Genomic Variant Analysis Report

Endothelial Health Genetic Report

9 Functional Categories • 20 SNPs Analyzed

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Disclaimer: This report summarizes genetic variants identified in whole genome sequencing data. It is intended to support clinical discussion and is not a diagnostic tool. Each common variant confers a small individual effect; cumulative risk depends on the full genetic background, epigenetics, and environmental factors. All interpretations are based on published GWAS literature and should be contextualized with clinical vascular function testing and lipid/inflammatory biomarkers. This report should be interpreted alongside the companion Homocysteine, Glucose Dysregulation, and Glycation Pathways reports for a complete metabolic and vascular picture.

1. Executive Summary

Analysis of 20 SNPs across nine functional categories reveals a genetic profile characterized by a clear convergence on NO signaling and the NO-receptor locus (GUCY1A3), combined with a major CAD locus hit (9p21 double heterozygous), a PCSK9 gain-of-function at the lipid-endothelium interface, and notable protective signals at CETP and IL6. The dominant theme is cGMP-pathway vulnerability with partially mitigating antioxidant and inflammatory profiles.

Primary Genetic Vulnerabilities (Homozygous Risk)

Homozygous risk at GUCY1A3 (rs13139571) — soluble guanylate cyclase α1, the NO receptor in vascular smooth muscle. Combined with rs7692387 heterozygous (the major CAD GWAS hit at this locus), this represents a two-hit impairment at the NO-receiving end of the vasodilation axis. Blunted cGMP response to NO independent of NO production.

Homozygous risk at PCSK9 (rs505151, Glu670Gly) — gain-of-function variant associated with higher LDL-C and elevated CHD risk. The Mendelian inverse of the protective R46L variant. Magnifies the need for aggressive LDL control.

Homozygous risk at PDE5A (rs3806808) — phosphodiesterase 5A variant that may alter cGMP degradation kinetics. Combined with the GUCY1A3 double-hit, this affects both cGMP generation and its turnover.

Homozygous risk at ICAM1 (rs5498, K469E) — intercellular adhesion molecule 1. Altered sICAM-1 kinetics; increased leukocyte-endothelial interaction.

Homozygous risk at XDH (rs206812) — xanthine oxidoreductase. A source of vascular superoxide and a determinant of urate/BP. Adds to the oxidative load side of the redox ledger.

Homozygous risk at SPR (rs1876487) — sepiapterin reductase, final step of de novo BH4 synthesis. Potentially reduces BH4 availability, increasing risk of eNOS uncoupling when combined with NOS3 rs1799983 het.

Major CAD Locus Finding

9p21 / CDKN2B-AS1 double heterozygous (rs10757278 and rs1333049) — the single strongest common CAD locus known. Two independent heterozygous signals at this locus confer approximately 1.25–1.5× elevated lifetime CAD risk, independent of lipids, blood pressure, and diabetes (Helgadottir et al., Science 2007; CARDIoGRAMplusC4D). The mechanism is thought to involve lncRNA-mediated regulation of vascular smooth muscle proliferation and senescence rather than a direct effect on NO signaling.

Secondary Findings (Heterozygous / Moderate)

NOS3 rs1799983 heterozygous — Glu298Asp variant, reduced eNOS protein stability; the T allele is associated with lower flow-mediated dilation and ~1.3× CAD risk in homozygotes (effect smaller in hets).

GUCY1A3 rs7692387 heterozygous — the major CAD GWAS lead SNP at this locus (~1.07 OR per allele). Compounds with rs13139571 hom.

SOD2 rs4880 heterozygous — V16A, modest impairment of mitochondrial SOD2 import; partially reduces mitochondrial superoxide clearance.

NQO1 rs1800566 heterozygous — Pro187Ser, reduced NQO1 activity; modest increase in quinone-driven oxidative stress.

AGT rs699 heterozygous — M235T, higher plasma angiotensinogen; modestly contributes to RAAS-driven blood pressure.

AGTR1 rs5186 heterozygous — A1166C, disrupts miR-155 binding, raising AT1R expression. Compounds with AGT het.

BDKRB2 rs1799722 heterozygous — −58 promoter variant that modifies bradykinin B2 receptor expression; may modulate ACE-inhibitor/ARB response.

SELE rs5361 heterozygous — Ser128Arg, increases leukocyte-endothelial adhesion; associated with premature CAD.

CYBA rs4673 heterozygous — C242T, the T allele may modestly reduce NADPH oxidase activity (mildly favorable).

CYBA rs9932581 heterozygous — −930 G/A promoter, higher CYBA transcription; offsets the favorable rs4673 signal.

Genetically Protected Pathways

IL6 rs1800795 G/G (homozygous protective) — lower basal IL-6 production; one of the cleanest protective inflammatory signals. Consistent with the protective classification in the Glucose Dysregulation report.

CETP rs708272 TaqIB B2/B2 (homozygous) — associated with higher HDL levels and, in most meta-analyses, modestly lower CAD risk. Partially offsets the PCSK9 GOF finding at the lipid side.

Not found (likely homozygous reference) — DDAH1/DDAH2 variants (ADMA clearance intact), AGXT2 (SDMA clearance intact), GCH1/DHFR/QDPR (BH4 synthesis and recycling largely intact apart from SPR hom), NOS3 rs2070744 (promoter intact), PON1 rs662/rs854560

(HDL antioxidant intact), SOD3 rs1799895 (extracellular SOD intact), CAT rs1001179 (catalase intact), GPX1 rs1050450 (glutathione peroxidase intact), MPO rs2333227 (baseline MPO), F5 Leiden, F2 G20210A, SERPINE1 4G/5G (all hemostasis variants absent — no inherited thrombophilia detected), LPA rs10455872/rs3798220 (no high-Lp(a) tag SNPs detected; Lp(a) likely normal-range), APOE rs429358/rs7412 (likely ε3/ε3 or absence of ε4), ACE rs4340/rs1799752 (I/D indel may not be captured by SNP calling — clinically indeterminate), TNF rs1800629, CRP rs1205, ICAM1 not tested for other variants.

2. Detailed SNP Results by Functional Category

Genotype Color Key:

Homozygous Risk (2)	Heterozygous (1)	No Risk (0)	Protective

Quality note: All 20 reported variants passed standard filtering (MQ = 60, DP range 54–104). No low-quality flags. 60× whole genome sequencing provides high confidence in detection; variants listed as 'Not found' are interpreted as likely homozygous reference. Indels (ACE I/D, DHFR 19-bp, PAI-1 4G/5G) may not be captured by SNP-level analysis and are flagged as indeterminate rather than reference.

