To evaluate the inflammatory response and distinghuish between autoinflammation and pathogen induced inflammation we offer quantification of the following biomarkers from blood samples requested (heaprinized and EDTA-anticoagulated whole blood (PB) or bone marrow (BM)), as well as cerebrospinal fluid (CSF) or other body fluids such as bronchial lavage (BAL), ascites (ASC), pleural excudate, etc.

Data are availabe within **2h** after receiving the blood sample due to rapid analysis by SIEMENS Immulite<sup>®</sup> highly sensitive chemiluminescent based ELISA. Best interpretation of the biomarker profiling can be done with the results of the immune phenotype (vailable on the next day after receiving the blood sample).

• LBP: lipopolysaccharide binding protein

LPS-binding protein (LBP) is a 481-amino-acid acute phase protein binding to lipopolysaccharide (LPS) derived from Gram-negative bacteria. LBP-LPS complexes improve interaction with CD14 and TLR4 activation (see cartoon on the right). Similarly, LBP can also complex lipoteichoic acid (LTA), peptidoglycan and lipopeptides and transfer them to CD14, suggesting that LBP may assist not only in the function of TLR4, but also in the function of TLR1, TLR2 and TLR6.



- **IL-1β** plays a major role to judge the activation of the inflammasome, associated with caspase 1 activation and release of pro-IL-1β from antigen presenting cells.
- **IL-6** is active as a B-cell stimulating cytokine, acute phase response cytokine and follows pathogen as well as autoinflammatory processes
- IL-8 is a major indicator of NFkB-activatied inflammation and toxicities
- **IL-10** is T-cell cytokine, an inhibitor of inflammation, often related to reactivation of Epstein Barr virus (EBV) and linked to downregulation of HLA-class II in monocytes (see immune phenotype analysis)
- **Ferritin** is also an indicator of inflammtion and infection as well as liver cell decay if not related to ion overload. Macrophages and liver cells may secrete ferritin into the blood.
- **Erythropoietin** indicates stimulated erythropoiesis due to bleeding of erythro-hemophagocytosis in the bone marrow
- sCD25 is the soluble form of the high affinity IL-2receptor, non-specifically released by massive T cell activation (often related to virus infections), by malignant T cells, as well as by hemophagocytes in a rare disease called hemophagocytic lymphohistiocytosis (HLH). sCD25 is higher in young children and plasma concentrations decrease with age and lymphopenia. Increased sCD25 is also a biomarker for macrophage activation syndromes in juvenile rheumatoid arthritis as well as sarcoidosis and during septic shock in intensive care patients.
- TNF-α is a product of monocytes and macrophages as well as lymphocytes and extremely elevated plasma concentrations may be related to insufficient concentrations of soluble TNFreceptors type I and type II (CD120a, CD120b), moerate elevations are related to inflammation and infections as well as relative increases of monocytes (see immune phenotype)