No Bones About It!

COMBINING NUTRIGENOMICS WITH THE CULINARY ARTS IN THE PREVENTION AND TREATMENT OF OSTEOPOROSIS

Susan Allen-Evenson, RDN, LDN, CCN: Functional Nutrition
Amanda Archibald, RDN: Nutrigenomics, Culinary Genomics
Highly recognized Functional Nutrition expert, Susan Allen-Evenson incorporates an overall focus on the Integrative and Functional Medicine approach in her work as a speaker, mentor, author and nutrition consultant. In addition to her own private practice, she was involved in one of the first nationally-based Integrative Medicine clinics and consulted for the development of a major hospital system’s Integrative Medicine Center in Chicago, IL. Ms. Allen has held board appointments with The International and American Association of Clinical Nutritionists, the Academy of Nutrition and Dietetics’ sub-specialty group: Dietitian’s in Integrative and Functional Medicine (DIFM), and on the Nutrition Board of the Institute for Functional Medicine (IFM).

In her more than two decades of practice, Susan has recognized the growing divide between traditional dietetics training and the emerging trends in Integrative and Functional Medicine. With her passion for educating and understanding many clinicians are missing a key opportunity; she originated a unique, first of its kind, international training initiative to provide advanced training in the nutritional aspects of this specialty. Considered an authority, she has appeared on numerous radio and television programs, has been invited to speak at many professional conferences, has been quoted extensively in the press, and is also a published author. She was Chief Nutritional Consultant for the Reader’s Digest book; Food Cures: Breakthrough Nutritional Prescriptions for Everything from Colds to Cancer and she was a contributing author to the first college textbook of its kind, Integrating Therapeutic and Complementary Nutrition. Ms. Allen has also authored a chapter in AAPI’s Nutrition Guide To Optimal Health: Using Principles of Functional Medicine and Nutritional Genomics – Part 2.

Although her professional training program keeps her very busy, Susan continues to enjoy a thriving private practice specializing in Integrative and Functional Medical Nutrition Therapy (IFMNT), where she also consults with healthcare professionals on their most challenging cases.
Amanda Archibald RDN

Amanda’s unique training as an analyst and a nutritionist (RDN), combined with her culinary expertise, has enabled her to develop a new lens through which we can understand the food and health conversation. Amanda’s trailblazing work is redefining the food, nutrition and cooking education footprint in ways that are understandable, meaningful and fundamentally achievable for all Americans. Her cutting-edge work in Culinary Genomics, unveiled in 2015 in South Africa (Translational Nutrigenomics) and at the Institute for Functional Medicine AIC (2015), has created a new frontier uniting the fields of Genomic Medicine with the Culinary Arts. Through this work, Amanda is placing food, clinicians and chefs and the kitchen at the epicenter of healing, igniting a new food and nutrition conversation for the world. Her work has been showcased in more than 30 states, over 100 U.S. cities, and in 7 countries. Amanda is currently working with a global foodservice management company to build genomic principles onto the patient and retail menu for a Southern California hospital system. In its preliminary phase, this work received a culinary award in 2016, for its innovation in healthcare.

Amanda is the founder of The Genomic Kitchen, a system of choosing, preparing and understanding food based on culinary genomics, a term she coined to express this revolutionary merging of genomic science (nutrigenomics) and the culinary arts. Widely recognized for her trailblazing work as a culinary nutritionist and dietitian, Amanda has a longstanding commitment to redefining the food, nutrition and cooking education footprint in ways that make them understandable, meaningful and fundamentally achievable for all.
No Bones About it!
Combining Nutrigenomics with the Culinary Arts in the Prevention and treatment of Osteoporosis

• The presenters have no conflicts of Interest
• This session is being recorded. Limited-time access will be shared tomorrow (NLFN Gold/Platinum members get extended access)
• CPE cert and slides are available in your control panel
Agenda –
Susan Allen-Evenson, RDN, LDN, CCN

• Prevalence of bone disease

• Opportunity for Integrative and Functional Healthcare professionals to work at a deeper, more targeted and effective level

• Review of bone metabolism and factors affecting bone health

• Identify Genomic factors influencing and biomarkers to monitor both bone formation and degradation
World-wide Statistics

• ~30% of women and 20% of men over 50 suffer from osteoporosis or osteoporotic fractures.
• Worldwide, osteoporosis causes >8.9 million fractures annually, resulting in an osteoporotic fracture every 3 seconds.
• Osteoporosis is estimated to affect 200 million women worldwide.
• Osteoporotic fractures are not only associated with increased mortality in both sexes, but are also responsible for about 1% of the worldwide disability caused by prevalent noncommunicable diseases.

NHANES: 10.2 million adults (8.2/women and 2.0/men) had osteoporosis and 43.4 million (27.3/women and 16.1/men) had low bone mass in 2010.

Health Care Providers Have a Golden Opportunity!

• The Functional Medicine model goes under the diagnosis to look at the root causes, or the set of circumstances that allows the progression of ill health to move into a disease state.

• Deeper assessment, food as medicine, and dietary supplements as indicated, are our valuable tools.

• The genomic assessment provides a missing piece to deeper understanding that we can now harness.
Systems Biology

Institute for Functional Medicine - The Functional Medicine tree
Genomics/Epigenetics

• Modification of DNA can influence biochemical and metabolic pathways
  – Single Nucleotide Polymorphisms (SNPs) represent disease risk

• Epigenetics: changes in organisms caused by modification of gene expression rather than alteration of the genetic code itself (e.g. environmental, stress, drugs/pharmaceuticals, diet, endotoxins).