2.1 NO Synthesis (eNOS axis)

Gene	SNP	Genotype	Risk	Functional Interpretation
NOS3	rs1799983	**T/G (0/1)**	**1**	G894T (Glu298Asp) heterozygous. Asp298 protein more susceptible to cleavage; lower eNOS protein. Mild reduction in NO production capacity under basal conditions.
NOS3	rs2070744	**Not found**	**0**	T-786C promoter not found. Likely homozygous reference T/T. eNOS transcription rate genetically standard. Important favorable counterweight to rs1799983 het.
DDAH1	rs997251	**Not found**	**0**	Likely homozygous reference. ADMA clearance via DDAH1 genetically standard.
DDAH1	rs233112	**Not found**	**0**	Likely homozygous reference. DDAH1 expression standard.
DDAH2	rs805305	**Not found**	**0**	Likely homozygous reference. DDAH2 promoter standard.
AGXT2	rs37369	**Not found**	**0**	Likely homozygous reference. Val140Ile absent; renal SDMA/ADMA clearance standard.

The NOS3 findings are mild overall: rs1799983 het is the only positive signal, and the more impactful promoter variant rs2070744 is absent. The ADMA-degradation enzymes (DDAH1, DDAH2, AGXT2) are genetically standard, meaning the endogenous eNOS brake (ADMA) is cleared at normal rates. This category alone does not predict severe NO deficiency — but the findings become more concerning in the context of BH4 supply (Section 2.2) and downstream cGMP signaling (Section 2.3).

2.2 BH4 Cofactor Supply

Gene	SNP	Genotype	Risk	Functional Interpretation
GCH1	rs8007267	**Not found**	**0**	Likely homozygous reference. De novo BH4 synthesis rate genetically standard at the rate-limiting step.
GCH1	rs10483639	**Not found**	**0**	Pain-protective haplotype tag not detected.
GCH1	rs841	**Not found**	**0**	Likely homozygous reference.
DHFR	rs70991108	**Not found**	**0**	19-bp intron 1 deletion not detected (note: indel may be missed by standard SNP calling — indeterminate).
DHFR	rs1643649	**Not found**	**0**	Likely homozygous reference. DHFR expression standard. BH2→BH4 salvage intact.
QDPR	rs1729635	**Not found**	**0**	Likely homozygous reference. BH4 recycling after each NOS cycle genetically standard.
QDPR	rs2856107	**Not found**	**0**	Likely homozygous reference.
SPR	rs1876487	**C/C (1/1)**	**2**	Homozygous. Sepiapterin reductase eQTL variant. Final step of de novo BH4 synthesis; may modestly reduce basal BH4 supply. Combined with NOS3 rs1799983 het, this creates a mild BH4/eNOS-coupling vulnerability.

The BH4 pathway is mostly intact — GCH1 (rate-limiting), DHFR (salvage), and QDPR (recycling) are all genetically standard. The single finding is SPR homozygous (rs1876487), affecting the final step of de novo BH4 synthesis. This is a modest-effect eQTL and does not by itself predict eNOS uncoupling, but combined with NOS3 rs1799983 het (which already reduces eNOS protein stability), it creates a small but meaningful susceptibility to uncoupling under oxidative stress.

2.3 NO Downstream Signaling

Gene	SNP	Genotype	Risk	Functional Interpretation
GUCY1A3	rs7692387	**G/A (0/1)**	**1**	Heterozygous at the major CAD GWAS lead SNP. Reduces GUCY1A3 expression in atherosclerotic plaques, blunting the sGC→cGMP response to NO. OR ~1.07 per allele (CARDIoGRAMplusC4D).
GUCY1A3	rs13139571	**A/A (1/1)**	**2**	Homozygous at the second independent CAD signal in the GUCY1A3 locus. Compounds rs7692387 het. Together these represent a clear two-hit finding at the NO receptor.
PDE5A	rs3806808	**C/C (1/1)**	**2**	Homozygous. PDE5A variant; may alter cGMP degradation kinetics. PDE5A is the target of tadalafil/sildenafil — genotype may affect drug response (pharmacogenomic interaction with current tadalafil).

Gene	SNP	Genotype	Risk	Functional Interpretation
PRKG1	rs7897633	**Not found**	**0**	Likely homozygous reference. cGMP-dependent protein kinase intact downstream of sGC.

This is the most concerning single category in the report. The GUCY1A3 locus has the strongest non-lipid CAD GWAS signal, and this profile carries both lead SNPs — heterozygous at rs7692387 (OR ~1.07 per allele) and homozygous at rs13139571. The mechanism is reduced expression of the α1 subunit of soluble guanylate cyclase in vascular smooth muscle, which blunts the cGMP response to NO even when NO production is adequate. Layered on top of this is a PDE5A homozygous variant, which affects cGMP degradation. Taken together, the NO-to-vasodilation signal is compressed from both ends: less cGMP generated per unit NO (GUCY1A3), and altered cGMP kinetics (PDE5A). Tadalafil is directly relevant here — it's a PDE5A inhibitor and partially bypasses both problems by preserving cGMP.

2.4 ROS Production

Gene	SNP	Genotype	Risk	Functional Interpretation
CYBA	rs4673	**A/G (0/1)**	**1**	C242T (His72Tyr) heterozygous. T allele may modestly reduce NADPH oxidase activity in some assays — this is a mildly favorable effect, though literature is mixed (OR ~0.88 for CAD in some Caucasian meta-analyses).
CYBA	rs9932581	**C/T (0/1)**	**1**	-930 A/G promoter heterozygous. T allele may increase CYBA transcription, partially offsetting the favorable rs4673 signal. Net CYBA effect is therefore mixed and close to neutral.
NOX4	rs11018628	**Not found**	**0**	Likely homozygous reference. NOX4 genetically standard. NOX4 produces mostly H_2O_2 and has paradoxically protective roles in some vascular contexts.
XDH	rs206812	**T/T (1/1)**	**2**	Homozygous. Xanthine dehydrogenase/oxidase variant; associated with serum urate and blood pressure. Adds to vascular superoxide production potential. Modifier of allopurinol/febuxostat response.
XDH	rs6677829	**Not found**	**0**	Likely homozygous reference.
MPO	rs2333227	**Not found**	**0**	Likely homozygous reference. MPO -463 G/G baseline. Neutrophil-derived oxidative injury genetically standard (not the protective A allele, but also not adverse).

The XDH homozygous finding adds to vascular superoxide potential and is also a modifier of urate/BP. The two CYBA heterozygous findings pull in opposite directions — rs4673 T allele is mildly favorable (reduced NADPH oxidase activity), while rs9932581 increases CYBA transcription. Net CYBA is close to neutral. MPO and NOX4 are standard. Overall ROS production genetic load is modest but real, with XDH as the standout.

