EFFECT OF NUTRIENTS ON THE GENE EXPRESSION:

Nutri-genomics.

INTRODUCTION

REGULATION OF GENE EXPRESSION BY DIETARY FAT

- In addition to its role as an energy source and its effects on membrane lipid composition, dietary fat has profound effects on gene expression, leading to changes in metabolism, growth and cell differentiation.

- The effects of dietary fat on gene expression reflect an adaptive response to changes in the quantity and type of fat ingested.

- **These factors are regulated by**

(*a*) direct binding of fatty acids, fatty acyl–coenzyme A, or oxidized fatty acids

(*b*) oxidized fatty acid regulation of G-protein–linked cell surface receptors and activation of signaling cascades targeting the nucleus

(*c*) oxidized fatty acid regulation of intracellular calcium levels, which affect cell signaling cascades targeting the nucleus.

- At the cellular level, the physiological response to fatty acids will depend on:

(a) the quantity, chemistry, and duration of the fat ingested;
(b) cell-specific fatty acid metabolism (oxidative pathways, kinetics and competing reactions);
(c) cellular abundance of specific nuclear and membrane receptors
(d) involvement of specific transcription factors in gene expression.

- These mechanisms are involved in the control of carbohydrate and lipid metabolism, cell differentiation and growth

Role of PUFA on Gene expression

- Lipogenic enzymes in liver decreased as result of feeding a diet containing 60 % linoleic acid.
- Fatty acids stimulated the expression of adipocyte fatty acid binding protein (ap2) mRNA
- In the 3T3–L1 adipocyte cell line, arachidonic acid (n-6) decreased SCD1 m RNA stability in a dose depedent manner (80% maximum repression), as did linoleic and eicosapentanoic acids.

EFFECT OF PROTEIN ON GENE EXPRESSION

- Protein is very essential for growth, to develop immunity, normal maintenance of body function and structure apart from reproduction and production.

- In many developing countries protein insufficiency is still remains a major and serious problem.

- The function of protein in body is not only at macro level but it also function at gene level.

- A variety or number of genes responds to dietary protein both protein quantity as well as quality influences gene expression.

- Insulin secretion was reduced in individuals which are fed with low protein diet due to reduction in pancreatic β-cell mass lower response of remaining β-cells to nutrients and lowered protein kinase activity (PKA).
- PKA is involved in potentiation of glucose induced insulin secretion by gastrointestinal hormones such as GIP and GLP-1.
- Low protein diet feeding to rats altered the many gene expression, which are responsible for proteins related to insulin biosynthesis, secretion and cellular remodeling.

- Normal insulin secretion is influenced by level of Protein Kinase C (PKC), K+ channel protein, calcium ion (Ca^{2+}) and PKAα.
- Increased ATP to ADP ratio achieved through glucose metabolism, close the K^{+} ATP channel, which leads to depolarization of β-cells.
- Depolarized β-cells opens the voltage dependent Ca^{2+} channels which results in influx of calcium leads to exocytosis of insulin granules.

- Feeding low protein diet also increased expression of PFK in islets results in defective glucose metabolism; it further leads to deceased glucose induced insulin secretion.

- Feeding low protein diet decreases insulin level, it also acts through decreased movement of intracellular calcium.

Influence of Amino Acids

- **The first step of protein translation is the formation of the 43s pre-initiation complex containing methionyl tRNA, eIF2, GTP.**

- **This is followed by the assocoiation of methionyl tRNA and eIF2–GTP that bind to the 40s ribosomal sub unit.**

- **The GTP is hydrolyzed late in the initiation process, and eIF2 is released from the ribosome as an inactive eIF2–GTP complex.**

- **Formation of eIF2 – GTP is mediated by the guanine –nucleotide exchange factor eIF2B.**

- **The mechanism to regulate eIF2B activity may be at the level of the ribosomal protein S6 and eukaroyotic elongation factor 2 (eEF-2) which is phosphorylated in response to many agents, including growth factors and hormones initiation process.**

- **Amino acids regulate protein translation through modulation of eIF2B activity, 4 E –BP phosphorylation and protein S6 phosphorylation.**

EFFECT OF MINERALS ON GENE EXPRESSION

- As similar to other nutrients, mostly minerals are involved in several gene expressions

Effect of Zinc on gene expression.

- Zn is an essential trace element with cofactor functions in a large number of proteins of intermediary metabolism, hormone secretion pathways and immune defense mechanism.

- **Zn is involved in regulation of small intestinal, thymus and hepatocytes gene expression.**

- **MTF-I (Metal Responsive element Factor- I) is a Zn dependent transcriptional activator regulates metallothionein I and II through MRE.**

- **Zn dependent KLF4 transcription factor is involved in protein preparation of HT-29 cells.**

- **The other protein have Zn in it as constituents are ATP synathase, cytochrome c, a, NADP dehydrogenase I and II regulated by Zn.**

- Deficiency of one or more mineral in diet lead to impaired body functions.

- Such as Iron, Iodine, Selenium deficiency or excess of heavy metal ions.

Example: Anaemia

EFFECT OF VITAMINS ON GENE EXPRESSION

- **Vitamins are micronutrients needed in very small quantity and are involved in gene expression.**
- **Vit A is involved in gene expression of PEPCK (Phospho Enol Pyruvate Kinase), IGF 9insulin like growth factor).**
- **Biotin is involved in various essential proteins (enzymes) synthesis at gene level.**
- **Vitamin C is involved in hepatic gene expression.**

Vitamin A and PEPCK gene expression

- PEPCK is vitamin A dependent enzyme.
- PEPCK is involved in conversion of oxaloacetate to phospho-enol-pyruvate, one of the important steps in gluconeogenesis.
- Vitamin A deficiency condition leads to changes in chromosomal structure of RARE (Retinoic Acid Responsive Element), which further leads to change in co regulator binding and activity.

- The above discussed role of various nutrients on gene expression is occurring normally in body.

- For any type of study in biological system is not complete until studied up to gene level.

- To exploit full genetic potential, its needs lots of nutrients to function at gene level

Other Factors Related to Nutrigenomics:

- **Nutrition and Diet**
- **Nutritional Status (deficiency or excess)**
- **Nutritional Behaviour (preference or rejection of any food)**

- **Demographic Nutritional changes**
- **Area Specific Deficiencies**
- **Environmental Factors (Tropical or Temperate)**

CONCLUSION:

- Nutritional genomics technologies can be integrated with data bases of genomic sequences, inter individual genetic variability, and disease susceptibility etc.

- By this knowledge we can elucidate the role of nutrients on hypertension, cancer, cardiovascular and other life threatening diseases.

Future Prospects

- Will it then be possible from nutrigenomics research to develop food products that can prevent or reduce onset and impact of complex diseases and some forms of cancers?

- Can food products be tailored to promote the health and well-being of groups in the population identified on the basis of their individual genomes?