Nutritional Genomics, or Nutrigenomics

- Study of gene-nutrient interactions; how foods affect our genes and how individual genetic differences can affect the way we respond to nutrients in the foods we eat
- Allows for personalized medicine and health, based upon an understanding of our nutritional needs, nutritional and health status, and our genotype
- New specialty – “Culinary Genomics”
  - Using food constituents/bioactives to mitigate the effects of gene SNPs

Bone Health

• Should be considered throughout all stages of women’s life (not just menopause) and for men too!

• General Considerations:
  – Genetics/Genomics
  – Hormone balance
  – Diet/ Nutritional status
  – Exercise
  – Oxidative stress
  – Inflammation
  – Medication interactions/effects
Drugs that may contribute to or exacerbate osteoporosis

- Aluminum-containing antacids
- Antiseizure medicines (only some) such as Dilantin® or Phenobarbital
- Aromatase inhibitors such as Arimidex®, Aromasin® and Femara®
- Cancer chemotherapeutic drugs
- Cyclosporine A and FK506 (Tacrolimus)
- Gonadotropin releasing hormone (GnRH) such as Lupron® and Zoladex®
- Heparin
- Lithium
- Medroxyprogesterone acetate for contraception (Depo-Provera®)
- Methotrexate
- Proton pump inhibitors (PPIs) such as Nexium®, Prevacid® and Prilosec®
- Selective serotonin reuptake inhibitors (SSRIs) such as Lexapro®, Prozac® and Zoloft®
- Steroids (glucocorticoids) such as cortisone and prednisone
- Tamoxifen® (premenopausal use)
- Thiazolidinediones (‘glitazones’ for DM2) such as Actos® and Avandia®
- Thyroid hormones in excess
Bone Metabolism Review

• Bone resorption: removing of mature bone tissues from the skeleton via osteoclast cells

• Bone remodeling - the formation of new bone matrix via the process of ossification (osteogenesis) by osteoblast calls

• Bone health is homeostasis between these two

• The imbalance between bone formation and bone resorption leads to changes in bone mass. Osteoporosis is more resorption vs remodeling
Inflammation and Bone Health

- Bone loss is due to the effects of inflammation, poor nutrition, oxidative stress, hormone balance, decreased lean body mass, hypothyroid, sedentary life and the effects of medications
- Chronic inflammatory diseases of almost any cause are associated with bone loss
  - Increase bone resorption (increased osteoclast activity)
  - Decrease bone formation (reduced osteoblast activity)

Oxidative Stress and Bone Health

• Oxidative stress may play a role by enhancing bone resorption
  – Increases bone-matrix degrading matrix metalloproteinases (MMPs)

• Example: Environmental pollution with cadmium and/or polychlorinated biphenyls (PCBs) are involved in the development of Osteoporosis

Estrogen and Bone Health

• Plays a fundamental role in skeletal growth and homeostasis.

• Estrogen deficiency is the major factor in the pathogenesis of postmenopausal osteoporosis.

• With less estrogen, other factors become that much more important to identify and address.

General Intervention/Support

• Supportive diet and optimal nutritional status (via diet or dietary supplements), especially bone building nutrients
  – Calcium, magnesium, other minerals
  – Vitamins D & K2 (MK-7), etc
  – Collagen supporting and sulfur containing amino acids
• Weight bearing exercise
• Monitor drug effects and drug-nutrient interactions
• Maintain optimal pH balance
• Avoid/reduce or counter oxidative stress
• Minimize inflammation
SOMETIMES IT'S JUST NOT ENOUGH.
Genomics & Osteoporosis Risk

• Bone Formation SNPs
  – COL1A1
  – GSTT1
  – GSTM1
  – MTHFR
  – IGF-1
  – BMP4
  – LRP5
  – GSTT1

• Inflammation SNPs
  – IL-6/6R
  – CRP
  – TNF-alpha
  – APOE

• Bone Resorption SNPs
  – CYP1A2
  – MTHFR
  – BMP2
  – SOST
  – GSTM1

• Calciotropic and Sex Hormone SNPs
  • PTH/PTHR
  • CT/CTR
  • AR
  • CYP19A1
  • CaSR
  • GR

• Other
  • BCMO1?
SNPs – Important to Know!

Expand your clinical toolbox:

• Identify your patient’s SNPs that are actionable through diet & lifestyle modifications
• Look for signs, symptoms, and biomarkers that show evidence of SNP expression
• Polygenic vs Monogenic: It’s not just about one SNP alone but how SNPs act together
• Apply appropriate intervention
• Monitor accordingly
COL1A1 (collagen type I alpha)

- Gene encodes for instructions for making part of a large molecule called type I collagen
  - most abundant form of collagen in the human body
  - major protein of bone matrix
- SNP: associated with decreased bone mass and osteoporotic fractures by reducing bone mineral density
- Smoking, low-protein diet/status and low calcium intake may negatively influence

GSTT1 & GSTM1
(Glutathione S-Transferase theta 1 & Mu 1)

• A member of a superfamily of proteins that catalyze the conjugation of reduced glutathione
  – Detoxification of a broad range of toxic substances (like Estrogen!)

• Genetic polymorphisms can result in reduced enzyme activity due to the null phenotype of the GSTM1 and GSTT1
  – More prevalent in Caucasians

• Absence of gene, and therefore reduced enzymatic activity, is associated with decreased bone mineral density
  – Affects both formation and remodeling and indirectly increases oxidative stress

• Increased oxidative stress may negatively influence

• Encodes for the protein that supports methylation by catalyzing the conversion of 5,10-methylenetetrahydrofolate to 5-methyltetrahydrofolate, a co-substrate for homocysteine remethylation to methionine.

