NUTRIGENOMICS

by

W. Jean Dodds, DVM
Hemopet/Hemolife
PET FOODS AND DIAGNOSTICS OF THE “NEAR” FUTURE

Key Point

“Wholesome nutrition is the key to a healthy immune system and resistance to disease.”
Deficiencies/Imbalances & Chemical/Drug/Toxin Exposure

- Continual immunological challenge
- Suppress immune function, especially genetically susceptible (immune deficiency, autoimmunity, allergies)
Nutrition & Immune Function

- zinc, selenium & vitamin E, vitamin B₆ (pyridoxine), linoleic acid.
- deficiency impairs both humoral and cell-mediated immunity
- requirement for essential nutrients increases during rapid growth/reproduction
- may increase in aging, as immune function & nutrient bioavailability wanes
The Gut-Skin Connection

- diet = potent mechanism to alter cellular environment
- especially in GI tract (intestinal biosis and dysbiosis)
- supports metabolism and vital functions of skin
Food Sensitivity & Intolerance

- diet long recognized cause of hypersensitivity-like skin reactions in dogs, cats, people
- Type I hypersensitivity well-documented
- Types III & IV suspected
- immediate (within mins-hrs) and delayed (hrs - days)
Food Sensitivity & Intolerance (cont’d)

- delayed sensitivities 2-72 hrs after eating; difficult to connect symptoms with foods
- high correlation of delayed sensitivity with amount and frequency of food eaten
Food Sensitivity & Intolerance (cont’d)

- primary food allergens: corn, wheat, soy, beef, eggs, milk
- secondary food allergens: lamb, rabbit, venison, buffalo, chicken, turkey, barley, millet, oatmeal, salmon, white fish, rice, quinoa, potatoes, peanut butter
Food Sensitivity & Intolerance (cont’d)

- 3rd most common after flea bite sensitivity and atopy
- 1-10% of all allergic skin disease
- no age, breed, sex predilection
- most affected animals eating offending foods for > 2 years
Food Sensitivity & Intolerance (cont’d)

- mimics other skin syndromes
- major complaints: pruritis
- pruritic bilateral otitis externa
- secondary seborrhea, pyoderma
Management & Therapy

- create healthy acid-base balance through optimal nutrition
- diet elimination trials for 3-6 weeks; often poor compliance
- must be individualized; use nutrigenomic principles
- avoid additives & supplements; avoid switching from diet-diet
1-15% have concurrent GI tract issues

some peripheral lymphadenopathy, especially cats

tension-fatigue, malaise, dullness

non-seasonal and poor response to steroids
Nutrigenomics

- emerging science that studies the molecular relationships between nutrition and the response of genes in promoting health
- different diets alter gene expression, and protein/metabolite production
- specific nutrients affect body responses in a form defined as a “signature”
- individual response = “molecular dietary signature”
Nutrigenomics (cont’d)

- Signature of a particular nutrient can vary between individuals according to their DNA.
- Nutrigenomics identifies the food for an individual according to the molecular dietary signature of that individual.
- Individualized diets proven for liver cleansing, arthritis, obesity.
Nutrigenomics (cont’d)

- genetic differences lead to quantitative variations in dietary needs for energy/nutrients to maintain health
- genetic defects may result in inborn errors of metabolism that affect one or more pathways involving nutrients or their metabolites
- wide variation in energy needs of dogs depending on their breed, age, sex, and size
NUTRIGENOMICS --
THE SCIENCE

by

W. JEAN DODDS, D V M

BRUNO STEFANON, Ph D
The science of nutrigenomics seeks to provide a molecular understanding for how common dietary ingredients (i.e. nutrition) affect health by altering the expression and/or structure of an individual’s genetic makeup.
5 Basic Concepts of Nutrigenomics

- diet can be a serious risk factor for a number of diseases
- common dietary ingredients act on animal genome directly/indirectly, to alter gene expression/structure
- degree of dietary influence on balance of healthy and disease states depends on individual's genetic makeup
5 Basic Concepts of Nutrigenomics (cont’d)

- certain diet-regulated genes play a role in onset, incidence, progression, and/or severity of chronic diseases
- dietary intervention based on animal’s nutritional requirement/status plus genotype used to prevent, mitigate or cure chronic disease
Nutrigenetics

- Genetic variations among individuals
- Clinical response to a specific nutrient
The simplest form of DNA variation among individuals is the substitution of one single nucleotide for another.
SNP Properties

