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NUTRIGENOMIX® CONTACT:
info@nutrigenomix.com

NUTRIGENOMIX®

PERSONALIZED NUTRITION FOR SKIN & HEALTH REPORT

Hello Caroline:

Nutrigenomix is pleased to provide you with your Personalized Nutrition for Skin & Health Report based on your individual genetic profile. This report was developed based on scientific research published in peer-reviewed journals and reviewed by our team of experts in nutrigenomics.

Our laboratory has used state-of-the-art genetic testing procedures to analyze your DNA to determine how your genes can influence your skin's ability to combat the signs of aging, and how your body metabolizes nutrients that support skin health. Based on these results, we have determined your propensity to develop signs of skin aging and provided nutrition recommendations aligned with your genetic profile. In addition, we have analyzed genes to determine recommendations related to antioxidant & inflammatory response, sensitivities & intolerances, bone & muscle health, weight management & body composition, glycemic management, and cardiovascular health, and gathered additional genetic insights for you and your healthcare provider to consider as part of a comprehensive approach to support your skin care goals and overall wellness.

You and your healthcare provider can now use the information contained in this report to help you create a personalized skin care protocol. As new discoveries in the fields of nutrigenomics and dermatology are made, you will have the opportunity to access this information to further fine-tune your personalized skin health plan.

The Nutrigenomix Team

The Science Behind Nutrigenomix

One man's food is another man's poison – Lucretius

Nutrition is one of the most important lifestyle factors affecting your risk for developing certain diseases and has a significant impact on overall well-being. Over the past decade, there has been growing recognition of the importance of how genes influence our nutritional status, which directly impacts our health. The human genome consists of about 25,000 genes and virtually all can exist in different forms. The variations in our genes make us unique from one another. Genetic variation determines not only the color of our eyes and hair, but how we metabolize and utilize the foods, nutrients and supplements we ingest. Nutrigenomics is the science that applies genomic information and advanced technologies to uncover the relationship between genes, nutrition and human health. The term nutrigenomics refers to both the study of how the food, beverages and supplements we consume affects our genes and how our genes can influence our body's response to what we consume.

Different versions of a gene can make us respond differently to certain components in food such as the lactose in milk, the gluten in bread, the caffeine in coffee, along with carbohydrates, fats, proteins vitamins and minerals found in various foods. We are all familiar with people who are lactose intolerant or cannot eat gluten. These differences between individuals can be explained by gene variations within the population. Through science and research we have learned that genetic variations in the population and between individuals affect a wide variety of responses to key components of the human diet. For instance, some individuals may benefit from limiting their consumption of caffeine or increasing their intake of omega-3 fat, while others can follow the general recommendation for either or both. Your best diet depends on the specific variants you have for these nutrient-related genes. Understanding your genetic profile and its implications on your unique response to the foods, supplements and beverages you consume will provide you with the tools needed to make the best dietary choices.

The science of how specific genes change how we respond to dietary components enables us to use nutrition to its fullest potential to prevent, manage or improve various health issues. These personalized diets can optimize an individual's nutritional status and empower them to focus on preventing diet-related diseases or conditions. A healthy, balanced diet should provide enough energy and nutrients to support optimal health, reduce the risk of disease and maintain a healthy body weight. While general dietary recommendations might be prudent to follow, the one-size-fits-all approach to nutritional advice could limit some individuals from reaching their full potential for health and wellness. By tailoring one's nutritional needs to their genetic profile, the benefits of nutrition on health status can be maximized.