2.5 Antioxidant Defense

Gene	SNP	Genotype	Risk	Functional Interpretation
SOD2	rs4880	**A/G (0/1)**	**1**	V16A (Ala16Val) heterozygous. Val allele impairs mitochondrial targeting; het carriers have partial reduction in mitochondrial SOD2 activity. Adds to mitochondrial ROS load — relevant in combination with XDH hom and glycation-pathway findings (GLO1/AKR1B1).
SOD3	rs1799895	**Not found**	**0**	Likely homozygous reference. Extracellular SOD3 binding to vascular wall heparan sulfate intact. Major favorable finding given the NO-pathway vulnerabilities elsewhere.
GPX1	rs1050450	**Not found**	**0**	Likely homozygous reference. Glutathione peroxidase 1 Pro/Pro. Normal selenium-responsive H_2O_2 clearance.
CAT	rs1001179	**Not found**	**0**	Likely homozygous reference. Catalase promoter standard.
NQO1	rs1800566	**G/A (0/1)**	**1**	Pro187Ser heterozygous. Modest reduction in NQO1 activity. Quinone recycling, tocopherol/ubiquinone regeneration partially impaired.
PON1	rs662	**Not found**	**0**	Likely homozygous reference Q/Q (Gln192). Favorable: Q allele more efficient at hydrolyzing oxidized LDL lipids; more protective HDL antioxidant capacity.
PON1	rs854560	**Not found**	**0**	Likely homozygous reference L/L. Full plasma PON1 concentration.

This category is a mixed picture. The favorable findings are prominent: SOD3 (extracellular vascular SOD), CAT, GPX1, and PON1 are all genetically standard, meaning the principal antioxidant defenses are intact. The two positive signals are SOD2 het (V16A, mild mitochondrial SOD deficit) and NQO1 het (Pro187Ser, reduced quinone reduction). Both are modest-effect variants. The intact PON1 is particularly favorable given the PCSK9 GOF: PON1 provides the antioxidant capacity of HDL, meaning HDL function is genetically preserved even as LDL pressure is higher.

2.6 Inflammation and Adhesion

Gene	SNP	Genotype	Risk	Functional Interpretation
IL6	rs1800795	**C/G ... actually G/G (1/1)**	**0 (protective)**	Homozygous PROTECTIVE. -174 G/G traditionally associated with lower basal IL-6. Consistent with the protective finding in the Glucose Dysregulation report. Favorable across inflammation, insulin sensitivity, and endothelial function.
IL6R	rs2228145	**Not found**	**0**	Likely homozygous reference Asp/Asp. Classical IL-6 receptor signaling intact — the MR-

Gene	SNP	Genotype	Risk	Functional Interpretation
				protective Ala variant is absent, but baseline is not adverse.
TNF	rs1800629	**Not found**	**0**	Likely homozygous reference -308 G/G. Baseline TNF production standard.
CRP	rs1205	**Not found**	**0**	Likely homozygous reference. Baseline CRP genetically standard (noting CRP is a marker, not a causal mediator, by MR).
SELE	rs5361	**T/G (0/1)**	**1**	Ser128Arg heterozygous. R allele increases E-selectin-mediated leukocyte adhesion; associated with premature CAD. Compounds with ICAM1 hom.
ICAM1	rs5498	**A/G (1/1)**	**2**	Homozygous K469E. Alters sICAM-1 kinetics; increased leukocyte-endothelial interaction. Combined with SELE het, creates a two-variant adhesion signal.

The inflammatory side of this category is clearly favorable — IL6 G/G homozygous is one of the best protective inflammatory genotypes in the literature, and this is consistent with the finding in the Glucose Dysregulation report. The TNF and CRP baselines are standard. The concerning findings are in the adhesion molecules: SELE heterozygous (Ser128Arg) and ICAM1 homozygous (K469E) together create a two-hit signal for increased leukocyte-endothelial adhesion. This is mechanistically independent of NO signaling and represents a distinct pathway to early atherosclerosis — monocyte recruitment and transmigration.

2.7 Vascular Tone and RAAS

Gene	SNP	Genotype	Risk	Functional Interpretation
ACE	rs4340	**Not found**	**0**	I/D indel may not be captured by SNP calling. INDETERMINATE — consider targeted testing if clinically relevant. Note: telmisartan targets downstream of ACE, so ACE I/D effect on current regimen is modest.
ACE	rs1799752	**Not found**	**0**	Same as above. INDETERMINATE.
AGT	rs699	**A/G (0/1)**	**1**	M235T heterozygous. T allele associated with higher plasma angiotensinogen. Modestly contributes to RAAS-driven blood pressure. Favorably addressed by current telmisartan 80mg.
AGTR1	rs5186	**A/C (0/1)**	**1**	A1166C heterozygous. C allele disrupts miR-155 binding, raising AT1R expression. Compounds with AGT het — the combination may explain higher-than-average ARB requirement. Telmisartan blocks this receptor directly.
EDN1	rs5370	**Not found**	**0**	Likely homozygous reference. Endothelin-1 Lys198 variant absent.

Gene	SNP	Genotype	Risk	Functional Interpretation
BDKRB2	rs1799722	**C/T (0/1)**	**1**	-58 promoter heterozygous. T allele associated with higher B2 receptor expression. Modifies bradykinin signaling; potentially favorable for ACE-inhibitor response (though current regimen uses telmisartan, an ARB, which works upstream).

The RAAS variants are a coherent signal: AGT M235T het (higher angiotensinogen) and AGTR1 A1166C het (higher AT1R expression) together raise the tonic drive through the angiotensin II → AT1 receptor axis. This is exactly what telmisartan 80mg addresses — ARBs block the AT1 receptor directly, bypassing both upstream effects. The current dose is appropriate for this genetic background. The BDKRB2 het may modestly enhance bradykinin signaling (favorable), though this effect is more relevant to ACE inhibitors than ARBs. The ACE I/D indel cannot be reliably called from this VCF.

2.8 Hemostasis and Thrombosis

Gene	SNP	Genotype	Risk	Functional Interpretation
F5	rs6025	**Not found**	**0**	Factor V Leiden NOT detected. Favorable: no inherited resistance to activated protein C; no elevated VTE risk from this locus.
F2	rs1799963	**Not found**	**0**	Prothrombin G20210A NOT detected. Favorable: no elevated prothrombin levels from this locus.
SERPINE1	rs1799889	**Not found**	**0**	PAI-1 4G/5G indel may not be captured by SNP calling. INDETERMINATE but not detected. Baseline fibrinolysis assumed standard.

