Proteome-wide Analysis of *Coxiella burnetii* for Conserved T-cell epitopes with Presentation Across Multiple Host Species

Lindsay M.W. Piel1, Codie J. Durfee1, Stephen N. White1,2,3

1 USDA-ARS Animal Disease Research Unit, Pullman, WA 99164, USA

2 Department of Veterinary Microbiology & Pathology, Washington State University, Pullman, WA 99164, USA

3 Center for Reproductive Biology, Washington State University, Pullman, WA 99164, USA

Correspondence: Stephen.White@usda.gov

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Locus Tag (Gene Name)** | **Species** | **Epitopes Found** | **Experimental Process** | **Epitope****Type** | **Ref.** |
| **CBU\_00771** | Human | 203-LTLLLNWVNY-212 | Bioinformatic Screening with IFN-γ Recall Production | MHCI | (1) |
| **CBU\_00921** **(*ybgF*)** | Murine | 185-LLTKKQYDKAQASFQ-199 | Immunologic Response in Immunized Mice | MHCII | (2) |
|  | Human |  | Serology against Protein Microarray | B-cell | (3) |
|  | Human | 196-ASFQNYLNDY-205 | Bioinformatic Screening with IFN-γ Recall Production | MHCI | (1) |
| **CBU\_01091\***  | Human |  | Serology against Protein Microarray | B-cell | (3) |
|  | Human | 247-SPAVLSAAKKIFGDGA-262105-KTFVYPMGLY-114 | Bioinformatic Screening with IFN-γ Recall Production | MHCII/I | (1) |
| **CBU\_03071**  | Murine | 146-GKLGVAYTYNRANAG-160 | Immunologic Response in Immunized Mice | MHCII | (2) |
|  | Human |  | Serology against Protein Microarray | B-cell | (4) |
|  | Human | 149-GVAYTYNRANAGLPTNK-165202-VPGYRNASSKRFVAP-216 | Bioinformatic Screening with IFN-γ Recall Production | MHCII | (1) |
|  | Goat &Human |  | Meta-analysis with Goat and Human Serology Testing | B-cell | (5) |
| **CBU\_03111**  | Murine | 70-PVSASITQFGPVGEL-84 | Immunologic Response in Immunized Mice | MHCII | (2) |
|  | Murine |  | IFN-γ and Antibody Production | B-cell | (6) |
| **CBU\_05451****(*lemA*)** | Human |  | Serology against Protein Microarray | B-cell | (3, 4) |
| **CBU\_06121** **(*ompH*)** | Human | 41-IKDINTRLEK-5076-DEAVMGKKEAENLR-8990-KEIQNDESTLRQQQQQ-105123-SKVNGAVKRVAE-134 | Bioinformatic Analysis  | MHCI/I/II/I | (7) |
|  | Murine | 13-VAMIWSVAAVAQTVG-27 | Immunologic Response in Immunized Mice | MHCII | (2) |
|  | Human |  | Serology against Protein Microarray | B-cell | (3, 4) |
| **CBU\_06301\*** **(*fkpA*)** | Murine | 159-FDSSYKRGQPATFPL-173 | Immunologic Response in Immunized Mice | MHCII | (2) |
|  | Murine |  | Protection from *C. burnetii* Infection using Antigen Stimulated BMDC | MHCII | (8) |
|  | Human |  | Serology against Protein Microarray | B-cell | (3) |
| **CBU\_07181** | Human | 21-VAKLRGDLSSIIHKL-3528-LSSIIHKLTSFSKTEA-43 | Bioinformatic Screening with IFN-γ Recall Production | MHCII | (1) |
|  | Goat &Human |  | Meta-analysis with Goat and Human Serology Testing | B-cell | (5) |
| **CBU\_07541** | Human |  | Serology against Protein Microarray | B-cell | (4) |
| **CBU\_08911** | Human |  | Serology against Protein Microarray | B-cell | (3, 4) |
|  | Goat &Human |  | Meta-analysis with Goat and Human Serology Testing | B-cell | (5) |
| **CBU\_09681\*** | Human | 144-AENVLIIHNKTLAHRYLA-161 | Bioinformatic Screening with IFN-γ Recall Production | MHCII | (1) |
| **CBU\_11431****(*yajC*)** | Human |  | Serology against Protein Microarray | B-cell | (3, 4) |
|  | Human | 94-GTEITVQKASIASVLPK-110 | Bioinformatic Screening with IFN-γ Recall Production | MHCII | (1) |
| **CBU\_11571** | Murine | 88-PWRYIRSFPILASSG-102133-LSLMLNYPNSADRYY-147202-DLRYHAPIYGAVHPR-216 | IFN-γ and Antibody Production | MHCII& B-cell | (6) |
|  | Human | 130-RFDLSLMLNYPNSADRY-146 | Bioinformatic Screening with IFN-γ Recall Production | MHCII | (1) |
