targeting the CGRP receptor or monoclonal antibodies targeting the CGRP molecule may provide therapeutic interventions of prostate cancer and its associated bone metastasis towards increasing the life expectancy of adult males particularly prostate cancer patients. It is very imperative to increase the debate, discussion and research in this area to further expand the scope of information and existing knowledge towards new drug discoveries and increased chemotherapeutic intervention against prostate cancer and its metastasis, hence this paper.

Biography

Lawrence Aka is a Professor of Veterinary Physiology in St. Matthew's University, Cayman Islands, British West Indies. He had his DVM degree in 1996 from the University of Nigeria, Nsukka. In 2004 and 2010, he obtained his Master of Science and Doctor of Philosophy degrees respectively from the same University. He taught Veterinary Physiology at the University of Nigeria, from 1998-2016. He served as Head of the Department of Veterinary Physiology of same University until his appointment in St. Matthew's University. He also taught Veterinary Physiology, as Visiting Professor, in various Universities including Usmanu Danfodiyo University Sokoto, Nigeria, from 2009-2016, University of Maiduguri, Nigeria, 2012-2014, University of Agriculture Markurdi, 2011-2013 e.t.c. He has supervised and examined several postgraduate projects in veterinary physiology. He has published several in reputable peer review journals. His areas of interest are 1. Hormonal regulation of digestive functions in ruminants and organic manipulation of rumen methane emission. 2. Impacts of environmental residues on animal reproduction. 3. Endocrine disruption and cancer biology. His current focus is on the antineoplastic properties of extracts from tropical plants. He is a recipient of several academic awards including the University of Nigeria faculty best student award at undergraduate and Doctoral levels. He has few research grants to his credit. He has authored several books including "Foundation of Veterinary Physiology" (1st edition, 2004, and 2nd edition, 2014) and others of general interest. He is a member of reputable professional organizations.

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