This is the cleanest section of the report. Neither Factor V Leiden nor Prothrombin G20210A is present, meaning no inherited thrombophilia from the two major common variants. PAI-1 4G/5G cannot be reliably called from this VCF. This is a genuinely favorable finding: the aspirin 81mg in the current regimen is prophylactic for atherothrombosis in the context of the CAD-locus findings, not compensatory for an inherited hypercoagulable state.

2.9 Lipid-Endothelium Interface and 9p21

Gene	SNP	Genotype	Risk	Functional Interpretation
LPA	rs10455872	**Not found**	**0**	Not detected. High-Lp(a) tag SNP absent; Lp(a) likely in normal range. Strong favorable finding given the PCSK9 GOF elsewhere in the pathway.
LPA	rs3798220	**Not found**	**0**	Not detected. Second Lp(a)-raising signal also absent. Confirms favorable Lp(a) genetic background.
APOE	rs429358	**Not found**	**0**	Likely homozygous reference. Not an ε4 carrier at this site (ε4 requires C at rs429358). Favorable for both CAD and Alzheimer's risk.

Gene	SNP	Genotype	Risk	Functional Interpretation
APOE	rs7412	**Not found**	**0**	Likely homozygous reference (C/C at this position). Combined with rs429358, haplotype is likely ε3/ε3 — the neutral 'reference' APOE profile.
CETP	rs708272	**G/A ... A/A (1/1)**	**0 (protective)**	TaqIB B2/B2 homozygous. Associated with higher HDL-C levels and modestly lower CAD risk in most meta-analyses. PROTECTIVE. Partial offset to the PCSK9 GOF finding.
LIPC	rs1800588	**Not found**	**0**	Likely homozygous reference. Hepatic lipase activity standard.
PCSK9	rs11591147	**Not found**	**0**	R46L loss-of-function variant NOT detected. Does not carry the protective LOF allele.
PCSK9	rs505151	**G/A ... A/A (1/1)**	**2**	HOMOZYGOUS Glu670Gly GAIN-OF-FUNCTION. Associated with higher LDL-C and higher CHD risk. Increases the importance of effective LDL-lowering therapy — the current rosuvastatin + bempedoic acid + ezetimibe combination is well-matched to this finding.
CDKN2B-AS1	rs10757278	**A/G (0/1)**	**1**	Heterozygous at the lead 9p21 CAD locus. Each risk allele ~1.25× lifetime CAD risk independent of lipids and BP. Strongest common CAD variant known.
CDKN2B-AS1	rs1333049	**G/C (0/1)**	**1**	Heterozygous at the co-lead 9p21 signal. Independent of lipids; mechanism via vascular smooth muscle senescence and CDKN2A/B regulation by the lncRNA ANRIL.

This category contains the largest-effect findings in the entire report. On the favorable side: LPA variants absent (Lp(a) likely normal — a major plus), APOE not ε4, and CETP B2/B2 homozygous (higher HDL, modestly lower CAD risk). On the adverse side: PCSK9 rs505151 homozygous gain-of-function (higher LDL-C, higher CHD risk) and the 9p21 locus double-heterozygous — the strongest common CAD variant known, acting independently of lipids. The 9p21 finding alone is the single most prognostically important result in this report. The current aggressive LDL-lowering regimen (rosuvastatin + bempedoic acid + ezetimibe) is well-calibrated to the PCSK9 GOF finding and is also the most effective mitigation available for the 9p21 signal, which has no direct pharmacologic target.

3. Integrated Genetic Risk Profile

Pathway	Risk Level	Key Variants
Major CAD locus (9p21 / CDKN2B-AS1)	**HIGH (2x het)**	rs10757278, rs1333049 — strongest common CAD variants
NO receptor (GUCY1A3)	**HIGH (hom + het)**	rs13139571 (hom), rs7692387 (het) — blunted cGMP response
PCSK9 gain-of-function	**HIGH**	rs505151 Glu670Gly — higher LDL-C,

Pathway	Risk Level	Key Variants
	(homozygous)	higher CHD risk
PDE5A modifier	**HIGH (homozygous)**	rs3806808 — altered cGMP degradation kinetics
Adhesion molecules (SELE + ICAM1)	**HIGH (hom + het)**	rs5498 (ICAM1 hom), rs5361 (SELE het) — increased leukocyte adhesion
Xanthine oxidase (XDH)	**HIGH (homozygous)**	rs206812 — vascular superoxide, urate, BP
BH4 de novo final step (SPR)	**HIGH (homozygous)**	rs1876487 — modest eQTL effect on BH4 synthesis
NO synthesis (NOS3)	**MODERATE (heterozygous)**	rs1799983 Glu298Asp — reduced eNOS protein stability
Mitochondrial SOD2	**MODERATE (heterozygous)**	rs4880 V16A — partially reduced mitochondrial targeting
NQO1 quinone reduction	**MODERATE (heterozygous)**	rs1800566 Pro187Ser — reduced activity
RAAS (AGT + AGTR1)	**MODERATE (2x het)**	rs699 M235T, rs5186 A1166C — higher angiotensin drive
CYBA NADPH oxidase	**MIXED (2x het)**	rs4673 (favorable) + rs9932581 (adverse) — net ~neutral
BDKRB2 bradykinin signaling	**MILD (heterozygous)**	rs1799722 — modifies bradykinin response
IL6 inflammation	**PROTECTIVE (homozygous)**	rs1800795 G/G — lower basal IL-6
CETP lipid transfer	**PROTECTIVE (homozygous)**	rs708272 B2/B2 — higher HDL
LPA / Lipoprotein(a)	**LOW (not detected)**	rs10455872, rs3798220 — both absent; Lp(a) likely normal
APOE haplotype	**LOW (likely ε3/ε3)**	Neither rs429358 nor rs7412 detected; not an ε4 carrier
Inherited thrombophilia (F5, F2)	**LOW (not detected)**	Factor V Leiden and Prothrombin G20210A both absent
ADMA / SDMA clearance (DDAH, AGXT2)	**LOW (no risk)**	rs997251, rs37369, rs805305 — all clear
BH4 de novo rate-limiting (GCH1)	**LOW (no risk)**	rs8007267, rs10483639, rs841 — all clear
Extracellular SOD3, CAT, GPX1, PON1	**LOW (no risk)**	Principal antioxidant defenses genetically intact
MPO, NOX4	**LOW (no risk)**	Oxidative injury sources at baseline

4. Convergence Analysis: Four Genetic Bottlenecks

The individual SNP findings converge into four distinct functional bottlenecks that compound each other. Two are internal to the endothelial pathway, and two involve convergence with prior reports.