Ahmed El-Sohemy, PhD
Chief Scientific Officer

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Summary of Results

Skin Physiology and Metabolism

Trait	Gene, rs Number	Gene Function	Risk Variant	Your Variant	Your Risk	Recommendations / Implications
Facial Pigmented Spots p. 10	IRF4, rs12203592	IRF4 is involved in melanin synthesis	TC or TT	CC	Typical	Typical risk of age-related facial pigmented spots.
Loss of Elasticity p. 11	MMP1, rs1799750	MMP1 is involved in collagen degradation	GG	GG	Elevated	Elevated collagen breakdown.
Choline p. 12	MTHFD1, rs2236225	MTHFD1 & PEMT involved in metabolism of choline	Algorithm	GG	Elevated	Meet the Adequate Intake (AI) level for choline daily.
	PEMT, rs12325817			CG		
Folate p. 13	MTHFR, rs1801133	MTHFR impacts dietary folate utilization	CT or TT	TT	Elevated	Meet the RDA for folate daily.
Iron Overload p. 14	SLC17A1, rs17342717	SLC17A1 & HFE regulate the uptake and metabolism of iron	Algorithm	CC	Low	Follow the recommendations provided in the Low Iron Status section.
	HFE, rs1800562			GG		
	HFE, rs1799945			CC		
Low Iron Status p. 15	TMPRSS6, rs4820268	TMPRSS6, TFR2 & TF influence the uptake and transport of iron	Algorithm	GA	Elevated	Meet the RDA for iron and consume sources of vitamin C with iron-rich foods.
	TFR2, rs7385804			CA		
	TF, rs3811647			AA		
Zinc p. 16	SLC30A3, rs11126936	SLC30A3 is a zinc transporter	CC	CC	Elevated	Focus on consuming bioavailable sources of zinc.
Vitamin B_{12} p. 17	FUT2, rs601338	FUT2 regulates circulating levels of vitamin B12	GG or GA	GA	Elevated	Focus on consuming bioavailable sources of vitamin B12.
Vitamin D p. 18	CYP2R1, rs10741657	CYP2R1 & GC regulate circulating levels of vitamin D	Algorithm	GA	Elevated	Consume 1000 IU (25 mcg) vitamin D daily.
	GC, rs2282679			GG		

Bone and Muscle Health

Trait	Gene, rs Number	Gene Function	Risk/ Response Variant	Your Variant	Your Risk/ Response	Recommendations / Implications
Vitamin D p. 18	CYP2R1, rs10741657	CYP2R1 & GC regulate circulating levels of vitamin D	Algorithm	GA	Elevated	Consume 1000 IU (25 mcg) vitamin D daily.
	GC, rs2282679			GG		
Calcium p. 19	GC, rs7041	GC impacts transport and uptake of calcium	Algorithm	TG	Elevated	Consume 1200 mg of calcium daily.
	GC, rs4588			CA		
Bone Mass p. 20	WNT16, rs2707466	WNT16 mediates signaling for bone density	TC or CC	TC	Elevated	You have an elevated risk for low bone mass.
Soft Tissue Integrity p. 21	COL5A1, rs12722	COL5A1 impacts the repair of connective tissue	CT or TT	CC	Typical	You have a typical risk for soft tissue injury.
Muscle Damage p. 22	ACTN3, rs1815739	ACTN3 impacts fast twitch muscle fibre repair	TC or TT	CC	Typical	Meet general guidelines for warming up and cooling down.
Pain Perception p. 23	COMT, rs4680	COMT is involved in pathways that process pain signals	GG or GA	GA	Enhanced	You have an enhanced pain tolerance and therefore tend to experience less pain.
Power and Strength p. 24	ACTN3, rs1815739	ACTN3 impacts fast twitch muscle fibre repair	TC or CC	CC	Ultra	You have a genetic advantage to excel in power sports.
Endurance p. 25	NFIA-AS2, rs1572312	ADRB3, NRF2, GSTP1, NFIA-AS2 & PGC1a impact endurance abilities	Algorithm	CC	Typical	Your endurance potential is typical.
	ADRB3, rs4994			TT		
	NRF2, rs12594956			CA		
	GSTP1, rs1695			AG		
	PGC1a, rs8192678			AA		

1in5

People with Risk Variant

Your Results

Gene	Marker
IRF4	rs12203592
Risk Variant	**Your Variant**
TC or TT	CC

Your Risk

Typical

Implications

Since you possess the CC variant of the IRF4 gene, you have a typical risk of developing facial pigmented spots. The best way to prevent the formation of pigmented spots is to practice sun safety by minimizing UV ray exposure and using sunscreen. Some topical treatments containing vitamin C and vitamin E have been shown to brighten skin pigmentation. In addition, daily moderate consumption of some foods including almonds, apples and mangoes has been shown to reduce the signs of photoaging.

Typical risk of age-related facial pigmented spots.

