Biosimilars-2013
OMICS Group Conferences
Accelerating Scientific Discovery
2nd International Conference and Exhibition on
Biowaivers & Biosimilars
September 23-25, 2013 Raleigh, North Carolina, USA

Alpha ENaC-b as a gene therapy in salt-sensitive hypertension

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Abstract

We previously reported the existence of an overly abundant alternatively spliced form of the alpha subunit of the epithelial sodium channel (alpha ENaC) named alpha ENaC-b. Interestingly, the abundance of the alpha ENaC-b salt-sensitive splice variant was significantly higher 4-weeks post high salt diet compared to normal salt diet in Dahl salt-resistant (R) rats [Shehata, 2009]. Alpha ENaC-b was also significantly elevated in Dahl R *versus* Dahl salt-sensitive (S) rats. As much as it is essential to identify the genetic differences between Dahl S and R rats that contribute to the above unique expression pattern of alpha ENaC-b in Dahl R *versus* S rats, it is equally important to expand our understanding of the biological role of the overly abundant alpha ENaC-b splice variant in salt-sensitive hypertension. What we now know about alpha ENaC-b might be used in a potential gene therapy for salt-sensitive hypertension in vivo. To test the role of alpha ENaC-b as a dominant negative regulator of ENaC, we will adopt the antisense approach to silence alpha ENaC-b expression in Dahl R rats. The antisense approach utilizes a short complimentary DNA sequence that inhibits the expression of alpha ENaC-b and thus silences the gene. We anticipate that silencing alpha ENaC-b in Dahl R rats would cause Dahl R rats to be similar to Dahl S rats in their hypertensive response to high salt-diet. In conclusion, the antisense oligonucleotide approach will serve as a test of the role of alpha ENaC-b in increasing blood pressure salt-sensitive subjects.

Biography

Dr. Marlene Shehata has received her PhD in Cellular and Molecular Medicine, specializing in Genetics of Cardiovascular Diseases from the University of Ottawa during the period of 2004-2010. Dr. Shehata is also a licensed Ontario Pharmacist practicing in Southwestern Ontario. Currently, she is working as a Clinical Pharmacist Consultant in numerous academic hospitals, nursing homes and community pharmacies in Southwestern Ontario. She has successfully completed her Administrative responsibilities as a Manager for the Pharmacy and Clinical Services Department. She is currently the Editor-in-Chief of the Journal of Pharmacology Research, Associate Editor for the Journal of Ecobiotechnology and The Journal of Biotechnology Applications. She sits on the editorial boards of numerous journals including the African Journal of Biotechnology and Hypertension-Open Access. Dr. Shehata has authored 23 research articles, 2 book chapters and 24 abstracts. She is a member of the Canadian Hypertension Society, Canadian Cardiovascular Society, Ontario Pharmacists Association and Ontario College of Pharmacists. She is the 2012 recipient of the Commitment to Care and Service Awards winner for Advanced Learning. She is the 2011 recipient of the Certificate of Excellence by Hypertension Canada and the 2007 Horizon Award recipient by Memorial University of Newfoundland. She was awarded numerous other awards including the Pfizer Canada, Canadian Hypertension Society (CHS) and the Canadian Institutes of Health Research (CIHR) Doctoral Research Award in 2005, the Ontario Graduate Scholarship in 2005, Merck Frosst Best Basic Science Presentation Award in 2006 and the Ontario Graduate Scholarship for Science and Technology in 2004 and 2006. Marlene was selected as one out of five Canadian pharmacists' finalists in Diabetes Management: Best Practices in Patient Care 2009 Competition; she was recognized on the "Volunteer Wall" on campus the University of Ottawa for sacrificially giving over 180 hours of volunteer work in 2007 academic year . Her motivation, enthusiasm, and perseverance made her an ideal candidate for receiving the 2008 Have a Heart Bursary by the Canadian Cardiovascular Society.