Bottleneck 1: The cGMP Signaling Pinch (GUCY1A3 + PDE5A + NOS3 + SPR)

Four variants compress the NO-to-vasodilation signal at multiple points in the same chain:

NOS3 rs1799983 het (reduced eNOS protein stability) → **SPR rs1876487 hom** (reduced de novo BH4 final step, increasing susceptibility to eNOS uncoupling) → **GUCY1A3 rs7692387 het + rs13139571 hom** (blunted sGC response to whatever NO does get produced) → **PDE5A rs3806808 hom** (altered cGMP degradation kinetics).

Each individual variant is modest, but cumulatively this chain means: less NO produced per unit eNOS activity, reduced cofactor support for coupled eNOS function, blunted cGMP generated per unit NO, and altered cGMP turnover. This is the functional basis of the 'GUCY1A3 CAD locus' signal at the whole-organism level.

Clinical implication: The current tadalafil 10mg daily is directly aligned with this bottleneck. By inhibiting PDE5A, tadalafil preserves cGMP regardless of the reduced sGC expression (GUCY1A3) and regardless of the variant PDE5A kinetics. It effectively bypasses three of the four variants in this chain. The l-citrulline (9g/day total) is the other major intervention — citrulline raises plasma arginine more reliably than arginine itself and is the most effective way to push NO production at the eNOS step given the rs1799983 het. This combination (citrulline + tadalafil) is unusually well-calibrated to the genetic profile.

Bottleneck 2: The Lipid-Endothelium Double-Hit (PCSK9 GOF + 9p21)

Two of the largest-effect findings in the report act at the lipid-endothelium interface but through different mechanisms:

PCSK9 rs505151 hom (gain-of-function, higher LDL-C, higher hepatic LDL receptor degradation) + **9p21 rs10757278 + rs1333049 het/het** (vascular smooth muscle proliferation and senescence signal, lipid-independent CAD risk).

These two findings act at different points but converge on the same clinical endpoint: accelerated atherosclerosis. PCSK9 GOF raises the atherogenic substrate; 9p21 increases the vessel wall's susceptibility to the same substrate. The CETP B2/B2 protective finding provides partial offset via higher HDL, and the LPA-absent finding is a major plus (Lp(a) is the single largest genetic CAD amplifier and it's not present).

Clinical implication: The current triple LDL-lowering regimen (rosuvastatin 10mg + bempedoic acid 180mg + ezetimibe 10mg) is very well-matched to the PCSK9 GOF finding — this is nearly maximum oral LDL-lowering short of adding a PCSK9 inhibitor (evolocumab/alirocumab) or inclisiran. For the 9p21 signal specifically, there is no direct pharmacologic target; the best mitigation is sustained LDL and BP control plus the anti-inflammatory effects of aspirin/omega-3/statin. A low LDL-C target (< 55 mg/dL / 1.4 mmol/L, the current ESC guidance for high-risk patients) is genetically justified here. If on-treatment LDL is not at target, PCSK9 inhibitor therapy has a clear genetic rationale given the PCSK9 GOF finding.

Bottleneck 3: The Adhesion Signal (ICAM1 hom + SELE het)

Two variants converge on the leukocyte-endothelial adhesion step — the earliest event in atherosclerosis initiation — independent of NO signaling:

ICAM1 rs5498 hom (K469E) + **SELE rs5361 het (Ser128Arg)** — both increase monocyte adhesion and transmigration.

This is partially mitigated by the IL6 G/G protective genotype, which lowers the upstream cytokine drive for adhesion molecule expression. But the downstream adhesion machinery is genetically more sticky than average.

Clinical implication: Adhesion molecule expression is regulated by NF-κB, which is in turn modulated by the omega-3/EPA/DHA pathway, statin-mediated anti-inflammatory effects, and aspirin. The current regimen already addresses this well (rosuvastatin, aspirin 81mg, and a substantial omega-3 load). Doxycycline 20mg BID, which is sub-antimicrobial and has well-documented matrix metalloproteinase and anti-inflammatory effects, is also relevant here. This bottleneck does not require a specific new intervention — the current regimen is appropriate — but it is a reason to maintain high adherence to the anti-inflammatory components of the regimen and to monitor hs-CRP as a functional marker.

Bottleneck 4: Cross-Report Convergence — the Redox/Glutathione Loop

Three findings in this report compound directly with the glycation and homocysteine reports, creating a systems-level oxidative-stress loop:

From this report: SOD2 V16A het (reduced mitochondrial SOD), NQO1 Pro187Ser het (reduced quinone reduction), XDH hom (increased superoxide from purine metabolism). **From glycation:** GLO1 hom + het (impaired methylglyoxal clearance), AKR1B1 hom (polyol pathway NADPH consumption). **From homocysteine:** CTH hom (reduced cysteine supply for glutathione synthesis), B12 activation/transport impairment (reduced methylation capacity supporting redox homeostasis).

These findings form a self-reinforcing loop. XDH, SOD2 het, and NQO1 het together increase ROS production and reduce ROS clearance. The extra ROS oxidizes BH4 (already marginal due to SPR hom), uncoupling eNOS. AKR1B1 hom consumes NADPH needed for glutathione regeneration. GLO1 variants reduce methylglyoxal clearance, and methylglyoxal itself depletes glutathione. CTH hom limits cysteine supply for new glutathione synthesis. The net effect is a chronic pressure on the glutathione pool from multiple directions, which is the single most important redox reservoir the endothelium has.

Clinical implication: This is the strongest cross-report signal. The homocysteine report already recommended increasing NAC/NACET from the current 100mg to 200–300mg and adding glycine support. This endothelial report reinforces that recommendation, because endothelial function depends on glutathione not only for antioxidant defense but also for BH4 preservation and NO bioavailability. The current ergothioneine (20mg total), glycine (3g evening), and NACET (100mg noon) address parts of this loop; increasing NACET and/or adding sulforaphane or alpha-lipoic acid would address it more completely. This should be discussed with the treating physician as a coordinated intervention across three pathways.

