CXCL9, a promising biomarker in the diagnosis of chronic Q fever

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Background: In the aftermath of the largest Q fever outbreak in the world, diagnosing the potentially lethal complication chronic Q fever remains challenging. Chronic Q fever is a persistent infection of aneurysms, aortic prosthesis or heart valves with the Gram-negative bacterium Coxiella burnetii. Laboratory investigations, such as PCR on blood, lack sensitivity and there is no agreement on cut-off values for anti-C. burnetii phase I IgG titers. Monitoring chronic Q fever during treatment is at least equally difficult and currently, treatment decisions are based on changes in IgG phase I titers and alterations in FDG-avidity of the lesion on a PET/CT. Because there is little evidence for treatment decisions based on IgG phase I titers, there is a need for additional biomarkers to diagnose and monitor chronic Q fever.
**Material/methods:** We performed a transcriptome analysis on *C. burnetii* stimulated peripheral blood mononuclear cells (PBMCs) of 4 healthy controls and 6 chronic Q fever patients and identified the genes that were most differentially expressed. These gene products were determined using Luminex technology in whole blood samples cultured with heat-killed *C. burnetii* and in serum samples of chronic Q fever patients and control subjects.

**Results:** Gene expression of chemokines CXCL9, CXCL10, CXCL11 and CCL8 was strongly upregulated in *C. burnetii*-stimulated PBMCs of chronic Q fever patients, in contrast to healthy controls. In whole blood cultures of chronic Q fever patients (n=36), all four chemokines were increased upon *C. burnetii* stimulation, but also healthy controls (n=15) and past Q fever infected individuals (n=20) showed increased production of CXCL9, CXCL10 and CCL8. However, CXCL9 and CXCL11 production were significantly higher for chronic Q fever patients compared to past Q fever infected individuals. In addition, CXCL9 serum concentrations of chronic Q fever patients (n=51) were higher than serum concentrations of past Q fever individuals (n=10). There was no relation between chemokine concentration and treatment duration.

**Conclusions:** CXCL9 is a promising biomarker for diagnosis of chronic Q fever and suitable for measurement of host response induced by *C. burnetii*.