Facial Pigmented Spots

Dark pigmented spots on the face and other skin areas are a common sign of aging. Pigmented spots, also known as solar lentigines, result from cumulative skin exposure to UV rays. Cells within the skin produce melanin, a pigment that acts as a natural sunscreen upon UV ray exposure. Over time, melanin build-up within skin cells can result in the dark pigmented spots characteristic of aging. Research shows that variation in the Interferon Regulatory Factor 4 (IRF4) gene is associated with facial pigmented spots. Individuals who carry the T variant of the IRF4 gene have a greater percentage of their facial skin covered by pigmented spots than those who do not carry this genetic variant.* Both topical application and oral intake of rich sources of vitamin C and E have been shown to brighten skin and reduce the signs of photo-aging.**, ***, ****

*Jacobs LC et al. A Genome-Wide Association Study Identifies the Skin Color Genes IRF4, MC1R, ASIP, and BNC2 Influencing Facial Pigmented Spots. Journal of Investigative Dermatology. 2015;135:1735–1742.
**Rattanawiwatpong, Pattarawan et al. "Anti-aging and brightening effects of a topical treatment containing vitamin C, vitamin E, and raspberry leaf cell culture extract: A split-face, randomized controlled trial." Journal of cosmetic dermatology vol. 19,3 (2020): 671-676.
***Rybak, Iryna et al. "Prospective Randomized Controlled Trial on the Effects of Almonds on Facial Wrinkles and Pigmentation." Nutrients vol. 13,3 785. 27 Feb. 2021
****Shoji, Toshihiko et al. "Administration of Apple Polyphenol Supplements for Skin Conditions in Healthy Women: A Randomized, Double-Blind, Placebo-Controlled Clinical Trial." Nutrients vol. 12,4 1071. 13 Apr. 2020

IRF4

The IRF4 gene affects the activity of an enzyme involved in melanin synthesis. Variation within this gene has been linked to skin, hair and eye colour, and even hair graying.* A large study showed that individuals who carry the T variant of the IRF4 gene have a greater percentage of their facial skin covered by pigmented spots than those who do not. This effect is observed consistently, regardless of the person's skin tone.

*Adhikari K et al. Genome-wide association scan in admixed Latin Americans identifies loci influencing facial and scalp hair features. Nature Communications. 2016; 7:10815.

Foods that may reduce signs of Photoaging

Almonds	Walnuts
Pomegranate	Grapes
Apple	Mango

Refer to the vitamin C and E sections for your DNA-based recommendations.

Loss of Elasticity

As skin ages, it loses its inherent elasticity. The resulting stiffness affects the skin's architecture, contributing to the appearance of fine lines and wrinkles. Collagen is a protein produced by skin cells which plays a role in the elasticity characteristic of youthful skin, but its production and turnover decreases as we age. Furthermore, damage from exposure to UV rays also decreases elasticity. This is partly mediated by enzymes called matrix metalloproteinases (MMPs) that break down and alter the structure of collagen and other connective tissue molecules. The presence of MMPs increases after UV ray exposure. Research shows that genetic variation in MMP1 is associated with increased enzyme activity, which results in more collagen breakdown.* This may lead to premature loss of skin elasticity and more wrinkling. A combination of foods containing nutrients such as collagen peptides, vitamin C, zinc, biotin, and vitamin E have been shown to improve skin elasticity.**

*Quan T et al. Matrix-degrading metalloproteinases in photoaging. Journal of Investigative Dermatology Symposium Proceedings. 2009;14(1):20-4.
**Bolke, Liane et al. "A Collagen Supplement Improves Skin Hydration, Elasticity, Roughness, and Density: Results of a Randomized, Placebo-Controlled, Blind Study." Nutrients vol. 11,10 2494. 17 Oct. 2019

MMP1

MMP1 encodes an enzyme that carries out a significant proportion of skin collagen degradation upon exposure to UV rays. Some individuals carry two extra copies of the G variant, which leads to increased production of the resulting MMP1 enzyme. This, in turn, results in a higher level of collagen breakdown.* Individuals who carry two G variants may experience a greater loss of elasticity over time, and they may be particularly vulnerable to the skin-aging effects of UV rays.

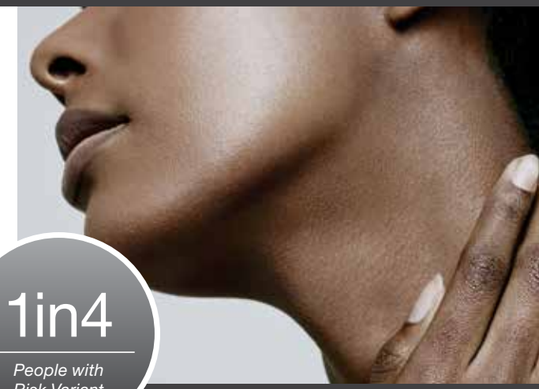
*Rutter JT et al. A single nucleotide polymorphism in the matrix metalloproteinase-1 promoter creates an Ets binding site and augments transcription. Cancer Res. 1998;58(23):5321–5325.