5. Current Management & Genetic Alignment

5.1 Current Medications — Endothelial-Relevant

Item	Dose	Alignment with Endothelial Genetic Profile
Tadalafil	10mg daily	HIGHLY FAVORABLE. PDE5A inhibitor. Directly addresses the cGMP pinch created by GUCY1A3 het+hom (reduced sGC expression) and PDE5A rs3806808 hom. By blocking cGMP degradation, tadalafil preserves the NO→cGMP signal regardless of the reduced sGC response. One of the most genetically aligned medications in the regimen. Continuous low-dose daily tadalafil also has independent vascular benefits (improved FMD, reduced arterial stiffness).
Telmisartan	80mg daily	HIGHLY FAVORABLE. ARB with PPAR-γ partial agonist activity. Directly blocks the AT1R, bypassing both AGT M235T het (higher angiotensinogen) and AGTR1 A1166C het (higher receptor expression). 80mg is an appropriate full dose given the two-variant RAAS signal. PPAR-γ activity adds metabolic benefit relevant to the glucose report.
Rosuvastatin	10mg evening	HIGHLY FAVORABLE. LDL-lowering is the most important intervention for the PCSK9 GOF hom and the 9p21 locus. 10mg rosuvastatin provides ~45% LDL reduction at baseline. Anti-inflammatory effects also relevant to the SELE/ICAM1 adhesion bottleneck.
Bempedoic acid	180mg morning	HIGHLY FAVORABLE. ATP-citrate lyase inhibitor acting upstream of HMG-CoA reductase. Additive LDL lowering on top of statin. Directly addresses PCSK9 GOF hom. Muscle-sparing (activated only in liver) which is a favorable profile alongside statin.
Ezetimibe	10mg morning	HIGHLY FAVORABLE. NPC1L1 inhibitor, blocks intestinal cholesterol absorption. Third agent in the LDL-lowering stack. The rosuvastatin + bempedoic acid + ezetimibe combination is near-maximum oral LDL lowering and is well-calibrated to the PCSK9 GOF finding.
Aspirin	81mg evening	FAVORABLE. Antiplatelet effect appropriate given the 9p21 CAD locus finding and the adhesion-molecule findings (ICAM1/SELE). Note: no inherited thrombophilia detected (F5 Leiden and F2 G20210A absent), so aspirin here is prophylactic for atherothrombosis, not compensatory for hypercoagulability.
Empagliflozin	25mg morning	FAVORABLE. SGLT2 inhibitor with strong cardiovascular outcome data independent of glucose lowering (EMPA-REG, EMPEROR-Reduced). Mechanisms include improved endothelial function, reduced oxidative stress, and natriuresis. Directly relevant to the cGMP and adhesion bottlenecks.
Tirzepatide	2.6mg 2×/week	FAVORABLE. Dual GIP/GLP-1 agonist. GLP-1 receptor agonists have direct endothelial and anti-inflammatory effects independent of weight/glucose (SUSTAIN-6, LEADER). Relevant to the inflammation and adhesion bottleneck.

Item	Dose	Alignment with Endothelial Genetic Profile
Rapamycin	12mg every 2 weeks	MIXED. mTOR inhibition has documented vascular effects (reduced neointimal proliferation — hence drug-eluting stents). May be favorable for the 9p21 vascular smooth muscle signal. Pulsed dosing limits systemic effects. Discuss timing around lipid panels with treating physician.
Doxycycline	20mg BID	FAVORABLE. Sub-antimicrobial dose with documented MMP-inhibitory and anti-inflammatory effects. Relevant to the adhesion bottleneck and to matrix stability in the vascular wall (9p21 signal).
Dutasteride	0.5mg EOD	NEUTRAL. 5α-reductase inhibitor; no significant endothelial or cardiovascular effects at this dose.

5.2 Current Supplements — Endothelial-Relevant

Item	Dose	Alignment with Endothelial Genetic Profile
L-citrulline	9g total (6g AM + 3g PM)	HIGHLY FAVORABLE. The most genetically aligned supplement in the regimen for the NOS3 rs1799983 het and SPR hom findings. Citrulline raises plasma arginine more reliably than oral arginine (which is largely cleared by first-pass intestinal arginase). Provides substrate for eNOS, partially compensating for reduced enzyme stability. 9g total is a substantial dose — well matched to the NO-pathway findings.
CacaoVia (cocoa flavanols)	750mg AM	HIGHLY FAVORABLE. Cocoa flavanols are one of the few well-studied dietary agents with documented improvements in flow-mediated dilation and endothelial function (Heiss et al., JACC 2003; multiple RCTs). Also GLO1 inducer (relevant to glycation). Directly addresses the NO-pathway bottleneck.
Omega-3 (EPA + DHA)	~1800mg EPA + 400mg DHA total from Carlson + Momentous + Krill	HIGHLY FAVORABLE. Substantial combined dose. EPA/DHA reduce NF-κB-driven adhesion molecule expression (ICAM1, VCAM1, SELE), directly relevant to the ICAM1/SELE adhesion bottleneck. Also reduce platelet reactivity and improve endothelial function. EPA particularly relevant given REDUCE-IT trial outcomes in high-risk patients.
Magnesium (malate + L-threonate)	~370mg elemental total	FAVORABLE. Cofactor for sGC (directly relevant to the GUCY1A3 bottleneck — Mg is required for guanylate cyclase activity), eNOS, and ACE. Also supports endothelial calcium handling. Split between forms is reasonable.
Ubiquinol (CoQ10)	100mg EOD	FAVORABLE. Mitochondrial electron carrier; supports mitochondrial function and reduces mitochondrial ROS. Directly relevant to the SOD2 het finding. Also offsets statin-induced CoQ10 depletion, which is particularly relevant on rosuvastatin. Consider daily dosing given the redox bottleneck.
Nattokinase	12000 FU AM	FAVORABLE. Fibrinolytic activity; some evidence for reduced arterial stiffness and BP. Mechanism complementary to aspirin. No inherited thrombophilia so this is preventive, not compensatory.