• MTHFR SNP associated with hyperhomocysteinemia, in some studies correlated with low BMD and Osteoporotic fracture

• Global methylation patterns of genes may also be directly associated with BMD in postmenopausal women
  – Major signaling pathways in osteoblasts affected by DNA methylation
  – DNA methylation affects osteoclast activity as well

Methylation and Sclerostin

• As a self-balancing mechanism, when necessary, Osteocytes produce the protein Sclerostin, which inhibits bone formation

• When bone density falls, our body normally counteracts this by inhibiting the expression of the Sclerostin-producing gene (SOST gene)
  – Inhibition achieved with increased methylation on the promoter region of the gene

• Proper methylation required to support SOST inhibition

SNPs for VITAMIN D
At Risk for Deficiency

• Absorption issues
  • Low fat diets/malabsorption
  • Older individuals
  • Celiac or other mucosal damage issues
  • Taking supplements without fat-containing food

• Vit D receptor issues and SNPs for Vit D metabolism
Vitamin D Metabolism Review

DHCR7
(7-Dehydrocholesterol Reductase)

• DHCR7 encodes 7-dehydrocholesterol reductase, which converts 7-dehydrocholesterol to cholesterol, thereby reducing availability for vitamin D synthesis in the skin.

• Decreased enzyme activity = less vitamin D from sun
  – Increases risk for lower bone mineral density, osteoporosis and fractures.

Kuan V, Martineau A, Griffiths C, Hyppönen E and Walton R. DHCR7 mutations linked to higher vitamin D status allowed early human migration to Northern latitudes. BMC Evolutionary Biology 2013;13:144
CYP2R1
(Cytochrome P450 family 2 subfamily R member 1)

• Member of the cytochrome P450 superfamily of enzymes that converts vitamin D into the active ligand for the vitamin D receptor.

• SNP is associated with decreased enzymatic function, increased risk of vitamin D deficiency and therefore higher risk of Osteoporosis

GC (Vitamin D binding protein)

- Encodes for the major carrier protein of 25-hydroxyvitamin D in circulation (GC-globulin)
  - Linked with alterations in bone density
  - Roles in 1) maintaining stable levels during times of decreased 25(OH) availability and 2) in regulating delivery of 25(OH) D to target tissues
  - Role in inflammatory response and bone development independent of vitamin D as well.
VDR BsmI and VDR FokI (Vitamin D Receptors)

- The VDR gene encodes for the vitamin D receptor; variants have been reported to influence bone mineral density
- VDR BsmI (rs1544410): SNP in the VDR associated with increased risk of low BMD (especially in women).
- VDR FokI (rs2228570): SNP in the VDR related with osteoporosis risk
- Other potentially relevant receptor SNPs: Cdx2, Apal, EcoRV and TaqI

**Other SNPs Related to Vit D**

- **CYP24A1**: Regulates the level of vitamin D
  - Therefore, plays a role in calcium homeostasis and the vitamin D endocrine system
- **CYP27A1**: Might be responsible for the conversion of vitamin D to 25(OH)D3
- **CYP27B1**: Regulates the level of biologically active vitamin D and plays an important role in calcium homeostasis

Vitamin D 25-OH Lab Limited

• D3 depends on lab values (not season!)
  – Off supplements for 1 week prior
  – Labs drawn fasting

• Lab may be normal but conversion to active may be suboptimal with SNP affecting kidney conversion
  – Check 1,25 OH

• Lab may be normal but utilization suboptimal with receptor SNPs.
  – Look at alternative markers and associated signs/symptoms
Bone Formation: Monitor Labs, especially as you see risk in SNPS

- Bone mineral density
- Collagen cross-linking markers
- Vitamin D (25-OH & 1,25-OH)
- Magnesium RBC
- Vitamin A
- Homocysteine
- Folate
- Vitamin B12/MMA
- Hormones/related markers
- PTH/calcitonin
- Phosphorus
Collagen Cross-linking Markers

• In post-menopausal women, the markers that have been studied the most and also have the strongest negative correlations with BMD are:
  – Alkaline phosphatase (ALP)
  – Carboxylated Osteocalcin (OC) – for K2 status
  – Type 1 cross-linked C-telopeptide (CTx)
  – Type 1 cross-linked N-telopeptide (NTx)

• Mostly used in research and perhaps more in functional medicine (may not be covered well by insurances)

1. Collagen Crosslinks and Biochemical Markers of Bone Turnover. UnitedHealthcare Commercial Medical Policy Effective 03/01/2017 PDF
Bone Formation: Supplement Support

- Vitamin D3
- Calcium
- Magnesium
- Hydroxyapatite
- Choline-stabilized orthosilica
- Strontium
- Boron
- MSM, SAMe
- Good-quality multi vitamin-mineral supplying: Vit C, A, E, Cu, Zn, and Mn
  - Additional antioxidants as needed
- K2 (as MK 7) – often needed in higher amt than what occurs in many supplements
More on Vitamin D/K2 Supplementation

• If any gut problems of malabsorption, dysbiosis, hx gall bladder removal – may be best to use an emulsified form of D so not dependent on adequate bile and absorption chemistry

• Be sure Calcium fasting blood level is not high before giving higher dose D

• Consider Vit K2 status & supplement K2-7

• Vit D and Vit A can use some same receptor sites – monitor both if supplementing D
The Role of K2 in Building Bone and Preventing Bone Loss

Vitamin D (inactive form) → Vitamin D3 (active form) → Stimulation by D3 → Osteoblast cells – bone building cells → Glu-osteocalcin (inactive form) → Calcium → Gla-osteocalcin (active form) → Release of osteocalcin → Vitamin K2-7

Calcium → Adding calcium and building bone → Breakdown of bone

Vitamin K2-7

Antioxidant Support

- Vitamins: A, C, and E
- Minerals: zinc and Selenomethionine (active selenium)
- Green tea extract
- Milk thistle
- Flavanoids
- Lipoic acid
- NAC/Reduced Glutathione
- CoQ 10 (Ubiquinol if NQ01 SNP)
Bone Formation
Diet and Lifestyle

• Adequate dietary protein intake
  – especially containing proline and glycine (collagen forming amino acids) and sulfur containing amino acids (methionine and cysteine)

• Ensure adequate intake of foods rich in folate, vit B6 & 12, silica, antioxidants, and bone building nutrients like Ca, Mg, vit D, K2-7, boron, etc

• Reduce Oxidative stress: smoking and other toxins

• Get regular (not excessive) exposure to sun – mind the DHCR7 SNP

• Exercise on a regular basis with strength/resistance training
Bone Resorption
CYP1A2
(Cytochrome P450 1A2)

• CYP1A2 is a member of the cytochrome P450 superfamily of enzymes, involved in the metabolism of xenobiotics/caffeine.

