

Effect of dietary shifts on infection progression and immune response in rabbits challenged with *Mycobacterium avium* subspecies *paratuberculosis*

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Introduction: The relation between nutrition and immunity has been accepted long ago. Diet can actively influence the immune system. The highest number of immune cells are located in the gut making it the largest immune organ in the body. We hypothesize that paratuberculosis, a gastrointestinal disease produced by *Mycobacterium avium* subspecies *paratuberculosis* (MAP) maybe influenced by dietary components. Recent studies carried out by our group have shown that MAP infection progression may be modulated by short term dietary changes during challenge with MAP in laboratory rabbits. In this case, our intention is to evaluate the effect of long term diet changes in the establishment of MAP infection in rabbits with special attention on the gut associated lymphoid tissue (GALT) in the rabbit model.

Aims and Methods: New Zealand white female rabbits (n=5/group) were assigned to a regular (Diet R), high protein (Diet HP) or high fiber (Diet HF) group and were all challenged with MAP at 7 weeks of age taking their corresponding diets on alternate weeks and regular diet the rest of the time. Animals were euthanized at 34 weeks of age. Faecal and blood MAP F57 qPCR were used to monitor the disease progression in the rabbits during the experiment. Post-mortem tissue bacteriological culture and qPCR, as well as histopathology were assessed to evaluate final disease status. PPA-3 ELISA and western blot analysis were performed to measure humoral response.

Results: MAP detection in faeces and blood was more common in the Diet R group, which did not undergo diet stress. Histological lesions were recorded in vermiform appendix, sacculus rotundus and mesenteric lymph node mainly in this diet group, as well. MAP was detected by qPCR in all previously mentioned GALT tissues as well as in liver and muscle in 68.2% of analyzed samples for diet R, 52% for diet HF and 64% for diet HP. Total lesion index was higher in diet group R animals compared to diet HP and diet HF (p=0,006). PPA-3 antibodies were detected after 150 days of the beginning the experiment being 3 and 2 fold higher in diet groups HF and HP respectively compared to those in diet R.

Conclusion: Data demonstrate that diet changes do affect immune response and MAP infection progression upon challenge with this microorganism. Diet R group showed highest infection parameters indicating that alternating diets may attenuate MAP infection establishment and progression in rabbits.

Keywords: *Mycobacterium avium* subsp. *paratuberculosis*; rabbit; animal model; dietary changes, immune response.