

Calprotectin

The superior inflammatory biomarker

Calprotectin is well known within the gastroenterology world as a non-invasive biomarker for active disease in patients with Inflammatory Bowel Disease (IBD). Its use, however, is not limited to differential diagnosis and follow-up of IBD patients; it is a general biomarker that has gained a lot of increased focus within research and drug development in the past decades, challenging traditional inflammatory biomarkers such as C-Reactive Protein (CRP).

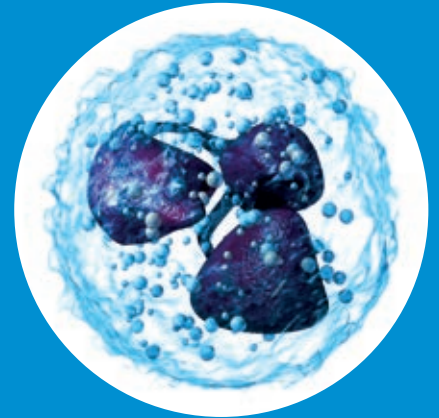
What is calprotectin?

Calprotectin belongs to a family of calcium-binding S100 proteins consisting of subunits of S100A8 and S100A9. Discovered and characterized in the 1980s, it was named “calprotectin” to reflect its calcium-binding properties as well as its anti-fungal and anti-microbial properties. It is also known as MRP8/14, Calgranulin A, leukocyte protein L1, and with other lesser common names within the literature.

Calprotectin is expressed in a variety of cells, and neutrophils stand out in this regard, where it makes up 45%-60% of their cytosolic protein content. Numerous studies show how calprotectin is involved in various intra and extracellular processes and that it is found in much higher concentrations in extracellular compartments and bodily fluids during infections and inflammations due to neutrophil activation and turnover. Neutrophils are one of the initial cells to respond to inflammation and infections in our body. Upon activation, the neutrophils will migrate to the site of inflammation or infection, where they will also release calprotectin into their surrounding environment, and the calprotectin concentration will therefore reflect the number of neutrophils activated.

Calprotectin is a general biomarker, as it becomes apparent from the above rationale: an increase in neutrophil activity will result in increased calprotectin concentration in a given matrix (blood, urine, CFS, etc.), and since neutrophils are a part of the innate immune response and general, the biomarker will also be general. Despite this, calprotectin has mainly been used by gastroenterologists in the diagnosis and follow-up of IBD patients. In the past 10-15 years, however, there has been an increase in interest in using calprotectin as a biomarker in studies centered around both acute and chronic inflammatory indications such as sepsis, Covid-19, various forms of arthritis, vasculitis, bacterial infections, SLE, and others. As calprotectin can be detected in various bodily fluids, it is also very versatile and easier to use in organ-specific indications by selecting a suitable sample.

Another thing that makes Calprotectin stand out is its stability and robustness. Its stability is clearly shown within the gastroenterology field, where stool samples stored at room temperature have stable calprotectin levels up to 5 days after collection.



DID YOU KNOW?

Calprotectin is:

- Naturally and abundantly occurring protein in neutrophils
- Released upon neutrophil activation, making it less prone to be affected by drugs
- A general biomarker for bacterial/fungal infection and inflammation
- Found in most bodily fluids
- Detectable earlier than CRP, and also has a shorter half-life, thus giving a closer to real-time indication of ongoing inflammation

Calprotectin or CRP?

CRP is by far the most common general inflammatory biomarker used in both clinical settings as well as in research and trials. In many ways, calprotectin has the same usage, but several studies have pointed out the differences between the two. Below are a few important highlighted differences:

	CRP	Calprotectin
Detection time during inflammation	6-9 hrs, peaks at 48 hrs	<3 hrs
Half-life in serum/ circulation	19 hrs	5 hrs
Site of production	Hepatocytic cells	Released from neutrophils upon activation
Synthesis/release signal	Cytokines for synthesis signalling	Neutrophil activation

Several studies comparing calprotectin and CRP in patient samples with various arthritic conditions also highlight the calprotectin's ability to differentiate low and no disease activity, which is somewhat more difficult to do with CRP, especially when the patient is treated with biological drugs. This difference might potentially be due to the biological drugs targeting cytokines associated with inflammation that are also involved in CRP propagation.

Calprotectin: the ideal biomarker for complement-based indications

The complement cascade is an integral part of our defense against pathogens, interacting with both the innate and adaptive parts of the immune system. In this, it has three major tasks: formation of the membrane attack complex, opsonization, and promoting inflammation through its anaphylatoxins.

The latter is mainly done by C5a, and it has been reported that neutrophils are activated by C5a resulting in increased membrane elasticity and cell size, making it possible for them to migrate and invade the site of inflammation and clear pathogens and molecular debris.

The connection between neutrophils and calprotectin is also well established: Activated neutrophils will release calprotectin during phagocytic activity as well as due to neutrophilic cell death, releasing calprotectin into the intracellular space. Increased calprotectin, therefore, is a good biomarker of neutrophil activation and, by extension, also for complement activation.

As the release and build-up of calprotectin results in a shorter cascade compared to CRP as it does not require any synthesis, and it has a significantly lower half-life, and is less prone to interference from potential drug candidates, calprotectin can easily be seen as an inflammatory biomarker suitable and ideal for academic research and clinical stages of drug development process.

Recommended reading

Wang *et al.* Front Immunol. 2018, 9:1298
Pruenster *et al.* Pharmacol Ther. 2016, 167:120-31
Hetland *et al.* Mol Pathol. 1998, 51(3):143-8

Our Calprotectin and Complement Solutions

Calpro is a world-leading provider of Calprotectin tests. Our aim is to provide solutions that are effective and user-friendly without compromising on the quality.

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Svar offers functional and biomarker assays that can be used to explore every angle of complement system involvement in a wide range of application areas.

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