• Related to low bone mineral density with caffeine intake.
  – Fast metabolizers may have an effect based on an increased concentration of caffeine metabolites (men in the literature, more then women)
  – Slow metabolizers may have an effect through increased concentration of caffeine itself.

• Addressed earlier: A member of a superfamily of proteins that catalyze the conjugation of reduced glutathione.
  – Involved in the detoxification of a broad range of toxic substances.
• Absence of gene and therefore enzymatic activity associated with decreased bone mineral density.
  – Affects both formation and remodeling.
• May counter benefits of Nrf2 pathway
  – Compounded by TNF-a

MTHFR: Methylenetetrahydrofolate reductase

- Addressed earlier: Encodes for the protein that supports methylation by catalyzing the conversion of 5,10-methylenetetrahydrofolate to 5-methyltetrahydrofolate
- A relationship exists between DNA methylation and level of transcription of genes highly associated with BMD
Receptor activator of nuclear factor-kB ligand (RANKL) is a key mediator of osteoclast differentiation, promoting the activation and survival of bone-resorbing cells.

For bone homeostasis, RANKL can be opposed by osteoprotegerin (OPG), which blocks RANKL from stimulating osteoclast formation and activation.

Increased DNA methylation in the RANKL transcriptional start site is associated with epigenetic silencing of RANKL.

Supporting DNA methylation capability may help to regulate RANKL expression and modulate bone resorption.

Methylation Influences RANKL and Sclerostin

ApoE4 associated with reduced fat soluble vitamin absorption

ApoE2 is genetic risk factor for low trabecular bone mass and vertebral fractures.

- May have impaired lipoprotein-associated vitamin K delivery affecting osteoblasts, via a lower degree of carboxylation of osteoblast-derived gla-proteins (carboxylated osteocalcin) which in turn contributes to a higher bone turnover and development of a lower trabecular bone mass.

More Inflammation SNPs
Gene encodes a cytokine that functions in inflammation and the maturation of B cells and plays a central role in inflammatory response.

IL-6 stimulates the development of osteoclasts and thereby the process of bone resorption, it is likely to be a pathogenic factor in bone loss, especially that triggered by estrogen deficiency.

- SNP (GG Genotype) associated with decreased bone density

IL6R associated with increased C-reactive protein and inflammation

CRP (C-Reactive Protein)

- C-reactive protein (CRP), a marker of inflammation and a hallmark of the acute-phase response, has been observed in immune and inflammatory diseases.
- Higher CRP concentration in premenopausal women was found to significantly correlate with decreases in BMD.
- SNPs on CRP can influence plasma levels of CRP or
  
  - Note: SNP on rs1205 can lower CRP and consequently mask an inflammatory status - look for other markers and symptoms of inflammation

Gene encodes for tumor necrosis factor alpha, a pro-inflammatory cytokine.

Induces ROS production that activates NF-κB

- There is a strong consensus that TNFα and RANKL can act synergistically to induce osteoclastogenesis

Specifically, NF-κB controls the differentiation/activity of the main skeletal cell types – osteoclasts, osteoblasts, osteocytes and chondrocytes. Activation increases inflammation - negatively affects bone health

NF-κB (Nuclear Factor-κB)

• Encodes this protein complex that controls DNA transcription, cytokine production, and cell survival

• NF-κB activation has been associated with
  – Low-grade inflammation
  – Accumulation of reactive oxygen species

• Inappropriate activation of NF-κB enhances RANKL-mediated osteoclastogenesis and bone resorption and may also inhibit bone formation by osteoblasts

Monitor Labs, especially as you see risk in SNPS

• Inflammation Markers
  – IL-6
  – TNF-a
  – Additional cytokines - look at balance between pro and anti-inflammatory (IL 4, IL 10 etc)
  – hsCRP and other acute phase reactants (Ferritin, Albumin, etc)
  – Sed rate (ESR)
  – EFA balance
Other SNPs Related to Bone Health

Calciotropic and sex hormones and their receptors

• Parathyroid hormone (PTH) and PTH receptor (PTHR).
  – Calcium homeostasis, endogenous vitamin D synthesis and regulation of bone cells activity.

• Calcitonin (CT) and its receptor (CTR).
  – Increases osteoblast activity, retains calcium in bones and prevents phosphorus and calcium loss.

• Aromatase (CYP19A1).
  – Catalyzes androgens conversion to estrogens.
Other SNPs Related to Bone Health

Calciotropic and sex hormones and their receptors

• Androgen receptor (AR).
  – Regulates osteoblast function and suppresses action on bone resorption.

• Calcium-sensing receptor (CaSR).
  – Regulates calcium homeostasis at parathyroid, kidney, bowel and bone level.

• Glucocorticoid receptor (GR).
  – Inhibition of bone formation, suppression of calcium absorption.
Other SNPs Related to Bone Health

Growth factors and local regulators
- Insulin-like growth factor 1 (IGF-I).
  - Stimulates bone formation, recruits pre-osteoblasts, growth factor for osteoblasts.
- Bone morphogenetic protein 4 (BMP4).
  - Involved in bone and cartilage development and in fracture repair.
- Bone morphogenetic protein 2 (BMP2).
  - Stimulates the differentiation and/or activity of osteoclasts.

