IVD.03 - Computational identification of *Coxiella burnetii* non-conserved B-cell epitopes: a rational strategy for Q fever diagnosis

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Introduction: *Coxiella burnetii* is the etiological agent of the zoonosis Q fever, a neglected disease which causes an acute or a chronic, life-threatening disease in humans. In its late course, Q fever can be complicated by fatal (eg, endocarditis) or debilitating (eg, chronic fatigue syndrome) disorders. Ruminants are considered as the main reservoirs for human infections but are usually asymptomatic or may manifest as late term abortions and therefore have significant economic impact. *C. burnetii* presents a highly stable and infectious cell form, which persists in the environment and is transmitted via inhalation of aerosols and/or consumption of contaminated milk. Q fever infection is most commonly diagnosed by serology tests but due to its impaired sensitivity, reliable clinic and veterinary diagnostic tests need to be developed. In this sense, recent immunoproteomic studies identified several proteins, which presented reactivity against *sera* from Q feverpatients, and are potential candidates for the development of new diagnostic tests.

Objective: To identify, through a combination of prediction algorithms, immunogenic and non-conserved B-cell epitopes present on *Coxiella burnetii* immunoreactive proteins (outer membrane protein A, YAJc and LemA).

Methodology: FASTA sequences of outer membrane protein A (ompA;CBU-1260), YAJc (yajC;CBU-1143) and LemA (lemA;CBU-0545) from *C. burnetii* were obtained from UNIPROT. The B-cell epitope prediction was carried out using two different algorithms, BepiPred and BCPred (threshold 0.5), whereas surface accessibility was predicted by Emini Surface Accessibility algorithm (threshold 1.0). We considered a potential B-cell epitope, sequences predicted by 2 or more algorithms that comprises, at least, 9 mers of length. Thereafter, the immunogenic potential from B-cell sequences were predicted by Vaxijen algorithm (threshold 0.4). The degree of sequence conservation between immunogenic B-cell epitopes and other *C.burnetii* related species (*Francisella tularensis, Legionella pneumophila, Escherichia coli, Pseudomonas aeruginosa, Campylobacter jejuni, Rickettsia rickettsia, Ehrlichia chaffeensis, Bartonella henselae, Brucella melitensis, Afipia felis*) were compared using protein BLAST databank.

Results: Combining different prediction algorithms, we described four B-cell epitopes present on OMP-A (OMP-AE1, OMP-AE2, OMP-AE3 and OMP-AE4). OMP-AE1 and OMP-AE2 appears as two potential highly immunogenic B-cell candidates (Vaxijen score: 1.2 and 2.1, respectively), both with a low degree of sequence conservation (E-value >20), whereas OMP-AE3 and OMP-AE4 were predicted as B-cell sequences poorly immunogenic (Vaxijen score: 0.3 and 0.01, respectively). YAJc and LemA possess potential B-cell epitopes (YAJ-E01, LEM-E01 and LEM-E02; Vaxijen score: 1.2, 1.5 and 1.1, respectively), but although highly immunogenic, the predicted sequences are highly conserved (E-value < 1) among phylogenetic *C. burnetii* related species.

Conclusion: Taken together, our *in silico* analysis suggests that OMP-AE1 and OMP-AE2, present on protein OMP-A, are potential highly immunogenic B-cell epitopes specific to *Coxiella burnetii* and could be used for development of Q fever diagnosis.

Keywords: B-Cell epitopes; Zoonosis; *Coxiella burnetii*