

## CLINICAL SPECIFICATIONS

### CITRULLINATED EBV

#### Pathogen Type:

Epstein-Barr virus (EBV) is a common virus from the herpes family. Citrullination or deimination is the conversion of the amino acid arginine in a protein into the amino acid citrulline. EBV infects the epithelial cells in the oropharynx and nasopharynx and hence is transmitted by the oral fluid.

#### Associated With:

Atherosclerosis<sup>1</sup>  
 Rheumatoid Arthritis<sup>2,3</sup>  
 Chronic inflammatory demyelinating polyneuropathy (CIDP)<sup>4</sup>  
 Multiple sclerosis<sup>5</sup>  
 Systemic lupus erythematosus<sup>6</sup>  
 Autoimmune thyroid disorders<sup>7</sup>

**Known Cross-Reactions:** Transaldolase,<sup>8</sup> lupus-associated antigen,<sup>9</sup> α-B crystallin,<sup>10</sup> HLA-DQw8β,<sup>11</sup> CYP2D6,<sup>12</sup> multiple food proteins<sup>13</sup>

#### Clinical Significance:

The detection of antibodies to Citrullinated EBV indicates the patient has increased risk of a variety of autoimmunities including joint, lupus, neurological, thyroid, and liver, and type 1 diabetes and multiple food immune reactivity. After reactivation of latent virus, EBV has been shown to encode an enzyme, deoxyuridine triphosphate nucleotidohydrolase (dUTPase), and this enzyme has been shown to induce peripheral blood monocytes to produce pro-inflammatory cytokines such as interleukin-6 as well as endothelial cell expression of intercellular adhesion molecule-1 (ICAM-1).<sup>1</sup> This can lead to acute coronary events. Rheumatoid arthritis patients appear to have elevated antibody levels to EBV,<sup>2,14</sup> yet the mechanism linking EBV pathogenesis in RA has not been elucidated.<sup>8</sup> Patients with CIDP show impaired B cell expression of the inhibitory Fcγ receptor (FcγRIIB), which alters the state of EBV persistence, leading to increased viral replication and antiviral immune responses.<sup>4</sup> Epidemiological studies suggest that childhood EBV exposure is an important determinant of MS risk.<sup>5</sup>

This array tests for IgG immune reactivity associated with Citrullinated EBV. This is not a measurement of acute infection. Equivocal or out-of-range results indicate IgG antibody reactivity to the tested antigen. We tested 288 blood donor sera against Citrullinated EBV antigens at optimal dilution, 6% of these donors were IgG reactive.

#### References:

- Binkley, et al. Evidence for the role of Epstein Barr virus infections in the pathogenesis of acute coronary events. *PLoS ONE*, 2013; 8(1):e54008.
- Panza, et al. Immunoglobulin G subclass profile of anticitrullinated peptide antibodies specific for Epstein Barr virus-derived and histone-derived citrullinated peptides. *J Rheumatol*, 2014; 41:407-408.
- Pratesi, et al. Deiminated Epstein-Barr virus nuclear antigen 1 is a target of anti-citrullinated protein antibodies in rheumatoid arthritis. *Arthritis Rheumatism*, 2006; 54(3):733-741.
- Lünemann, et al. Dysregulated Epstein-Barr virus infection in patients with CIDP. *J Neuroimmunol*, 2010; 218:107-111.
- Nociti, et al. Epstein-Barr virus antibodies in serum and cerebrospinal fluid from multiple sclerosis, chronic inflammatory demyelinating polyradiculoneuropathy and amyotrophic lateral sclerosis. *J Neuroimmunol*, 2010; 225:149-152.
- Gross, et al. EBV and systemic lupus erythematosus: a new perspective. *J Immunol*, 2005; 174:6599-6607.
- Janegova, et al. The role of Epstein-Barr virus infection in the development of autoimmune thyroid diseases. *Endokrynol Pol*, 2015; 66(2):132-136.
- Esposito, et al. Human transaldolase and cross-reactive viral epitopes identified by autoantibodies of multiple sclerosis Patients. *J Immunology*, 1999; 163:4027-4032.
- Pool, et al. Epstein-Barr virus and molecular mimicry in systemic lupus erythematosus. *Autoimmunity*, 2006; 39(1):63-70.
- van Sechel, et al. EBV-induced expression and HLA-DR-restricted presentation by human B cells of alpha B-crystallin, a candidate autoantigen in multiple sclerosis. *J Immunol*, 1999; 162(1):129-135.
- Fujiya, et al. Fulminant type 1 diabetes mellitus associated with a reactivation of Epstein-Barr virus that developed in the course of chemotherapy of multiple myeloma. *J Diabetes Investig*, 2010; 1(6):286-289.
- Bogdanos, et al. Virus/self double reactivity characterises the humoral immune response in autoimmune hepatitis-2. *J Hepatol*, 2000; 32(Suppl 2):45.
- Vojdani. Reaction of monoclonal and polyclonal antibodies made against infectious agents with various food antigens. *J Clin Cell Immunol*, 2015; 6:359. doi:10.4172/2155-9899.1000359
- Costenbader and Karlson. Epstein-Barr virus and rheumatoid arthritis: is there a link? *Arthritis Res Ther*, 2006; 8:204.