Miscellaneous
- Low-density lipoprotein receptor-related protein 5 (LRP5).
  - Regulates osteoblasts proliferation and bone formation.
- Sclerostin (SOST).
  - Potent osteocyte expressed negative regulator of bone formation in vitro.

General Intervention/Support & To Quiet SNP Expression

• Supportive/varied diet and optimal nutritional status, especially bone building nutrients
  • 8-12 srvgs fruit/veggies a day (all colors of rainbow!)
  • Keep insulin in check
  • Keep processed foods to a minimum
  • Assure good protein balance and amino acid status
  • Avoid excessive caffeine intake, especially if CYP1A2 SNP
  • Stay hydrated

• Identify and reduce inflammation from all sources
  • Gut health/Microbiome diversity
  • Diet
    – Balance fatty acid intake
Anti-inflammatory Supplements
(Many cross over for oxidative stress!)

• EPA/DHA
• Curcumin
• Quercetin
• Ginger
• Alpha-lipoic acid
• Resveratrol
General Intervention/Support & To Quiet SNP Expression

• Reduce Oxidative stress
  • Monitor/Reduce heavy metals/toxic burden
  • Remember oil quality/cooking methods
• Exercise, but not too much
• Maintain optimal pH balance
• Maintain optimal Microbiome
• Monitor drug effects and drug-nutrient interactions
• Get enough good quality sleep
• Balance work/play – stress management
• Experience joy and gratitude everyday
And to get more targeted....
Agenda

• Definitions

• Culinary Genomics: the art of translating biochemistry to the plate: example: oxidative stress

• Applying Culinary Genomics to Bone Formation SNPs

• Applying Culinary Genomics to Bone Resorption SNPs

• Case Study: Polygenic thinking and applied culinary genomics
Definitions

- **Nutrigenomics**: sometimes called nutritional genomics, investigates how nutrients and bioactive compounds in the food we eat interact with our genes to affect our health.

- **Culinary Genomics**: uniting the science of genomics with the knowledge of the kitchen. Preparing & serving specific nutrient rich foods to trigger specific genes on/off and promote overall health. Or *Cooking the Language of our DNA*.
The application of the culinary arts to the science of genomics... yields a new food conversation
Culinary Significance

- Nutrigenomics elevates the importance of food for our innate biochemistry
- Culinary genomics showcases the power, relevance and potential of the kitchen
Culinary Genomics requires an implicit understanding of the following:

- How genes function
- Which ingredients contain bioactives that can trigger genes into action, or turn them off
- Which nutrients are needed to support the functionality of the proteins that our genes produce
- How to cook with these ingredients!
CULINARY GENOMICS EXAMPLE: OXIDATIVE STRESS
Painting biochemistry on the plate

1. **Bioactives + Gene NrF2** \(\textit{plus}\) target nutrient cofactors (vitamins and minerals) = successfully reduced oxidative stress

2. Bioactives + Gene NrF2 \(\textit{minus}\) nutrient cofactors = unmitigated oxidative stress via endogenous enzymes
Putting biochemistry on the plate

**Bioactives + Gene NrF2** = Superoxide Dismutase (SOD), Catalase (CAT) and Glutathione Peroxidase (GPX)

**SOD, CAT and GPX** + selenium, copper, manganese, iron and zinc

**Oxidative stress mitigation** = **bioactives + NrF2** = (SOD + CAT + GPX + se + cu + mn+ zn +fe) + (Exogenous antioxidants)
Culinary Genomics creates recipes from biochemistry for biochemistry.
Recipe Formulation Considerations

- Genes / SNPs + their impact
- Prioritization of culinary intervention based on level of impact on critical biochemical pathways
- Recipe formulation utilizing bioactives and supporting nutrients
- Knowledge of impact of heat (turmeric = example)
- Outcomes measurement and adjustment of intervention
Culinary innovation & translation just got more real...
Culinary Genomics in action.
Genomic specific: 
Bone Formation

- Bone formation SNPs, including Vitamin D SNPs
- Oxidative stress SNPs

- Ca, Mg, Vitamin D rich foods
- Mineral-rich
- Add fermented foods
- Cruciferous vegetables
- Alliums/quercetin-rich foods

Polygenic thinking drives culinary solutions
Food-Gene Cross Talk

Bone Formation

......100 foot painting of assorted biochemistry for the plate
Build an ingredient matrix specific to SNPs in relevant Biochemical Pathways.
Build an ingredient matrix

Vitamin D is not found abundantly in a wide variety of foods. Food supplies vitamin D in a form that must be converted to its 1,25-(OH)2D3 form.

Sword Fish, salmon, trout, mackerel, eel, tuna fish, whitefish, sardines

SEAFOOD

VITAMIN D

Fortified Products check label

Dairy products, orange juice, cereals

Other

Cod liver oil

Egg yolk

Mushrooms

Best = raw Shitake, Maitake Chanterelle, Morel
Build an ingredient matrix specific to SNPs in relevant Biochemical Pathways.
Culinary thought informed by science
Genomic specific: Bone Resorption

- Bone Resorption SNPs
- Methylation SNPs
- Inflammation SNPs

Vitamin D rich foods (induce)  
Crucifers (induce)  
(Cumin/turmeric/grapefruit inhibit)

Vitamin B complex rich foods, choline, betaine

Upregulate NrF2  
/downregulate TNF-alpha/NfkB cascade +  
Omega-3 FA
The **methylation cycle** is dependent on many cofactors including B vitamins and amino acids. Critical nutrient drivers of the cycle are B2, B6, B12, folate, magnesium, zinc, methionine, betaine, choline. This roadmap illustrates foods which, when combined, provide a rich source of both of these key nutrients. **NOTE:** Animal proteins are the richest source of Methionine. All other food groups are poor sources of methionine. Best plant sources are Brazil nuts, sesame seeds, seaweed (spirulina).
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<td>Downregulate TNF-alpha/NfkB: Quercetin/curcumin</td>
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Upregulate NrF2: Offset oxidative stress
TNF-alpha: widespread implications
Tamp down TNF-alpha & NF-κB
TARGET FOODS
TNF-Alpha & INFLAMMATION MANAGEMENT

Omega-3 FA

Vegetables
- Alliums
  - Radishes & Leeks
  - Fennel
  - Kale
  - Sweet Potatoes
- Ample
- Berries
- Chickpeas

Quercetin-Rich Foods

Fruit
- Lovage, dill, cilantro, scorp
- Capers

Herbs

Other

Animal
- Grass-raised/wild
- Herring, mackerel, oysters, sardines, salmon, tuna

Seafood

Plant
- Avocados, olives, chia, flax, pumpkin, sunflower seeds, Brazil nuts, walnuts

Curcumin
- Turmeric

Whole Soy
- Rosemary

Mediterranean Herbs

Clove

Ginger

Pomegranate

Revered

Epigallocatechin gallate

Other

Thyme, sage, oregano

Other

Root
Case Studies
Female, age 52

Ht 62”/Wt 125#

Med Hx: Lap Chole, Tubal Ligation, 2 x breast abcess

Family Hx: mother – bilateral hip replacement, curvature of spine

Activity level: high but not excessive. Road-mountain cycling/yoga/hike

Diet: healthy and varied. Lots of vegetables, adequate protein intake (includes fish and animal protein), healthy fats, fermented foods

Caffeine: 1 cup coffee/day, 2 teas

Alcohol: avg 1 glass of wine/day

Meds: none

Supplements: Woman over 50, Omega 3, D3/K2, DIM, Ubiquinol, Calcium: 900 mg/d (in supplements). Diet: avg 500mg/d
Polygenic Assessment and Application
Bone Formation & Resorption

High Impact
- VDR FokI
- VDR Taq1
- IL 10

Moderate Impact
- DHCR7
- GC
- GSTT1
- CRP
- IL-6
- IL-6R
- MTHFR-1
Polygenic Assessment and Applications

Beyond Bone: looking deeper under the hood

- NQ01 (Inflammation/estrogen metabolism)
- FUT2 (folate/HCY)
- TCN2 (folate/HCY)
- CβS (folate/HCY)
- COMT
- SOD2
- GPx
- HMOX1
- NRF2L2
Genomics Was Key!

• Genomic results showed potential risk
• With family history, dictated a closer look at lab biomarkers
  • Dexa
  • Blood
<table>
<thead>
<tr>
<th>Location</th>
<th>BMD (g/cm²)</th>
<th>T-score</th>
<th>Z-score</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>L1-L4</strong></td>
<td>0.814</td>
<td>-3.1 STD</td>
<td>-2.3 STD</td>
</tr>
<tr>
<td><strong>Right Femoral Neck</strong></td>
<td>0.847</td>
<td>-1.4 STD</td>
<td>-0.3 STD</td>
</tr>
<tr>
<td><strong>Left Femoral neck</strong></td>
<td>0.924</td>
<td>-0.8 STD</td>
<td>0.2 STD</td>
</tr>
<tr>
<td><strong>Right Femur Total</strong></td>
<td>0.903</td>
<td>-0.8 STD</td>
<td>-0.1 STD</td>
</tr>
<tr>
<td><strong>Left Femur Total</strong></td>
<td>0.895</td>
<td>-0.9 STD</td>
<td>-0.2 STD</td>
</tr>
</tbody>
</table>

**DEXA Results:**

**Osteopenia-Osteoporosis**
Bloodwork

- B12: 613 pg/mL (180-914 pg/mL)
- Folate: >20 ng/mL (>5.9 ng/mL)
- Vit B6 (P5P): 342.6 nmol/L (20.0  125.0 nmol/L)
- Plasma Homocysteine: 7 umol/L (5-15 umol/L)
- hsCRP: 1.303 mg/L (0.000 – 3.000 mg/L)
- Vit D 25-OH: 33 ng/mL (13 – 62 ng/mL)
- Vit D 1,25-OH: 61.4 pg/mL (19.9 – 79.3 pg/mL)

- Other markers earmarked for future testing...
  - Osteocalcin
  - IL-6
  - TNF-a
  - Collagen cross-linking markers
  - C-telopeptide
  - EFA testing
Genomic Informed Culinary Intervention

- Preventive Inflammation management
  - CRP
  - IL-6
  - IL-6R
  - SOD2
  - GPx
  - HMOX1
  - NRF2L2
  - + Omega-3 foods

- Optimizing bone metabolism
  - Fermented Foods
  - D-rich + mineral rich

- Strength regimen
Knowledge of how biochemical pathways work, drives selection of ingredients and recipe/menu formulation
Culinary Translation
Female, age 55

<table>
<thead>
<tr>
<th>Ht 65”/Wt 130#</th>
</tr>
</thead>
<tbody>
<tr>
<td>Med Hx: IBS (since childhood), Diverticulosis, Raynaud's, Frequent Sinusitis, Thyroid nodules, Osteopenia (Spine) – BMD: 9% loss 2010 to 2013.</td>
</tr>
<tr>
<td>Family Hx:Cancer, CVD, Thyroiditis, Osteopenia (paternal)</td>
</tr>
<tr>
<td>Activity level: 3x/week, varied and included wt bearing.</td>
</tr>
<tr>
<td>Diet: Varied, avoids lactose, focuses on calcium rich foods. Eats modified FODMAPS, consumes coffee.</td>
</tr>
<tr>
<td>Sun exposure – seasonal and with travel. Always wears sunscreen</td>
</tr>
<tr>
<td>Alcohol: 2 glasses wine/wk</td>
</tr>
<tr>
<td>Meds: none</td>
</tr>
<tr>
<td>Supplements: Woman over 50, Omega 3</td>
</tr>
</tbody>
</table>
## DEXA Results – Spine

### Before Intervention

<table>
<thead>
<tr>
<th>Yr</th>
<th>BMD</th>
<th>T score</th>
<th>Z score</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>1.015</td>
<td>-0.3</td>
<td></td>
</tr>
<tr>
<td>2013</td>
<td>0.919</td>
<td>-1.2</td>
<td>-0.2</td>
</tr>
</tbody>
</table>

(9.5% loss)
Previous Bloodwork

2015
• T Pro, albumin – functionally low
• CRP – WNL
• Folate - elevated
• Vit D 34 – WNL (no intervention needed?)
• Monos – elevated (inflammation)

2016
• Mag RBC - fxn low
• 1,25 OH Vit D – WNL
• Phos – WNL
Polygenic Assessment

High Impact
- COL1A1
- CYP2R1
- DHCR7
- CG
- GSTT1
- IL6
- FUT2

Moderate
- VDR Bsml
- VDR FokI
- CRP
- Cyp1A2
- MTFHR-1/2
- SLC19A1
- Gpx
Intervention

- Add Vitamin D, 2000mg qd
- Add Calcium Citrate, 250 mg qd
- Add Vitamin K2 (MK7), 160 mg bid
- Add Magnesium citrate 150 mg bid
- Add Curcumin/Boswellia combo qd
- Add beta-sitosterol (address IL-6/optional)
- Add spore-based Probiotic
- Protein at every meal
- Off coffee
- No dairy, focus on other calcium rich food sources
- Focus on antioxidant, magnesium, and K2 foods
- Anti-inflammatory diet
- Address source of inflammation – GUT/SIBO confirmed!
Current Bloodwork

- C-Telopeptide – WML
- Calcitonin WNL
- Osteocalcin – WNL
- Protein and calcium – WNL
- Monos – WNL
- Mag – WNL
- 25 OH – 97 (forgot to go off supplement)
- Folate – WNL
- Still need IL6
<table>
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<tr>
<td>2010</td>
<td>1.015</td>
<td>-0.3</td>
<td></td>
</tr>
<tr>
<td>2013</td>
<td>.919</td>
<td>(9.5% loss)</td>
<td>-1.2</td>
</tr>
<tr>
<td>2016</td>
<td>.897</td>
<td>(only 3% loss)</td>
<td>-1.4</td>
</tr>
</tbody>
</table>
Culinary Intervention
Goals

• Support anti-inflammatory protocol (multiple SNPs)
• Optimize dietary folate/methylation cycle
• Optimize protein intake/sources
• Magnesium
• Gut support as tolerated
FOODS THAT MAY DEPLETE NUTRIENTS AND IMPACT METABOLISM

- Caffeine
- Sugar
- Some Medications

All Vegetables
- Onion, sweet potato, "Sea vegetables" most alkaline
- Lemons, limes, raspberry, pineapple, tangerine, watermelon: most alkaline
- Pumpkin seed, cashew: most alkaline
- Lentils most alkaline

Fruit

Nuts & Seeds

Legumes

BUILDING HEALTH BONES

ALKALIZING FOODS

- All Vegetables
- Fruit
- Nuts & Seeds
- Legumes

BROTHS

MAKE A NUTRIENT-RICH BONE OR VEGETABLE BROTH

BUILDING HEALTH BONES

BASIC GUIDANCE

VITAMINS

- Vitamin C
- Vitamin D
- Vitamin D Roadmap
- Vitamin K1
- Green Vegetables
- Fermented foods Ripe cheese, Yogurt, Kefir, Natto, Sauerkraut
- Organ Meats
- Vitamin K2

MINERALS

- Calcium
- Magnesium

OPTIMIZE GUT FUNCTION

- Cultured Foods
- Fermented Foods
- Foods rich in prebiotics
- See Roadmaps

MAKE A NUTRIENT-RICH BONE OR VEGETABLE BROTH

THE GENOMIC KITCHEN

- Kale, Collards
- See Fermented Foods Roadmap
- Microflora 101
- Optimizing G.I. Health
- Health Value of Fermented Foods
SAMPLE CULINARY BLUEPRINT FOR OXIDATIVE STRESS MANAGEMENT
VIA Nrf2 ACTIVATION bioactives + co-factors

- GRAINS
  - Oats

- LEGUMES
  - Garbanzo beans, lentils

- FRUIT
  - Apples, blackberries, elderberries, pineapple, pink grapefruit, (cooked) tomatoes, watermelon

- HERBS
  - Cilantro, dill, lovage

- SPICES
  - Turmeric

- ANIMAL PROTEIN
  - Turkey, Lamb

- SEAFOOD
  - Shrimp, Scallop

- VEGETABLES
  - Alliums, asparagus, chard, cruciferous vegetables (raw optimal), fennel, radishes and their leaves

- NUTS AND SEEDS
  - Walnuts, flax, pumpkin, sesame

- FUNGHI
  - Cremini, shiitake
Support methylation
Pumpkin, sesame, hemp, sunflower, chia, flax, poppy
Nuts and seeds maintain their potency from raw to prepared state.