Foods that may improve Skin Elasticity

Aloe vera	Eggs
Avocados	Red bell peppers
Broccoli	Sardines
Citrus fruits	Strawberries
Edamame	Salmon

Sources: Canadian Nutrient File and USDA Database

Refer to the vitamin C and E sections for your DNA-based recommendations.



1in4

People with Risk Variant

Your Results

Gene	Marker
MMP1	rs1799750
Risk Variant	**Your Variant**
GG	GG

Your Risk

Elevated

Implications

Since you possess two copies of the MMP1 G variant, you produce more MMP1 enzyme and your rate of collagen breakdown is higher than average. Therefore, you are at a higher risk of premature loss of skin elasticity, especially if you are exposed to UV rays regularly. To slow down this loss of elasticity and better manage wrinkles and fine lines, reduce your exposure to UV rays and practice sun safety by wearing sunscreen or protective clothing, and avoiding tanning beds. In addition, collagen peptides, vitamin C, zinc, biotin, and vitamin E rich foods have been shown to improve skin elasticity. You can include these foods in your diet; sardines, aloe vera, broccoli, berries, chicken bone-broth, citrus fruits, peppers, eggs, beans, whole grains, avocados and fish.

Elevated collagen breakdown.

1in5

People with Risk Variant

Your Results

Gene	Marker
ADORA2A	rs5751876

Risk Variant	Your Variant
TT	CT

Your Risk

Typical

Recommendation

Since you possess the CT or CC variant of the ADORA2A gene, you have a typical risk for an increase in feelings of anxiety after caffeine consumption. Aim to follow your DNA-based caffeine intake recommendations for the CYP1A2 gene included in your report.

Follow the recommendations provided by the CYP1A2 gene section of this report.

Caffeine

Anxiety

Many commonly consumed foods and beverages, such as coffee, tea, soft drinks and chocolate, as well as functional beverages such as energy drinks, contain caffeine. There are also hidden sources of caffeine found in pain medications, weight loss supplements, as well as chocolate or coffee-flavored beverages and food products. Caffeine is widely used to promote wakefulness and vigilance, reduce sleepiness and mitigate fatigue related to various shift-work occupations or travel across time zones. In the brain, the effects of caffeine are primarily due to its blocking action of adenosine, a neuromodulator that increases drowsiness and builds up over the day as bedtime approaches. Despite its widespread use, caffeine may cause anxiety in some people. A common variation in the ADORA2A gene contributes to the differences in subjective feelings of anxiety after caffeine ingestion,* especially in those who are habitually low caffeine consumers.**

*Childs E eta al. Association between ADORA2A and DRD2 polymorphisms and caffeine-induced anxiety. Neuropsychopharmacology. 2008 Nov;33(12):2791-800
**Rogers PJ, et al. Association of the anxiogenic and alerting effects of caffeine with ADORA2A and ADORA1 polymorphisms and habitual level of caffeine consumption. Neuropsychopharmacology. 2010. (9):1973–1983.

ADORA2A

The ADORA2A (adenosine A2A receptor) gene encodes one of the main receptors for adenosine. Adenosine has many functions in the body, including promoting sleep and calmness and suppressing arousal. Caffeine blocks adenosine receptors, resulting in the stimulating effects of coffee, tea, chocolate and other caffeinated food products and supplements. Individuals who possess the TT variant of the ADORA2A gene are more sensitive to the stimulating effects of caffeine and experience greater increases in feelings of anxiety after caffeine intake than do individuals with either the CT or CC variant.

Cardiovascular Health

Caffeine is the most widely consumed stimulant in the world and coffee is the most significant source of caffeine, with tea, soda and chocolate also contributing to intakes. Research has shown that caffeine can influence cardiovascular health. However, the reported effects of coffee on the cardiovascular system have been inconsistent and at times have appeared contradictory. Some studies reported a link between high coffee consumption and an elevated risk of high blood pressure and heart disease, while other studies have shown no effect or even a protective effect with moderate intake. Two landmark studies*,** have now shown that the effect of coffee on cardiovascular disease depends on a variation in a gene called CYP1A2.

