National Institutes of Health workshop: Role of Nutrient Regulation of Signal Transduction in Metabolic Diseases[1,2]

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FOREWORD

Nutritive and nonnutritive dietary constituents can promote or hinder the development of several chronic diseases, including cancer, obesity, inflammatory diseases, diabetes, and cardiovascular diseases. Understanding at the molecular level how dietary constituents influence the outcome of these chronic diseases requires new knowledge, and rapidly advancing research is providing this knowledge base. Specifically, research on signal-transduction pathways has unveiled some of the molecular and cellular events leading to disease development.

Recently, the hypothesis that oxidants may be important mediators in the expression of genes involved in degenerative pathophysiologic states, such as inflammation and cancer, has gained momentum and is now a subject of intense investigation. In particular, nuclear transcription factor κB (NF-κB) and activator protein 1, multisubunit nuclear transcription factors, have been implicated in the expression of a variety of genes in response to oxidants or changes in cellular oxidation-reduction (redox) status. Fatty acids and their metabolites, by functioning as ligands for a family of steroid-like receptors termed peroxisome proliferator-activated receptors (PPARs), were recently found to modulate gene transcription and the differentiation of many cell types. The PPARs interact with other steroid-like receptors (eg, T3) and with retinoid transcription factors to modulate the expression of a wide array of genes, particularly those involved in terminal fat cell differentiation. Long-term regulation of body adiposity is accomplished by the action of hormones, such as leptin and insulin, that are secreted in proportion to fat stores and that act in the brain to reduce food intake and body weight. The obesity protein, leptin, is believed to be an important signal regulating metabolic balance. Defects in leptin signaling (due to mutations in leptin or its receptor or to the ability of brain pathways to respond to the leptin signal) can lead to obesity, diabetes, or both.

Intrigued by the possibilities of such scientific developments and as a result of the increasing number of grant applications being reviewed in this area, the National Institutes of Health Nutrition Study Section organized a workshop on the nutrient regulation of signal transduction in metabolic diseases. The primary objective of the workshop was to overview current research on the nutrient modulation of signaling pathways.

The overview included 4 general areas of signaling pathways. Hwang (1) opened the workshop by reviewing several major receptor-mediated signaling pathways and by identifying targets that may be modulated by nutrients. Aw (2) discussed the redox regulation of gene expression via the activation of transcription factors, such as NF-κB, and summarized the current strategies used in studies of transcription factor activation and nuclear translocation. Clarke (3) covered the function of PPAR, ligand-protein interactions, and the action of other steroid-like and retinoid transcription factors when modified by PPAR. Finally, Billington described how leptin can act within the brain to modify appetite and how leptin may alter the sympathetic nervous system by signaling to fat cells as one route of modifying energy metabolism.

The workshop participants were mainly members of the Nutrition Study Section, staff members at the National Institutes of Health, and representatives from the US Department of Agriculture. The workshop emphasized informal discussion among the speakers and the audience. Because a broad spectrum of subjects are reviewed by the Nutrition Study Section, the workshop served as an educational forum to facilitate the evaluation of grant applications. In addition, the state-of-the art information presented in the workshop should be valuable for the general nutrition research community.

REFERENCES

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