Kenneth K Wu, J Diabetes Metab 2018, Volume 9
DOI: 10.4172/2155-6156-C2-081

International Conference on
METABOLOMICS AND DIABETOLOGY
May 23-24, 2018 | New York, USA

Cell-specific 5-hydroxytryptophan (5-HTP) metabolism and its relevance to cell function

Kenneth K Wu
China Medical University, Taiwan

5-HTP is derived from L-tryptophan via the catalysis by tryptophan hydroxylase (TPH). It is a common precursor of several bioactive molecules including serotonin (5-hydroxytryptamine), melatonin (N-acetyl-5-methoxytryptamine) and cytoguardin (5-methoxytryptophan). Enzymes catalyzing serotonin and melatonin synthesis are well characterized. In serotonergic neurons, 5-HTP is converted to serotonin by aromatic amino acid decarboxylase (AADC) while its conversion to melatonin in pineal cells is catalyzed sequentially by AADC, alkylamine N-acetyltransferase (AANAT) and N-acetylserotonin methyltransferase (ASMT also known as hydroxyindole O-methyltransferase or *HIOMT*). 5-HTP catabolism in non-neuron, non-pineal cells are less clear. We have shown that human fibroblasts and endothelial cells (EC) possess enzymatic machinery to convert 5-HTP to 5-methoxytryptophan (5-MTP). Neither cell type expresses AADC and hence is unable to synthesize serotonin or melatonin. 5-MTP suppresses pro-inflammatory mediator-induced COX-2 and cytokine expressions and plays a fundamental role in defending against inflammatory tissue damage and tumorigenesis. Thus, there is cell-specific utilization of 5-HTP to generate distinct bioactive metabolites to carry out anti-inflammatory, neurotransmission and circadian rhythm regulatory functions. Our preliminary results show that A549 cancer cells express AADC to convert 5-HTP to serotonin. Metabolomic analysis detected miniscule quantities of 5-MTP or melatonin which is correlated with low level of *HIOMT*. Stable transfection of *HIOMT* reprogrammed 5-HTP catabolism resulting in a switch from serotonin to 5-MTP synthesis. *HIOMT* overexpressed A549 cells had slow growth and low metastasis when compared to vector controls. In contrast with production of CNS bioactive metabolites, i.e. serotonin and melatonin by neurons and pineal cells, peripheral cells such as fibroblasts, EC and epithelial cells convert 5-HTP to 5-MTP to defend against inflammation. Cancer cells have an aberrant transcription program which can be corrected by *HIOMT* gene transfer.

Biography

Kenneth K Wu is Professor Emeritus at University of Texas Health Science Center in Houston, Distinguished Investigator and President emeritus at National Health Research Institutes (NHRI) in Taiwan. He is currently a Distinguished Professor and the Director in the Metabolomics Medicine Research Center at China Medical University (CMU) in Taichung, Taiwan. He also holds Hou Jindui Chair at National Tsing-Hua University in Hsin-Chu, Taiwan and Distinguished Chair Professorship at National Taiwan University in Taipei, Taiwan. His research experiences and expertise are in the areas of hematology, vascular biology and prostaglandin cellular and molecular biology.

kkgo@nhri.org.tw

Notes: