



## GlycA – A New Inflammation Marker

This new acute phase reactant marker can be more useful than hsCRP.

### Cogence Clinical Pearl

In this Cogence clinical pearl, we look at GlycA, a new, widely available marker of inflammation that is often elevated when hsCRP is normal.

#### *What the research says...*

This group of papers, from the *Journal of Translational Medicine*, *Circulation Research*, and *Journal of Crohn's and Colitis*, describe the importance of GlycA, a recently emerging marker of inflammation that may be quite useful in tracking the inflammatory process. These papers discuss its **application in patients with CVD, psoriasis, and IBD, showing up abnormal when the inflammation associated with autoimmune flares is activated, even when CRP levels are normal.** GlycA is elevated in both acute and chronic inflammation. Though the papers discuss particular diseases, GlycA is broadly applicable.

#### *Application...*

As you work with an autoimmune patient, you can use GlycA to assess the extent of inflammatory drive of their flare activation. When you combine this with other markers, like TGF $\beta$  and the wbc components of a cbc, you can begin to build a picture.

Remember that different patients with autoimmunity will have flares at different levels of inflammation, depending upon the mechanism of the flare and what parts of the biological dysfunction are driving symptoms, so you can't compare GlycA levels from one patient to another, to see whose flare is worse.

**It's also important to recognize that all of us and all of our patients will eventually die, most commonly from either cardiovascular disease or cancer of one form or another. Both of these diseases are fundamentally immunological. CVD is driven by inflammation and the clogging of arteries by foam cells that are specialized macrophages. Cancer surveillance depends on adequate Th1 cell activity. Th1 response is inhibited by inflammation, through the activity of MDSC's.**

So, tracking GlycA is important for autoimmune patients in connection with both their current status and also their long term trajectory.

#### *The Research...*

**GlycA, a novel biomarker of systemic inflammation and cardiovascular disease risk.**  
Connelly MA, Otvos JD, Shalurova I, Playford MP, Mehta NN. *J Transl Med.* 2017 Oct

27;15(1):219.

### **Abstract**

Background: GlycA is a novel spectroscopic marker of systemic inflammation with low intra-individual variability and other **attributes favoring its clinical use in patients with chronic inflammatory and autoimmune diseases**. GlycA is unique in its composite nature, **reflecting both increased glycan complexity and circulating acute phase protein levels during local and systemic inflammation**. Recent studies of GlycA from cross-sectional, observational and interventional studies have been highly informative, demonstrating that **GlycA is elevated in acute and chronic inflammation, predicts death in healthy individuals and is associated with disease severity in patients with chronic inflammatory diseases such as rheumatoid arthritis, psoriasis and lupus**. Moreover, following treatment with biological therapy in psoriasis, reduction in skin disease severity was accompanied by a decrease in GlycA levels and improvement in vascular inflammation. Conclusions: Collectively, these findings suggest GlycA is a marker that tracks systemic inflammation and subclinical vascular inflammation. However, larger prospective studies and randomized trials are necessary in order to assess the impact of novel therapies on GlycA in patients with chronic inflammatory conditions, which may be concomitant with cardiovascular benefits.

### **GlycA Is a Novel Biomarker of Inflammation and Subclinical Cardiovascular Disease in Psoriasis.**

Joshi AA, Lerman JB, Aberra TM, et al. *Circ Res*. 2016 Nov 11;119(11):1242-1253.

### **Abstract**

Rationale—GlycA, an emerging inflammatory biomarker, predicted cardiovascular events in population-based studies. **Psoriasis, an inflammatory disease associated with increased cardiovascular risk**, provides a model to study inflammatory biomarkers in cardiovascular disease (CVD). Whether GlycA associates with psoriasis and how it predicts subclinical CVD beyond hsCRP in psoriasis is unknown.

Objective—To investigate the relationships between GlycA and psoriasis, and between GlycA and subclinical CVD.

Methods and Results—Psoriasis patients and controls (n=412) participated in a two-stage study. We measured GlycA by NMR spectroscopy. NIH participants underwent 18-FDG PET/CT scans to assess vascular inflammation (VI) and coronary CT angiography to quantify coronary artery disease (CAD) burden. Psoriasis cohorts were young (mean age=47.9), with low cardiovascular risk and moderate skin disease. HsCRP and GlycA were increased in psoriasis compared to controls [GlycA: (PENN: 408.8±75.4 vs. 289.4±60.2, p<0.0001, NIH: 415.8±63.2 vs. 346.2±46, p<0.0001)] and demonstrated a dose-response with psoriasis severity. In stage 2, VI ( $\beta=0.36$ , p<0.001) and CAD ( $\beta=0.29$ , p=0.004) associated with GlycA beyond CV risk factors in psoriasis. In ROC analysis, GlycA added value in predicting VI (p=0.01) and CAD (p<0.01). Finally, initiating anti-TNF therapy (n=16) reduced psoriasis severity (p<0.001), GlycA (463.7±92.5 vs. 370.1±78.5; p<0.001) and VI (1.93±0.36 vs. 1.76±0.19; p<0.001), while GlycA remained associated with VI ( $\beta=0.56$ , p<0.001) post-treatment.

**Conclusions—GlycA associated with psoriasis severity and subclinical CVD beyond traditional CV risk and hsCRP. Moreover, psoriasis treatment reduced GlycA and VI. These findings support the potential utility of GlycA in subclinical CVD risk assessment in psoriasis and potentially other inflammatory diseases.**

### **GlycA, Nuclear Magnetic Resonance Spectroscopy Measure for Protein Glycosylation, is a Viable Biomarker for Disease Activity in IBD.**

Dierckx T, Verstockt B, Vermeire S, van Weyenbergh J. *J Crohns Colitis*. 2019 Mar 26;13(3):389-394.

### **Abstract**

Background and Aims: Glycoprotein acetylation [GlycA] is a novel nuclear magnetic resonance

[NMR] biomarker, measured in serum or plasma, that summarizes the signals originating from glycan groups of certain acute-phase glycoproteins. This biomarker has been shown to be robustly associated with cardiovascular and short-term all-cause mortality, and with disease severity in several inflammatory conditions. **We investigated GlycA levels in a cohort of healthy individuals [HCs], patients with Crohn's disease [CD] and patients with ulcerative colitis [UC] prior to and after therapeutic control of inflammation...**

Results: **GlycA levels were significantly higher in patients with active inflammatory bowel disease [IBD] compared with those in healthy controls, and accurately reflected the mucosal recovery to a 'healthy' state in both CD and UC patients achieving mucosal healing.** In CD patients who experienced an endoscopic response without achieving full mucosal healing, GlycA levels also decreased but did not normalize to HC levels. Overall, **GlycA correlated well with CRP and fCal, and accurately tracked disease activity in CRP-negative patients [ $<5$  mg/dL].**

Conclusion: **GlycA holds promise as a viable serological biomarker for disease activity in IBD, even in patients without elevated CRP, and should therefore be tested in large prospective cohorts.**