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Systems biology and bioinformatics help decipher *Brucella* antigens involved in clinical manifestation of the disease

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A commentary on

Antigen-specific acquired immunity in human brucellosis: implications for diagnosis, prognosis,and vaccine development *by Cannella, A. P., Tsolis, R. M., Liang, L., Felgner, P. L., Saito, M., Sette, A., Gotuzzo, E., and Vinetz, J. M. (2012) Front. Cell. Inf. Microbio. 2:1. doi: 10.3389/fcimb.2012.00001*

Brucellosis, induced by Gram negative bacteria of genus *Brucella*, is one of a few severe zoonoses with worldwide distribution. *Brucella* species are partly characterized by their association with a natural host in which they cause last trimester abortions. The *Brucella* infection of domestic animals (e.g., small ruminants, cattle, and swine) facilitates the spread of the disease in nature and becomes an important factor in sustaining a poor socio-economic standard of living in nomadic populations. Nowadays classification studies have led to the identification of novel species such as *B. microti* in common voles and red foxes and in soil. The discovery of these *Brucella* strains has challenged the traditional *Brucella* taxonomy and minimal standards that characterize the genus members and distinguish them from closer relatives such as *Ochrobactrum* spp. Given the unappreciated zoonotic potential of brucellosis, debates emerge on the relevance that clinical manifestation may play in classifying a newly identified isolate into the genus *Brucella*.

Cannella et al. (2012) published an article in this issue that aims at identifying serum antibodies associated with clinical manifestation of human brucellosis. They hypothesized that these antibodies can predict potential *Brucella* antigenic candidates, and may also have diagnostic, prognostic, and vaccine value. The authors also predicted that by elucidating the antibody profiles of groups of people (including *Brucella* culture or Rose Bengal assay positive or negative patients, or a naïve population from *Brucella*-free regions), without knowing specific infection details, common *Brucella* antigens significant in the clinical manifestation of the disease would be revealed. Based on this hypothesis, many *Brucella* proteins, including the Type IV secretion system protein VirB8 (Table 1) and VirB5 (Table 3), Outer membrane lipoproteins Omp10, Omp16, and Omp19 (Table 1), and iron metabolism protein Bacterioferritin, were identified to generate antigen-specific antibody immune responses and could be used as potential diagnosis markers or vaccine targets.

This approach assumes that the immune system would respond by a similar antibody repertoire in correlation with a manifested clinical situation. Using a proteome microarray expressing nearly all *B. melitensis* genes, such a systems biology method systematically analyzes *Brucella* antibody profiles of human sera in response to physiological and environmental cues.

We believe classical bacteriology, biochemistry, cell biology, and immunology still remain critical disciplines for understanding basic variables affecting host pathogen interactions. Systems biology and bioinformatics have emerged as tools in this field, thereby assisting the continuous cross-talk between researchers in different disciplines and guiding future developments in control and eradication of the disease. Intriguingly, the new tools are not only valuable in clinical studies but also in epidemiological, epizootic, and ecological studies. Computational progress and development of new algorithms could thus be envisioned as an integral part of the new world.

REFERENCE

Cannella, A. P., Tsolis, R. M., Liang, L., Felgner, P. L., Saito, M., Sette, A., Gotuzzo, E., and Vinetz, J. M. (2012). Antigen-specific acquired immunity in human brucellosis: implications for diagnosis, prognosis,and vaccine development. *Front. Cell. Inf. Microbio.* 2:1. doi: 10.3389/fcimb.2012.00001

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