

In Focus: Immune Activation Biomarkers

Th1 Immune Activation Biomarkers: Neopterin & Quinolinate

Immune system activation is known to be involved in the progression of a vast number of diseases including well-known autoimmune disorders such as rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). Conditions underpinned by heightened immune activation also typically exhibit high levels of oxidative damage due to increased levels of hydrogen peroxide and reactive oxygen species resulting from the activation of macrophages.¹ The extent of immune activation often correlates with the severity or stage of disease.² It follows that biomarkers of cellular (Th1-type) immune activation are important in monitoring the extent of disease progression. Urinary neopterin and quinolinate are two non-invasive biomarkers of cell-mediated immune system activation to receive recent attention in the literature. Recent advances in bioanalytical methods have seen the evolution of assays of urinary neopterin and quinolinate amendable to routine use in the clinical laboratory.³

Neopterin

In chemical gobbledegook, neopterin is an aromatic pteridine derived from intracellular guanosine triphosphate (GTP) and released primarily by human macrophages and monocytes on stimulation by T-lymphocyte-derived interferon-gamma (IFN- γ). Urinary levels of neopterin have been shown to be elevated in numerous infectious, malignant and inflammatory disorders. Furthermore, levels of neopterin correlate with disease activity in rheumatic diseases including SLE, RA and Wegener granulomatosis.⁴⁻⁶ To review the findings of the study on patients with SLE, click the link below:

<http://www.pubmedcentral.nih.gov/picrender.fcgi?artid=1005067&blobtype=pdf>

Quinolinate

Similarly, in chemical gobbledegook, quinolinate is an endogenous N-methyl-D-aspartate (NMDA) receptor agonist synthesized from L-tryptophan via the kynurenine pathway. It has been shown to mediate NMDA neuronal damage and dysfunction. The kynurenine pathway is active in liver, macrophages and brain tissue. Similar to neopterin, IFN- γ is the primary inducer of quinolinate production. Quinolinate levels are increased in patients with central nervous system inflammatory diseases.⁷

IFN- γ the Common Link

The diagram below serves to illustrate the dual effects of IFN- γ on the enzymes indoleamine dioxygenase (IDO) and GTP cyclohydrolase-1 to produce end products quinolinate and neopterin respectively. The mechanism of activation of NMDA receptors by quinolinate is also shown.

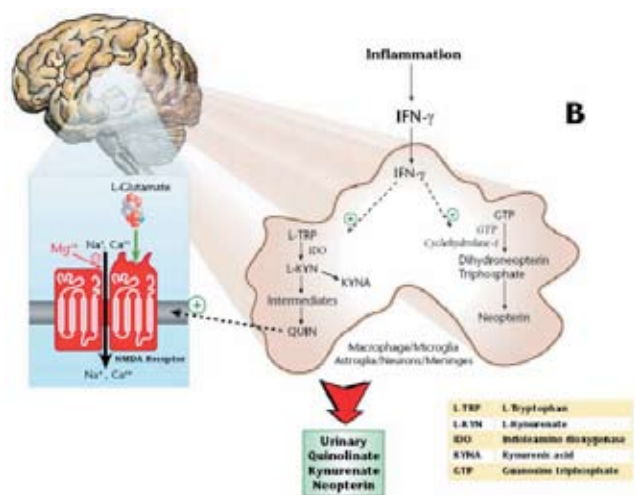


Figure 1. CNS Kynurenine Pathway Products (Figure adapted from: Lord RS, Bralley JA, eds. Laboratory Evaluations for Integrative and Functional Medicine. Duluth, GA: Metamatrix Institute; 2008.)

Simultaneous Neopterin & Quinolinic Acid Elevation

Combined elevations of neopterin and quinolinate have been found in conditions such as autism⁸, rheumatoid arthritis⁹ and juvenile idiopathic inflammatory myopathies¹⁰, where chronic inflammation is central to the etiology of the disease.

Immune Activation Assessment

Dual measurement of neopterin and quinolinate offer the clinician the ability to assess the degree of immune activation central to their patient's underlying conditions and treat accordingly. Because of quinolinate's action as an agonist for NMDA receptors of glutamatergic neurons, high levels signify neuronal degeneration. However, high levels of quinolinate can also indicate inflammatory bowel conditions as the gut is a frequent source of chronic inflammatory signal induction

via INF- γ .³

Neopterin on the other hand serves as an accurate broad-spectrum marker for monitoring cell-mediated (Th1-type) immune activation. Neopterin has been utilized as a marker in inflammatory conditions and a measure of immune system activation. Neopterin is elevated in infections; cardiovascular disease; autoimmune diseases; atopic asthma; malignant diseases; immunomodulatory treatment monitoring; psychiatric disorders; and sleep-disordered breathing.^{11, 12-17}

Neopterin & Quinolinate Unique to Metamatrix

Neopterin and quinolinate are markers that are both unique to Metamatrix. Neopterin can be ordered as part of the Neopterin/Biopterin profile (#0088), while quinolinate is part of both the Organix™ Comprehensive (#0091) and Organix™ Basic (#0291) profiles.

References

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