*Cornelis et al. Coffee, CYP1A2 genotype, and risk of myocardial infarction. Journal of the American Medical Association. 2006;295:1135-41.
**Palatini P et al. CYP1A2 genotype modifies the association between coffee intake and the risk of hypertension. Journal of Hypertension. 2009;27:1594-1601.

CYP1A2

The CYP1A2 gene produces an enzyme called cytochrome P450 1A2 (CYP1A2), which is the main enzyme responsible for breaking down caffeine in the body. Variations in the CYP1A2 gene affect the rate at which caffeine is broken down, which determines the impact of caffeine on heart health. Individuals who possess the GA or AA variant of CYP1A2 break down caffeine more slowly and are at greater risk of high blood pressure and heart attack when caffeine intake is high. Those who have the GG variant actually have a lower risk of heart disease with moderate coffee consumption than those who consume no coffee at all.

Sources of Caffeine

	Amount (mg)
Coffee (1 cup)	100
Energy drinks (1 cup)	80
Espresso (1 shot)	85
Black tea (1 cup)	50
Green tea (1 cup)	45
Cola (1 can)	26
Chocolate, dark (40g)	27
Decaf coffee, espresso, tea (1 cup)	0-15
Herbal tea (1 cup)	0

Source: Canadian Nutrient File and USDA Nutrient Database

1in2

People with Risk Variant

Your Results

Gene	Marker
CYP1A2	rs2472300

Risk Variant	Your Variant
GA or AA	AA

Your Risk

Elevated

only when caffeine intake is high

Recommendation

Since you possess the AA or GA variant of the CYP1A2 gene, there is an increased risk of high blood pressure and heart attack if consuming more than 200 mg of caffeine daily, which is approximately 2 small cups of coffee. Limit caffeine consumption to no more than 200 mg per day in order to reduce this risk. Caffeine occurs naturally in coffee, tea, cocoa, kola and guarana. It is also manufactured synthetically and added to cola, energy drinks, and certain over the counter cold remedies.

Limit caffeine intake to 200 mg/day.

International Science Advisory Board

Ahmed El-Sohemy, PhD

Dr. Ahmed El-Sohemy is a Professor and Associate Chair and held a Canada Research Chair in Nutrigenomics at the University of Toronto. He is also the founder of Nutrigenomix Inc., serves as the company's Chief Science Officer and is Chair of the company's International Science Advisory Board. Dr. El-Sohemy obtained his PhD from the University of Toronto and completed a postdoctoral fellowship at Harvard. He has published in the top scientific and medical journals with almost 200 peer reviewed publications and has given more than 300 invited talks around the world. He is currently Editor-in-Chief of the journal Genes & Nutrition, serves on the editorial board of 10 other journals, and has served as an expert reviewer for more than 30 different scientific and medical journals and 12 research granting agencies. He has been a member of international expert advisory panels and scientific advisory boards of several organizations. Dr. El-Sohemy is the recipient of several awards for excellence in research by the American College of Nutrition, the Canadian Society for Nutrition and the American Nutrition Association.

Sara Mahdavi, RD, MSc, PhD

Dr. Sara Mahdavi is a clinical scientist and holds a clinical instructor and research appointment with the Department of Community and Family Medicine at the University of Toronto. Dr. Mahdavi received her doctorate from the Faculty of Medicine at the University of Toronto in the field of gene-environment interactions and cardiometabolic disease. She has been practicing clinical dietetics over the last decade at several hospitals as well as private practices. Dr. Mahdavi has been an invited speaker at medical conferences and for government agencies. She has published over a dozen original scientific articles in top medical journals, has been an invited reviewer for several clinical journals and serves on the editorial board of the Canadian Journal of Kidney Health and Disease. Dr. Mahdavi's clinical research and practice have varied from early insulin sensitivity to kidney disease, rare genetic disorders, and innovative dermatological interventions.

Lynnette R Ferguson, D.Phil. (Oxon.), DSc

Dr. Lynn Ferguson is Program Leader of Nutrigenomics New Zealand. She obtained her D.Phil. from Oxford University working on DNA damage and repair. After her return to New Zealand, she began working as part of the Auckland Cancer Society Research Centre, using mutagenicity testing as a predictor of carcinogenesis. In 2000, she took on a 50% role as Head of a new Discipline of Nutrition at The University of Auckland. She has recently been investigating the interplay between genes and diet in the development of chronic disease, with particular focus on Inflammatory Bowel Disease. As Program Leader of Nutrigenomics New Zealand she is working with a range of others to bring nutrigenomics tools to the New Zealand science scene. She has supervised more than 30 students and has more than 300 peer reviewed publications. Dr. Ferguson serves as one of the managing Editors for Mutation Research: Fundamental and Molecular Mechanisms of Mutation, as well as on the Editorial Boards of several other major journals.

