MOLECULAR MIMICRY OF BRUCELLA MELITENSIS EPITOPES IN MOUSE AND HUMAN ARTHRITIS

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Introduction. Brucellosis is one of the most frequent zoonosis worldwide. Infection is transferable to humans, where brucellosis is associated with high incidence of osteoarticular disease including osteomyelitis, arthritis and spondyloarthritis. Peripheral arthritis and sacroiliitis often develop in patients with no or low count of live Brucella. Recently, we demonstrated that mice develop spontaneous arthritis several weeks after acute infection when bacteria are already eradicated. We aim to decipher immune mechanism of the brucellosis-associated delayed arthritis that has not been elucidated so far.

Materials and methods. Protein multi-sequence BLAST tuned for a perfect similarity of short sequences and implemented in Geneious software was used. Primary sequences of arthritogenic bacteria of *Brucella, Salmonella, Micobacteria, Klebsialla, Caprilobacter, Yershinia* and *Shigella* species were retrieved from NCBI database along with mouse and human host sequences. BALB/c female mice were immunized subcutaneously with 25 microgram peptide in 100 microliters complete Freund's adjuvant. Two weeks later, mice received boost immunization of same peptide in incomplete Freund's adjuvant. Mice were visually scored for paws" redness and edema (arthritis).

Results and discussion. Using murine models of brucellosis, immunodominant cytotoxic T cell epitope RYCINSASL derived from *Brucella melitensis* has been recently reported by Prof. Gary Splitter group (University Wisconsin Madison, USA). Using protein BLAST, we found that this epitope is extremely conservative among species and also homologous to both human and mouse hosts sequences. Some amino acid changes are conservative and do not change amino acid class. Additionally, we analyzed proteolytic cleavage prediction for MHC class I peptides in mice and in humans, and we found that generation of similar peptide by human proteasome machinery is feasible. We designed a set of bacteria/ human peptides to study their binding kinetics with HLA-B*2705 molecule, the MHC class I haplotype that most strongly associates with reactive arthritis and spondyloarthritis. To parallel human and mouse diseases, we immunized BALB/c females with RYCINSASL peptide and directly demonstrated its arthritogenic potential in rodents.

Conclusions. We showed that immunodominant epitope is able to induce arthritis in mice. Using bioinformatics approaches, we showed (i) the epitope conservancy among humans and arthritogenic bacteria, and (ii) plausibly correct protein processing in human class I proteasome pathway, and (iii) binding potential of the epitope towards the HLA-B*B27 class I molecule leading to antigen presentation for cytotoxic T cells.

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