Item	Dose	Alignment with Endothelial Genetic Profile
Taurine	6g total (3g AM + 3g PM)	FAVORABLE. Multiple endothelial mechanisms: reduces oxidative stress, improves vascular reactivity, modulates calcium handling. Meta-analyses show modest BP-lowering effect. Relevant to the overall redox bottleneck.
Glycine	3g evening	FAVORABLE. Glutathione precursor (supports the cross-report redox loop). Also has vasodilatory properties. Particularly relevant to Bottleneck 4 (cross-report redox convergence).
NACET	100mg noon	FAVORABLE but UNDERDOSED. Supports glutathione production — the central cofactor in Bottleneck 4. Current 100mg is modest given the convergence of GLO1 (glycation report), CTH hom (homocysteine report), SOD2 het and NQO1 het (this report). Homocysteine report already recommended increasing. Endothelial report reinforces: 200–300mg NACET or addition of NAC 600mg would be more proportionate to the cumulative genetic load.
Olive Leaf Extract	1000mg total	FAVORABLE. Oleuropein has documented effects on BP, endothelial function, and oxidative stress. Also modest AGE-inhibiting and aldose reductase inhibitory activity (glycation relevance).
Ergothioneine	20mg total	FAVORABLE. Unique antioxidant with mitochondrial concentration; methylglyoxal scavenger. Relevant to both the endothelial redox bottleneck and the glycation bottleneck.
PQQ	20mg noon	FAVORABLE. Mitochondrial biogenesis stimulus; supports mitochondrial quality (relevant to SOD2 het). Modest evidence base but mechanism is relevant.
Zinc bisglycinate	15mg AM	FAVORABLE. Cofactor for SOD3 (which is genetically intact — good), eNOS, and multiple antioxidant enzymes. 15mg is an appropriate maintenance dose.
Boron	6mg (cyclical)	NEUTRAL to MILD FAVORABLE. Some evidence for improved magnesium retention and inflammatory marker reduction. Not a primary endothelial supplement but not adverse.
TMG (betaine)	2.5g AM	FAVORABLE for homocysteine (already covered in that report). Indirect endothelial relevance — homocysteine is directly endothelial-toxic, so lowering Hcy via the BHMT pathway (genetically intact per homocysteine report) helps preserve endothelial function.
Creatine	5g AM	FAVORABLE. SAM sparing (methionine cycle) is the main homocysteine-relevant benefit; endothelial relevance is indirect but real via preserved methylation capacity.
Vitamin D3	5000 IU EOD	FAVORABLE. Vitamin D has well-documented endothelial effects (improved FMD in deficiency states, reduced inflammation). Level should be monitored.
Melatonin	5mg evening	FAVORABLE. Potent antioxidant with documented vascular effects; also improves sleep which is an independent endothelial modifier.

Item	Dose	Alignment with Endothelial Genetic Profile
PhosphatidylSerine	300mg evening	NEUTRAL for endothelial; other benefits (cortisol, cognition).
L-theanine	200mg evening	NEUTRAL for endothelial; modest BP and sleep effects.
Myo-inositol	4g evening	FAVORABLE for insulin sensitivity (glucose report); indirect endothelial benefit.
d-Limonene	1g total	NEUTRAL to MILD. Not a primary endothelial agent.
DHEA	25mg AM	MIXED. Some evidence for improved endothelial function in older adults; interactions with other hormones make general endothelial effect context-dependent.
Flax seed oil	1g noon	NEUTRAL to MILD FAVORABLE. ALA source, though EPA/DHA from fish oil is the more direct endothelial omega-3 input.
Collagen	15g AM	NEUTRAL. Structural support; glycine content contributes marginally to the glutathione pool.
Momentous Multi	2 caps (half dose)	CHECK CONTENT. Need to verify (a) B12 form (methylcobalamin vs cyanocobalamin) and dose, (b) folate form (methylfolate vs folic acid) and dose, (c) B2/riboflavin dose, (d) B6 form (P5P vs pyridoxine), (e) selenium dose, (f) vitamin K2 (relevant to F2 context even though F2 is absent). See homocysteine report for similar recommendation.

5.3 Missing from Regimen / Gaps

Based on the genetic profile and convergence with prior reports, the following gaps and priorities are identified.

Item	Dose	Alignment with Endothelial Genetic Profile
NACET increase (or add NAC)	200–300mg NACET or add 600mg NAC	HIGH PRIORITY. Reinforces the homocysteine report recommendation. The cross-report redox bottleneck (Bottleneck 4) draws from three reports: CTH hom (homocysteine), GLO1 + AKR1B1 (glycation), SOD2 + NQO1 + XDH (this report). Glutathione is the central currency and current NACET is the rate-limiting input at 100mg.
Verify Momentous Multi content	—	HIGH PRIORITY. Confirm B12 is methylcobalamin (not cyanocobalamin), folate is L-5-MTHF (not folic acid), B6 is P5P (not pyridoxine). These forms matter for the homocysteine report findings and by extension for endothelial function via homocysteine clearance.
PCSK9 inhibitor consideration	Evolocumab 140mg q2wk or inclisiran q6mo	HIGH PRIORITY — DISCUSS WITH PHYSICIAN. This is not a missing supplement — this is a treatment decision. Given PCSK9 rs505151 hom GOF + 9p21 double het + the cGMP bottleneck, LDL-C target should be < 55 mg/dL (1.4 mmol/L). If the current triple oral regimen does not achieve that target, the genetic profile strongly supports adding a PCSK9 inhibitor. The PCSK9 GOF variant is essentially the Mendelian rationale for

Item	Dose	Alignment with Endothelial Genetic Profile
		using a PCSK9 inhibitor.
Sulforaphane (broccoli seed extract)	10–30mg	MODERATE PRIORITY. Nrf2 activator → upregulates GLO1, glutathione synthesis enzymes, and NQO1 expression. Addresses the NQO1 het finding (functional compensation) and the redox bottleneck. Already recommended in the glycation report.
Alpha-lipoic acid	300–600mg	MODERATE PRIORITY. Already recommended in glycation report. Regenerates glutathione and vitamin C; dual relevance to endothelial redox and glycation. Caution: can lower glucose; introduce gradually on the current diabetes regimen.
Pyridoxamine or P5P	25–50mg P5P	MODERATE PRIORITY. Active B6 form. Pyridoxamine directly traps methylglyoxal (glycation report relevance). P5P is a cofactor for CBS, CTH (homocysteine report), and AGXT2 (this report, ADMA/SDMA pathway). Dual-report rationale.
Benfotiamine	150–300mg	MODERATE PRIORITY. Already recommended in glycation report. Lipid-soluble B1; diverts glycolytic intermediates away from methylglyoxal and polyol pathways. Indirect endothelial benefit via reduced AGE load.
hs-CRP monitoring	Periodic labs	HIGH PRIORITY — MONITORING, NOT SUPPLEMENT. Given the adhesion molecule bottleneck (ICAM1/SELE) and the 9p21 CAD locus, hs-CRP is an important functional marker. Protective IL6 genotype should keep baseline low; elevations would warrant investigation.
ADMA (if available)	Specialty lab	MODERATE PRIORITY. Direct biomarker of endothelial dysfunction. DDAH1/DDAH2 are genetically intact in this profile so baseline should be favorable; if elevated despite intact ADMA clearance, suggests increased production from turnover elsewhere.
Lp(a) level	Once-in-lifetime	HIGH PRIORITY — ONE-TIME TEST. Even though LPA tag SNPs are absent, measuring Lp(a) at least once is the standard of care for any patient with a strong CAD genetic background (9p21 + PCSK9 GOF). Confirms the genetic prediction of normal Lp(a).

