Corus® CAD Algorithm Overview

Corus CAD is the only clinically validated blood test that helps clinicians in the office setting evaluate whether a patient's symptoms are due to obstructive coronary artery disease (CAD).* Genes that are expressed in cells of the innate and adaptive immune systems were examined during the development of Corus CAD. The algorithm genes reflect cellular and molecular processes associated with:

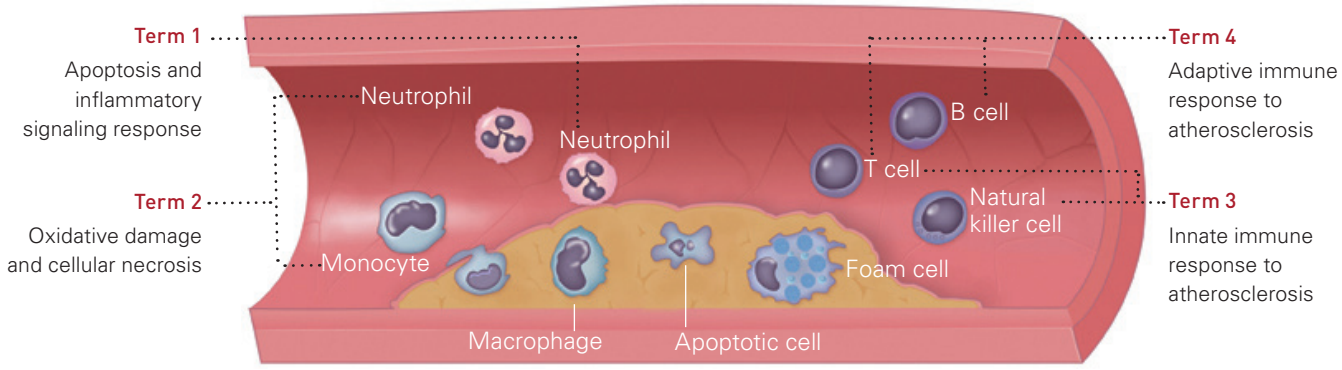
- Cellular apoptosis and necrosis
- Inflammatory cell migration into atherosclerotic plaque
- Innate and adaptive immune response to LDL oxidation and other inflammatory processes

The Corus CAD algorithm incorporates age, sex, and gene expression and was validated in the PREDICT and COMPASS multi-center studies.[1,2]

Algorithm Terms

The genes in the Corus CAD algorithm are grouped into six terms based on correlation of gene expression. The Corus CAD algorithm integrates age, sex, and gene expression to calculate a score. The complete algorithm generates a score that helps inform the clinician on the likelihood of obstructive CAD.

FIGURE 1: CORUS CAD GENE TERM SCHEMATIC



Term 1

This term contains genes that likely reflect increased neutrophil apoptosis (CASP5, TNFRSF10C),[3,4] activation of the interleukin-18 and anti-inflamatory signaling pathways (IL18RAP, TNFAIP6),[5,6] and other genes involved in the innate immune response and the recruitment of neutrophils to sites of inflammation (TLR4, IL8RB/CXCR2).[7,8,9]

Term 2

The main component of this term is comprised of three genes primarily found in granulocytes and neutrophils. Two of the genes (S100A12, S100A8)[10,11] have been implicated in coronary disease and cardiovascular events, and the third (CLEC4E)[12] has been shown to play a role in the surveillance of cellular necrosis.

(Continued on reverse)

*Obstructive coronary artery disease (CAD) is defined as at least one atherosclerotic plaque causing ≥50% luminal diameter stenosis in a major coronary artery (≥1.5mm lumen diameter) as determined by invasive quantitative coronary angiography (QCA) or core-lab computerized tomography angiography (CTA) (≥2.0mm lumen diameter).

Term 3

This term is comprised of two pairs of genes reflecting natural killer cell activation (SLAMF7, KLRC4)[13,14] normalized to genes expressed in T lymphocytes (TMC8, CD3D).[15,16]

Term 4

This term consists of two groups of genes reflecting levels of B (SPIB, CD79B)[17,18] and T lymphoctyes (TMC8, CD3D). The B to T cell ratio is likely sensitive to the presence of atherosclerosis.

Term 5

This term includes AF289562, a gene for which the underlying biology has yet to be determined. AF289562 is normalized to two genes (TFCP2, HNRPF) that are cell-type independent in their blood expression.

Term 6

This term consists of TSPAN16,[15] a gene for which the exact mechanism and associated biological pathways are unknown. TSPAN16 is normalized to two genes (TFCP2, HNRPF) that are cell-type independent in their blood expression. This term is used only in males.

For the Corus CAD Intended Use Statement please refer to www.cardiodx.com/corus-cad-intended-use

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CardioDx
600 Saginaw Drive
Redwood City, CA 94063
www.cardiodx.com

Customer Service
service@cardiodx.com
P 866.941.4996

Medical Affairs
medicalaffairs@cardiodx.com
P 866.941.4996

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