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Nutrigenomics Modeling of Performance Phenotypes in Sport: An Evidence-Based Systematic Review

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1. INTRODUCTION & OBJECTIVE

Physical performance is contingent upon adequate **nutrition input**; yet subjects display **variability** in their **physiological responses to identical diets,** nutrients, and supplement regiment. **Nutritional plans of action** must therefore be **adapted**, aligned with each athletes' **metabolic profile, biochemical individuality**, and **specific demands.** These strategies encompass **dietary patterns, macronutrient ratios, micronutrient sufficiency,** and **certain requirements** (e.g., nutrient-timing practices), and the evidence-based utilization of supplements and ergogenic aids. In sports, **nutrigenomics** explain how **genetic variants** modulate the answer to nutrition intake and dietary patterns, **affecting aerobic performance, anaerobic power output,** and **post-exercise recovery kinetics.** For example, the **CYP1A2 −163C>A (rs762551)** gene variant targets the erogenicity of caffeine. **Fast metabolizers (AA)** commonly experience clearer cognitive benefits**, slow metabolizers (CC)** often have null or detrimental responses, and those with the **AC alleles** exhibit **intermediate/variable** outcomes. Effects are **task- and dose-dependent,** with more noticeable genotype-related differences in **endurance** and at higher doses. However, the body of evidence is hindered by the scarcity of **CC** samples and methodological **heterogeneity**. Hence, **this systematic review evaluated the evidence regarding the influence of nutrigenomics on metabolic and phenotypic modulation of sport performance to support implementing personalized nutrition interventions.**

2. SYSTEMATIC METHODOLOGY

Records identified from (n = 742): PubMed, Scopus, and Web of Science (2010–2024) using keywords:"nutrigenomics", "sport", "athlete", "ACTN3", "ACE", "CYP1A2", "COL5A1", "nutrient–gene interaction", "performance"

Records excluded (n = 489)
- Animal-only studies
- Case reports
- Non–peer reviewed abstracts
- Not relevant outcomes
- Wrong study design

Records screened (n = 615)

Reports not retrieved (n = 18)
- Full text not accessible
- Only available as abstract
- Not retrievable from source

Reports sought for retrieval (n = 126)

Reports assessed for eligibility (n = 108)

Extracted data included:
1. Gene/SNP
2. Dietary factor or supplement
3. Outcome measure (physiological, performance, or injury)
4. Study design
5. Sample size

Studies included in review (n = 41)

Included articles were human studies that reported associations between genetic variants and responses to nutrients, supplements, or exercise-related phenotypes (endurance, power, recovery, injury).

Risk of bias and heterogeneity: qualitatively evaluated

3. GENES ASSOCIATED WITH SPORT NUTRITION

Gene (variant)	Function	Dietary factor	Source	Related outcome
CYP1A2 (rs762551)	Caffeine metabolism (fast/slow)	Caffeine	Coffee, black/green tea, yerba mate, cocoa, cola drinks	Cardiovascular response, endurance
ADORA2A (rs5751876)	Adenosine signaling, CNS arousal	Caffeine	Coffee, tea, caffeine-based supplements, energy drinks	Vigilance, sleep sensitivity
BCMO1 (rs11645428)	β-carotene – retinol conversion efficiency	Vitamin A	Kale, eggs, liver, tuna	Vision, immune function
MTHFR (rs1801133)	Folate activation – 5-MTHF formation	Folate	Lentils, chickpeas, beans, spinach, asparagus	Folate-related anemia, homocysteine levels
HFE (rs1800562/ rs1799945)	Iron absorption and regulation	Iron	Red meat, poultry, shellfish, legumes	Hemochromatosis predisposition
TMPRSS6 / TFR2 / TF	Hepcidin-mediated iron regulation	Iron	Red meat, poultry, mussels, sardines	Iron-deficiency anemia risk
FUT2 (rs602662)	Vitamin B12 absorption (secretor status)	B12	Shellfish (clams, mussels), beef, liver, salmon, tuna	B12-related anemia, homocystein
GSTT1 (Ins/ Del)	GST detoxification; vitamin C utilization	Vitamin C	Citrus fruits, kiwi, bell peppers, strawberries	Antioxidant capacity, vitamin C status
GC (rs2282679))	Vitamin D transport and activation	Vitamin D	Salmon, sardines, egg yolks, fortified milk	Immunity, bone health, recovery
GC (rs7041, rs4588)	Vitamin D–binding protein affinity	Calcium	Dairy, yogurt, cheese, tofu, sardines, almonds	Bone density, fracture risk, muscle function
PEMT (rs12325817)	Endogenous choline synthesis	Choline	Eggs, salmon, cod, turkey, beef, soybeans, chickpeas	Liver integrity, neurotransmitter synthesis
MTHFD1 (rs2236225)	Folate–choline – methylation pathway	Folate/ Choline	Leafy greens, eggs, legumes, animal liver	Muscle/liver damage risk
FTO (rs1558902/ rs9939609)	Energy balance and appetite regulation	Protein	Dietary patterns rich in SFA/ PUFA, meat	Body composition optimization
TCF7L2 (rs7903146)	Wnt signaling; adiposity regulation	Dietary fat	Nuts, seeds, olive oil, fish, avocado, dairy fats	Body composition optimization
PPARγ2 (rs1801282)	Adipocyte differentiation	MUFA	Olive oil, avocados, nuts, seeds, olives	Body composition optimization

4. INTERPRETATION OF EVIDENCE

Nutrient-gene interactions are well-recognized as key modulators of physiological pathways. **Polymorphisms** in **CYP1A2** and **ADORA2A** remain the most **robustly replicated genetic determinants** of inter-individual variability **in the ergogenic responsiveness to caffeine.** Moreover, variants in vitamin-related pathways (e.g., **MTHFR, GC/VDBP, and VDR**) can modulate micronutrient status and enhance metabolic efficiency.