| **CBU\_12601** | Human | 178-LPPVTSSVAVKVPSS-192 | Bioinformatic Screening with IFN-γ Recall Production | MHCII | (1) |
| **CBU\_18531\*** | Human |  | Serology against Protein Microarray | B-cell | (4) |
| **CBU\_18691** | Human |  | Serology against Protein Microarray | B-cell | (4) |
|  | Human | 200-GKHFDGIKVLKLSPQNTI-217 | Bioinformatic Screening with IFN-γ Recall Production | MHCII | (1) |
|  | Murine |  | IFN-γ and Antibody Production | B-cell | (6) |
| **CBU\_19101** **(*com1*)** | Human | 59-QKKTEAQQEEHAQQAIKEN-77121-VKQNKNLRV-129214-QLAGTPTFVI-223 | Bioinformatic Analysis | MHCII/I/I | (7) |
|  | Murine | 42-HYLVNHPEVLVEASQ-56 | Immunologic Response in Immunized Mice | MHCII | (2) |
|  | Murine |  | Protection from *C. burnetii* Infection using Antigen Stimulated BMDC  | MHCII | (8) |
|  | Murine | 42-HYLVNHPEVLVEASQ-5680-KLFNDPASPVAGNPH-94 | IFN-γ and Antibody Production  | MHCII & B-cell | (6) |
|  | Human |  | Serology against Protein Microarray | B-cell | (3) |
|  | Human | 218-TPTFVIGNKALTKFGF-23397-VTLVEFFDY-10534-KDIQSIVHHY-43 | Bioinformatic Screening with IFN-γ Recall Production | MHCII/I/I | (1) |
| **CBU\_19431\*****(*atpA*)** | Goat &Human |  | Meta-analysis with Goat and Human Serology Testing | B-cell | (5) |
| **CBU\_19671** | Human |  | Serology against Protein Microarray | B-cell | (4) |
| **CBU\_20651** | Human |  | Serology against Protein Microarray | B-cell | (4) |
| **CBU\_02292\*****(*rplL*)** | Human |  | Serology against Protein Microarray | B-cell | (3) |
|  | Human | 71-KIGVIKAIRTITGLGLKEA-89 | Bioinformatic Screening with IFN-γ Recall Production | MHCII | (1) |
| **CBU\_03832****(*tag*)** | Murine | 74-RDSFNNFDASIISKY-88 | IFN-γ and Antibody Production  | MHCII& B-cell | (6) |
|  | Goat &Human |  | Meta-analysis with Goat and Human Serology Testing | B-cell | (5) |
| **CBU\_12002****(*icd*)** | Human | 139-LRPVRYFTGVPSPVKTPE-156 | Bioinformatic Screening with IFN-γ Recall Production | MHCII | (1) |
| **CBU\_13982\*****(*sucB*)** | Human |  | Serology against Protein Microarray | B-cell | (3, 4) |
|  | Human | 231-RLGFMSFFTKAVVEALKRF-249382-REAVLFLVTIKELLEDP-398 | Bioinformatic Screening with IFN-γ Recall Production | MHCII | (1) |
|  | Goat &Human |  | Meta-analysis with Goat and Human Serology Testing | B-cell | (5) |
| **CBU\_14162** | Human | 74-IARYFMVNISQLIGEE-89 | Bioinformatic Screening with IFN-γ Recall Production | MHCII | (1) |
| **CBU\_15132\*** | Human |  | Serology against Protein Microarray | B-cell | (3) |
|  | Human | 137-QGHIINIGSISSHQV-151208-EAVYKGFTPLKAEDIAEA-225 | Bioinformatic Screening with IFN-γ Recall Production | MHCII | (1) |
|  | Goat &Human |  | Meta-analysis with Goat and Human Serology Testing | B-cell | (5) |
| **CBU\_16452****(dotB)** | Murine | 193-YDSLTTPTASVCQSE-207269-RLVGSFPAEERIGRT-283 | IFN-γ and Antibody Production  | MHCII & B-cell | (6) |
| **CBU\_17062\*** | Goat &Human |  | Meta-analysis with Goat and Human Serology Testing | B-cell | (5) |
| **CBU\_17162\*****(gcvT)** | Human | 373-KIPVKIIKPPFVRRG-387 | Bioinformatic Screening with IFN-γ Recall Production | MHCII | (1) |
| **CBU\_17182\*****(groEL)** | Murine | 474-DVNYGYNAATGEYGD-488 | Immunologic Response in Immunized Mice | MHCII | (2) |
|  | Goat &Human |  | Meta-analysis with Goat and Human Serology Testing | B-cell | (5) |
| **CBU\_17192\*****(groES)** | Human |  | Serology against Protein Microarray | B-cell | (3) |
| **CBU\_18352** | Human | 291-PDYVLNAVNHIRYKP-305416-MMEHLQNITNLVSTGRQGA-434 | Bioinformatic Screening with IFN-γ Recall Production | MHCII | (1) |
| **CBU\_00083\*** | Murine |  | IFN-γ and Antibody Production | B-cell | (6) |