J. Bruce German, PhD

Bruce German is the Director of the Foods for Health Institute at the University of California Davis, and is Professor of Food Science and Technology (http://ffhi.ucdavis.edu/). Dr German received his PhD from Cornell University and joined the faculty at the University of California (Davis) in 1988. In 1997, he was named the first John E. Kinsella Endowed Chair in Food, Nutrition and Health. His research interests in personalized nutrition include the structure and function of dietary lipids, the role of milk components in food and health and the application of metabolic assessment to personalizing diet and health. Dr German has published more than 350 papers and holds a number of patents related to various technologies and applications of bioactive food components. The research articles from his lab rank in the top 5 most cited in the field.

David Jenkins, MD, DSc, PhD

Dr. Jenkins earned his MD and PhD at Oxford University, and is currently a Professor in both the Departments of Medicine and Nutritional Sciences at the University of Toronto. He is also a staff physician in the Division of Endocrinology and Metabolism and the Director of the Clinical Nutrition and Risk Factor Modification Center, St. Michael's Hospital. Dr Jenkins has published over 300 peer reviewed articles and given hundreds of invited talks around the world. He has served on numerous international committees to set guidelines for the treatment of diabetes and most recently on the new joint United States-Canada DRI system (RDAs) of the National Academy of Sciences. His team was the first to define and explore the concept of the glycemic index of foods and demonstrate the breadth of metabolic effects of viscous soluble fibre. He has received many national and International awards in recognition of his contribution to nutrition research. Dr Jenkins currently holds a Canada Research Chair in Nutrition and Metabolism.

Jose Ordovas, PhD

Jose M. Ordovas is Professor of Nutrition and Director of the Nutrigenomics Laboratory at the United States Department of Agriculture, Human Nutrition Research Center on Aging at Tufts University in Boston. After obtaining his PhD from the University of Zaragoza, Spain, he completed postdoctoral work at Harvard, MIT and Tufts University. Dr Ordovas' major research interests focus on the genetic factors predisposing to cardiovascular disease and their interaction with environmental factors. Dr Ordovas has published ~700 articles in peer reviewed journals, and written numerous reviews and edited 5 books on nutrigenomics. He has been an invited speaker at hundreds of International meetings all over the world and is currently a member of the Institute of Medicine's Food and Nutrition Board (National Academies). He serves as Editor for Current Opinion in Lipidology (Genetics Section), and on the Editorial Board of numerous journals. Dr. Ordovas is a Member of Honor of the Spanish Society of Atherosclerosis and has received other awards for his contributions to the field of nutrigenomics.

Ben van Ommen, PhD

Dr. Ben van Ommen is Director of the Nutrigenomics Organization (NuGO) and Principal Scientist at TNO, one of the largest independent research organizations in the area of nutrition world-wide. He is also Director of the TNO systems biology program and leading the activities on nutrigenomics, nutritional systems biology, personalized health and personalized medicine. His research applies systems biology to metabolic health and metabolic disease, focusing on understanding all relevant processes involved in maintaining optimal health and causing specific disease sub-phenotypes, developing new biomarkers and treatment strategies.

Nanci S. Guest, PhD, RD, CSCS

Dr. Nanci Guest is a registered dietitian (sport specialty), certified personal trainer and a certified strength and conditioning specialist, and she has been working in private practice in this field for two decades. She completed her doctoral degree in the area of nutrigenomics and athletic performance at the University of Toronto. She obtained her BSc in agriculture and dietetics, and her MSc in nutritional sciences with a sport focus at the University of British Columbia. Dr. Guest has published her research in top journals, presented at international conferences and has given dozens of invited talks around the world. She also teaches advanced sport nutrition courses at the college level. Dr. Guest is a global consultant to professional and amateur athletes and teams, and she was also involved in creating past athlete nutrition guidelines for the International Olympic Committee. She was the Head Dietitian at both the Vancouver 2010 Olympics and the Toronto 2015 Pan Am games and served as a consultant to a variety of international athletes in preparation for the past four London, Sochi, Rio and PyeongChang Olympics.