Baseline diet, training load, and **inherent metabolic variability** significantly influence these effects. As a result, interpretations of **single nucleic polymorphisms (SNPs)** provide limited **predictive power complex performance phenotypes.** A **multi-locus, systems-based framework** is required to translate **nutrigenomic** evidence into **actionable, athlete-specific nutrition strategies**.

To set the molecular triggers that shape the response to performance-relevant nutritional input into context, **Figure 1** illustrates the principal pathways modulating the expression of the **CYP1A2 gene**, which serves as a precedent for a **nutrigenomic** biomarker and can be used as a reference for subsequent genetic testing.

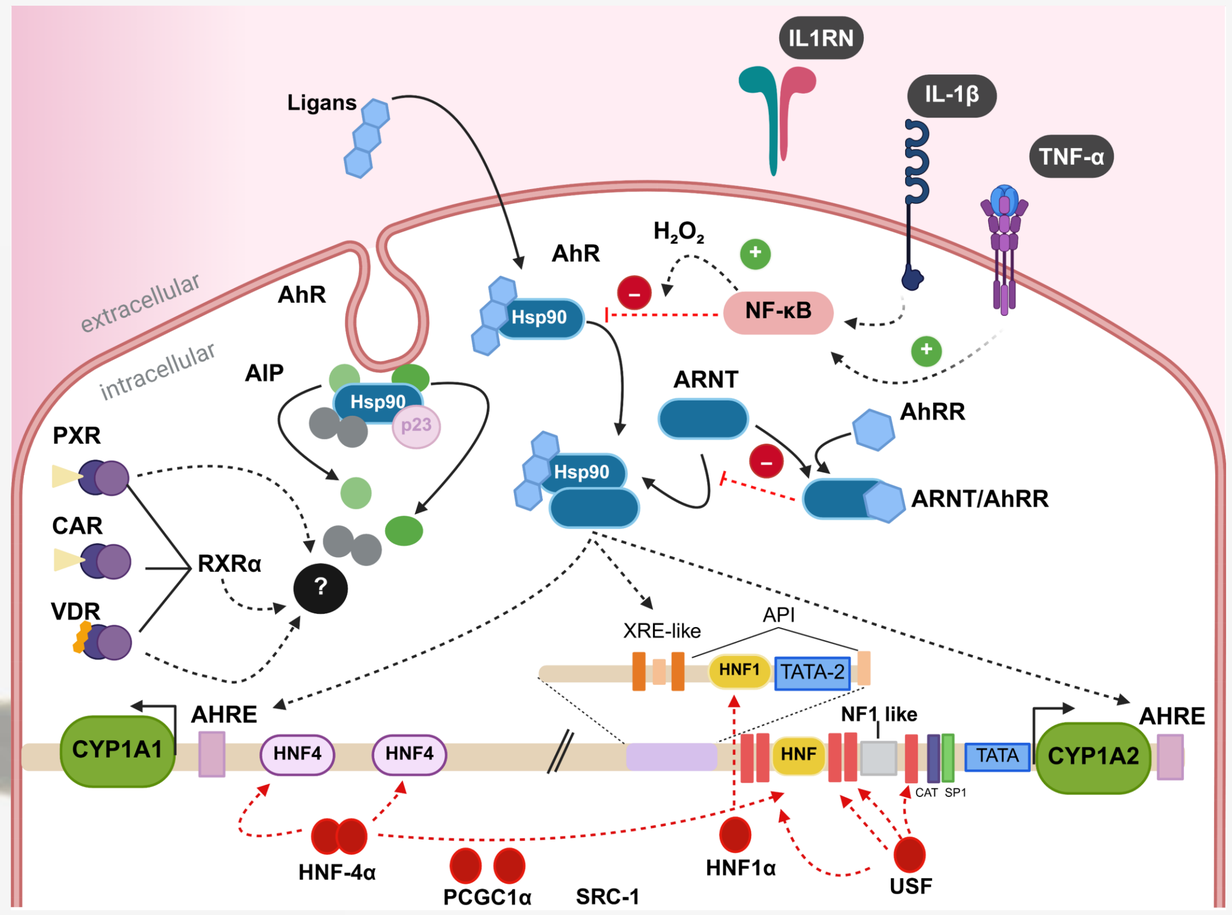

Figure 1. Overview of the cytochrome P450 1A2 (CYP1A2) pathways involved in transcriptional regulation. Created in https://BioRender.com.

5. CONCLUSION

Overall, **few studies are available** on the interaction between **genes** and **diet** on sport performance, so this may be a promising line of research. Futhermore, it has been found that **serum levels and/or dietary intake of several nutrients** and **food bioactives do influence health, body composition,** and **exercise performance.** The **CYP1A2** genotype is the **strongest evidence**, as it can modulate the **ergogenic effects** of **caffeine**. The differences across **genotypes**, however**, are inconsistent or restricted to domain-specific exercise scenarios.** Further testing of clinical usefulness is required to advance the application and translation of **nutrigenomic** into routine practice.

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