1. Scholzen A, Richard G, Moise L, Baeten LA, Reeves PM, Martin WD, et al. Promiscuous Coxiella burnetii CD4 Epitope Clusters Associated With Human Recall Responses Are Candidates for a Novel T-Cell Targeted Multi-Epitope Q Fever Vaccine. Front Immunol. 2019;10:207.

2. Xiong X, Qi Y, Jiao J, Gong W, Duan C, Wen B. Exploratory study on Th1 epitope-induced protective immunity against Coxiella burnetii infection. PLoS One. 2014;9(1):e87206.

3. Vigil A, Ortega R, Nakajima-Sasaki R, Pablo J, Molina DM, Chao CC, et al. Genome-wide profiling of humoral immune response to Coxiella burnetii infection by protein microarray. Proteomics. 2010;10(12):2259-69.

4. Beare PA, Chen C, Bouman T, Pablo J, Unal B, Cockrell DC, et al. Candidate antigens for Q fever serodiagnosis revealed by immunoscreening of a Coxiella burnetii protein microarray. Clin Vaccine Immunol. 2008;15(12):1771-9.

5. Miller HK, Kersh GJ. Analysis of recombinant proteins for Q fever diagnostics. Sci Rep. 2020;10(1):20934.

6. Chen C, Dow C, Wang P, Sidney J, Read A, Harmsen A, et al. Identification of CD4+ T cell epitopes in C. burnetii antigens targeted by antibody responses. PLoS One. 2011;6(3):e17712.

7. Jaydari A, Forouharmehr A, Nazifi N. Determination of immunodominant scaffolds of Com1 and OmpH antigens of Coxiella burnetii. Microb Pathog. 2019;126:298-309.

8. Xiong X, Meng Y, Wang X, Qi Y, Li J, Duan C, et al. Mice immunized with bone marrow-derived dendritic cells stimulated with recombinant Coxiella burnetii Com1 and Mip demonstrate enhanced bacterial clearance in association with a Th1 immune response. Vaccine. 2012;30(48):6809-15.