- 50% of SNPs are in the molecular regions not relevant for changes in cell bioactivities
- 25% lead to missense mutations; they change cell bioactivities
- 25% are silent mutations; they do not change cell bioactivities
Retrospective:
- Applied Science
- Individual Response to diet

Prospective:
- Discovery Science
- Nutritional Systems

MOLECULAR NUTRITION

Nutrigenetics (Polymorphisms)

Nutrigenomics (Gene Expression)
DIET

NUTRIENT

METABOLISM

(\textit{B})

GENE EXPRESSION

SIGNAL TRANSDUCTION

(NORMAL CELL GROWTH)
Nutrient Compounds

DNA
- gene regulation, SNPs
- transcriptional control
- histone interaction

RNA
- transcriptional control
- processing, stability
- transport of RNA

PROTEIN
- receptor interaction
- gene control, signal transduction
- enzyme regulation
- inhibition modification
- transport regulation
- channel or pump interaction

METABOLITE
- several functions

Effect on Health and Production
Multifactorial Chronic/Age-Related Diseases

- Cardiovascular Disease
- Metabolic Syndrome
- Cancer
- Hypertension
- Diabetes
Marker of Oxidative Stress

(Stefanon et al., 2000)
Limitations of the SNP approach

- Studies to date not always conclusive
- Response of extracts includes dozens of genes, with multiple SNPs
- Variability of extract response is affected by:
  - genotypic–environmental factor interaction
  - breeds
  - inheritance patterns in extract response
  - genetic variance response to medicine
What is the Alternative?

MDS
Molecular Dietary Signature
Dog
Heat Map
Dog
Liver Cleansing
MDS
Molecular Dietary Signature
Methodological Issues in Nutrigenomics

The high-throughput screening (HTS) era
From: http://www.accessexcellence.org
Dietary Diagnostics

Food Sensitivity -- Prior Testing

- typically based on IgE, IgG 4 and immune complexes with complement
- high sensitivity but lower individual specificity
- measures more immediate-type reactions
Dietary Diagnostics

Food Sensitivity -- Newer Testing -- ● ● ● 1, 2, 3

- newer tests can use serum, saliva or feces
- ELISA or other immunoassay platforms
- identify IgG, IgA, or immune complexes to foods in serum
- IgA or IgM antibodies to foods in saliva
- antibodies to foods appear in saliva before GI tract clinical/biopsy diagnosis of IBD or “leaky gut syndrome”
- saliva testing can thus reveal the latent or pre-clinical form of food sensitivity
Food Sensitivity
-- Future Testing

Three Levels of Testing ...Testing • • • 1, 2, 3

❖ Saliva Screening Kit --- POS owner/ vet clinic testing; 65 % of market, several times annually for life

❖ Tests for salivary IgA and IgM reactants in healthy pets and those with known or suspected food intolerances

❖ Client obtains test kit [from vet or pet supply store], follows directions, adds saliva, seals kit, sends to diagnostic laboratory
Food Sensitivity -- Future Testing

Three Levels of Testing

- Serum Screening Kit -- vet and laboratory serum testing; 30% of market, several times in pet’s life
- For those dogs reacting to saliva test, client goes to veterinarian, blood drawn and serum sent to diagnostic laboratory
Food Sensitivity

-- Future Testing

Three Levels of Testing

- DNA/RNA Microarray “Heat Map” -- vet and laboratory heat map genetic testing; 5-10% of market, a few times in pet’s life (identifies pets needing individualized nutrigenomic foods)

- For individual dogs with significant reactants in saliva/serum testing

- DNA/RNA Microarray “Heat Map” performed to identify which specific nutrients, botanicals or micronutrients needed to cleanse and “cure” the food intolerances
Conclusion

Nutritional efficacy is subject to both external and internal variability

- NUTRIGENOMICS: Effect of bioactive compounds on nutrition and gene expression and the resulting change in physiology
- NUTRIGENETICS: genetic variation, interindividual differences in response, with implication towards susceptible subgroups in the population
Trends and Technologies in Nutrition Science

(Gillies and Faha, 2003)

- Geographic epidemiology
- Identify and document
- Nutripharmacology
- Bioanalytical profiling
- Health claims
- Molecular nutrition
- Biomarkers
- Home test kits
- Internet dieticians
- DNA-nutrient databases
- Molecular epidemiology
- Biotech foods
- Food as primary prevention
- Food-drug complexes

Consumer insight surveys forecast 33% of consumers may collect and act on nutrigenomics by 2010.