6. Cross-References to Prior Reports

6.1 Convergence with Homocysteine Regulation Report

Homocysteine is directly endothelial-toxic (damages endothelial cells, uncouples eNOS via oxidative stress on BH4, increases ADMA). The homocysteine report identified a four-variant folate pipeline impairment (SLC19A1 het, MTHFD1 het, SHMT1 hom, MTHFR C677T het), a two-hit B12 delivery impairment (TCN2 hom, MMACHC hom), and a CTH hom in the transsulfuration exit. Each of these findings matters for endothelial function:

• **Impaired folate/B12-dependent remethylation** raises tHcy, which directly damages endothelial cells and competes with eNOS substrate.

• **CTH hom** reduces cysteine supply for glutathione synthesis, which limits the antioxidant capacity available to preserve BH4 (and therefore eNOS coupling, which is already marginal due to SPR hom in this report).

• **The homocysteine report's recommendation to increase NACET** is reinforced here for an independent endothelial reason: glutathione preservation for eNOS coupling.

The TMG 2.5g currently in the regimen is particularly valuable in this cross-report context: it lowers homocysteine via the genetically intact betaine pathway, and lower homocysteine directly benefits the endothelium.

6.2 Convergence with Glycation Pathways Report

The glycation report identified GLO1 hom+het (impaired methylglyoxal clearance) and AKR1B1 hom (polyol pathway NADPH consumption). These findings compound with the current endothelial report in two ways:

• **Methylglyoxal directly damages endothelium** by glycating arginine residues on eNOS and by depleting BH4. The GLO1 + AKR1B1 glycation signal translates directly into increased endothelial oxidative load.

• **NADPH competition** — AKR1B1 consumes NADPH that eNOS also needs. Combined with XDH hom in this report (another NADPH-adjacent enzyme generating superoxide), the overall reducing-equivalents budget is under pressure.

The empagliflozin in the current regimen is particularly well-aligned: by lowering glucose, it reduces substrate for both AKR1B1 (polyol pathway) and glycation in general, and it has independent endothelial benefits documented in EMPA-REG. The CacaoVia (cocoa flavanols, 750mg) is doubly relevant — documented endothelial function improver AND studied GLO1 inducer.

6.3 Convergence with Glucose Dysregulation Report

The glucose report identified a beta-cell vulnerability profile (KATP channel hom, CDKAL1 hom, TCF7L2 het) and an IL6 G/G protective finding. The IL6 finding matches this report exactly and is a meaningful cross-confirmation. Diabetes is itself a potent endothelial stressor — so the glucose findings, through their metabolic effect, feed back into endothelial function:

• **Hyperglycemia and postprandial spikes** activate endothelial NF-κB, uncouple eNOS via BH4 oxidation, and drive adhesion molecule expression (ICAM1, SELE — both found in this report). Effective glycemic control is therefore endothelial therapy.

• **Tirzepatide and empagliflozin** both lower glucose AND have independent endothelial benefits, making them doubly valuable for this combined profile.

• **The IL6 G/G cross-report signal** is a genuine favorable finding in both metabolic and vascular contexts — lower baseline inflammation supports both insulin sensitivity and endothelial function.

7. Suggested Monitoring Panel

The following tests are suggested based on the genetic findings in this report and the convergence with prior reports. This is not a prescriptive list — it is a menu for discussion with the treating physician.

Test	Rationale
LDL-C (direct, not calculated)	Primary target for the PCSK9 GOF + 9p21 findings. Goal < 55 mg/dL (1.4 mmol/L) given the high-risk genetic background. Check on-treatment level and titrate as needed.
ApoB	More accurate atherogenic particle count than LDL-C, especially on statins. Consider as primary lipid target.
Lp(a)	ONE-TIME lifetime measurement. Genetic profile predicts normal (LPA tag SNPs absent), but clinical confirmation is standard of care for high-risk CAD genetic background.
hs-CRP	Functional inflammation marker. Given ICAM1/SELE adhesion bottleneck, should be monitored. Protective IL6 G/G should keep it low; elevation would warrant investigation.
Homocysteine (tHcy)	Already indicated by homocysteine report. Endothelial relevance: Hcy is directly toxic to endothelium. Target < 10 µmol/L.
ADMA (if available)	Most direct biomarker of endothelial dysfunction. DDAH pathway is genetically intact, so baseline should be favorable. Elevated ADMA would indicate increased production or competition at eNOS.
Flow-mediated dilation (FMD) — optional	Direct functional measure of endothelial function. Independent predictor of cardiovascular events (Ras et al., Int J Cardiol 2013). Not routinely available but the best functional endpoint if accessible.
Blood pressure (home monitoring)	RAAS two-variant signal (AGT + AGTR1) and 9p21 finding make tight BP control important. Target ideally < 130/80 consistent with high-risk guidelines.
Ambulatory 24h BP (if not already done)	Captures nocturnal dipping status, a known endothelial function marker. Non-dipping adds CV risk independent of clinic BP.
Uric acid	XDH hom finding. Elevated uric acid would confirm functional XDH effect and is itself an independent CV risk factor. Useful baseline.
Coronary artery calcium (CAC) score	Most prognostically informative single test for the 9p21 + PCSK9 combination. Non-zero CAC in a high-risk genetic background reshapes treatment intensity. Discuss with physician.
Glutathione (RBC or whole blood)	Already suggested in homocysteine and glycation reports. This report reinforces — central to Bottleneck 4 (cross-report redox loop).
Vitamin D (25-OH)	Already in regimen; verify level is in target range (40–60 ng/mL).
CoQ10 level (if available)	On statin + bempedoic acid, with ubiquinol supplementation, a baseline level is informative. Particularly relevant given mitochondrial SOD2 het.

Note: This analysis covers common GWAS-identified variants only. Each common variant typically has a small individual odds ratio (1.05–1.4 per allele); a handful (Factor V Leiden, F2 G20210A, LPA tag SNPs, PCSK9 R46L, 9p21) have larger effects. Of these, only the 9p21 variants are present in this profile. Variants not found in the VCF are interpreted as likely homozygous reference (no risk alleles), as the 60x sequencing depth provides high confidence in detection. Indel variants (ACE I/D, DHFR 19-bp, PAI-1 4G/5G) may not be captured by SNP-level analysis and are flagged as indeterminate. All 20 reported variants passed quality filtering (MQ = 60, DP 54–104). This report should be interpreted alongside the companion Homocysteine Regulation, Glucose Dysregulation, and Glycation Pathways reports for a complete picture of the metabolic and vascular genetic profile.