Brazil nuts, almonds, pine, walnuts (English walnuts), hazelnuts, chestnuts (Japanese), macadamia, pistachio, pecans, cashews

Sun-dried tomatoes, artichokes, wasabi root, kale, okra
cooked

Swiss chard, spinach, beet greens, purslane, red and white skin potatoes, kale, acorn squash, green peas, butternut squash, sweet potato, collards

Mollusks, salmon, mackerel, pollock, tuna, crab, herring, sardines, lobster,
Sea Vegetables: seaweed spirulina (dried)

BEF: Beef, poultry, pork, game meats are not the richest sources of magnesium when compared to other food groups.

NUTS & SEEDS

LEGENUMES

Peanuts (raw and roasted), Cowpeas (catjang), soybeans, yellow, black, white, pink, mungo, lentils, lupins, navy, adzuki, great northern, cranberry (roman), pinto

Grains

Buckwheat, wheat bran/germ, oats, rye, triticale, wheat, corn, millet, brown rice/wild rice, sorghum, amaranth; quinoa, teff, barley, bulgur

Herbs & Spices

Celery seed, fennel seed, cumin seed, mustard seed, fenugreek seed, ground turmeric, anise seed, dried basil, chili powder, coriander seed, curry powder, dill seed, ground ginger, paprika, savory, ground turmeric,

VEGETABLES

Cooked

Seafood

Seavegetables: seaweed spirulina (dried)

ANIMAL

Fruit

Other

The Genomic Kitchen

**Bold** denotes sources > 200 mg/1 cup svg. **Blue** denotes sources > 100 mg/1 cup svg
Black (not bold) denotes >50 mg/1 cup svg. Herbs & Spices: Sources provide <10 mg per svg
Sources of food rich in CALCIUM and MAGNESIUM

- Sea Vegetables
  - Hijiki, kelp, kombu, nori, wakame

- Seafood
  - Sardines, salmon, bluefish, halibut, mackerel

- Animal
  - Chicken
  - Ground Beef
  - Eggs

- Dairy
  - Yogurt
  - Milk
  - Cheese

- Vegetables
  - Kale, collards, cabbage, spinach, parsley, turnip greens, watercress

- Grains
  - Amaranth, quinoa, brown rice

- Legumes
  - Garbanzo, black, pinto,

- Nuts & Seeds
  - Almonds, hazelnuts, Brazil, sunflower, pistachio, sesame, walnuts
Supportive References: Culinary Genomics

• The Nrf2-Antioxidant Response Element Signaling Pathway and Its Activation by Oxidative Stress: J Biol Chem. 2009 May 15; 284(20): 13291–13295

• Omega-3 fatty acids protect the brain against ischemic injury by activating Nrf2 and upregulating heme oxygenase 1. J Neurosci. 2014 Jan 29;34(5):1903-15

• The cytoprotective role of the Keap1-Nrf2 pathway. Arch Toxicol. 2011;85:241–272

• Crosstalk of reactive oxygen species and NF-κB signaling: Cell Research (2011) 21:103-115

• The Nuclear Factor NF-κB Pathway in Inflammation: Cold Spring Harb Perspect Biol. 2009 Dec; 1(6)

• Downregulation of tumor necrosis factor and other proinflammatory biomarkers by polyphenols: Archives of Biochemistry and Biophysics 559 (2014) 91–99

• Bioactive Nutrients and Nutrigenomics in Age-Related Diseases. Molecules. 2017 Jan 8;22(1).

• Carotenoids, inflammation and oxidative stress - implications in cellular signaling pathways: Nutrition Research · November 2014

• Omega-3 Fatty Acids and Inflammatory Processes: Nutrients 2010, 2, 355-374

Genomic Testing: What to Look For...

- Evaluate Genomic Testing Companies
  - Are SNPs relevant, modifiable, measurable
    - Do specialty panels fit clinical needs
  - Are reports and interpretation user-friendly
    - Name/show biochemical pathways for SNP relevance and interplay (polygenic versus monogenic)
  - Provide evidenced-based recommendations
  - Listing of biomarkers to monitor SNP expression
- Clinical Lab or Research Lab
  - Want more than just raw data
  - Clinical/educational support provided
Concluding Remarks

• Genomic information is one tool among many in the clinician toolbox
• Genomic information provides informed insights into the individual health blueprint and deep insights into prioritizing health intervention
• Polygenic versus monogenic approach requires an understanding of the multiple nutrients and compounds that inform our innate biochemistry
• Biochemistry informs culinary intervention
Concluding Remarks

• Deep level assessment, and corresponding nutritionally-focused intervention, represent the pinnacle of a personalized approach to patient care and ensure better outcomes.

• Additional learning is recommended. Further still, Medical practitioners and their patients can benefit from the services of a Dietitian/Nutritionist who is comprehensively trained in Integrative and Functional Medical Nutrition Therapy (IFMNT), genomics/nutrigenomics and culinary genomic application!

Thank you to genomics experts, Dr Joe Veltman PhD, DCCM, FAAIM and Dr Roberta Kline MD, FACOG, for all their guidance and expertise.
Additional Resources

• The “Genomic Resources” research group: http://www.genomic-resources.eus/
• Human Ageing Genomic Resources: http://genomics.senescence.info/
• Genomia International – Education/Training:
  https://genomainternational.com/clinician-training-certification/
• SNPedia: https://www.snpedia.com/
• International Osteoporosis Foundation: https://www.iofbonehealth.org/facts-statistics#category-14
Thank You!

This webinar was recorded - Limited time access is available to all registrants starting tomorrow.
Announcements

• IFMNT Spring training starts April 24!
• NLFN members get 10% off! (get in on NLFN Spring membership special savings now!)
• Spring Special (Through April 17 ONLY):
  Use code: S18 to receive an additional 10% off! (Yes, both discounts apply)
• Visit: https://www.nextlevelfunctionalnutrition.com/