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04.019 **Rapamycin Treatment might Prolong the Life of Diabetic Mice Infected with** *Sporothrix brasiliensis.* Oliveira MA[1], Albuquerque RC[2], Pereira BV[2], Tavares YPST[1], Silva CC[2], De Almeida SR[2], Martins JO[1] [1]FCF-USP, Lab Immunoendocrinology, Dept of Clinical and Toxicological Analyses, [2]FCF-USP, Lab Mycology, Dept of Clinical and Toxicological Analyses

Introduction: Type 1 diabetes mellitus (T1DM) is a chronic metabolic disease caused by an autoimmune response, which leads to the destruction of pancreatic ? cells. It is known that the chronic hyperglycemia present in these patients leads to a compromised immune response, making them more susceptible to infection diseases, such as sporotrichosis, with high incidence rates in the Rio de Janeiro and São Paulo, caused by the fungus *Sporothrix brasiliensis* (Sb). In addition, autophagy has been studied as a crucial component in innate defense against a wide range of infectious agents, having a central role in controlling several aspects of immunity in multicellular organisms. Our aim is to analyze the role of autophagy against Sb infection in healthy and diabetic animals, through induction with Rapamycin (RAPA). **Material and Methods:** For the induction of diabetes, treatment with streptozotocin (STZ) was performed intraperitoneally in mice of the C57BL/6J strain (CEUA Protocol No. 642). Then, mice were infected subcutaneously with 10^7 viable yeasts of *Sporothrix brasiliensis* M1168, with a period of 14 days of infection, in which 3 doses of RAPA were applied via gavage, intermittently every 5 days. Samples of liver, brain, spleen, lymph nodes, lesions and kidneys were collected for further analysis. **Results:** Infected T1DM mice with and without treatment with RAPA had 100% mortality at 36 days of infection, starting at 16 days post-infection, while the infected CT mice showed no mortality for 35 days post-infection, at which point they were euthanized ($p<0.0001$). In addition, infected mice had a higher percentage of monocytes (CT infected 4.7% and T1DM infected 6%) compared to uninfected mice (CT 2.03% and T1DM 3.1%). As well as a higher percentage of granulocytes (CT infected 49.3%, T1DM infected 62.88%, CT 17.11% and T1DM 23.65%) ($p<0.05$). However, the infected T1DM mice showed a depletion of lymphocytes when compared to the CT group (CT infected 45.93%, T1DM infected 31.41%, CT 80.85% and T1DM 73.18%) ($p<0.05$). With regard to the cytokine profile, the T1DM mice infected with Sb showed a higher concentration of IFN-γ (6.50 pg/mL) in the liver compared to the CT group with (0.69 pg/mL) or without treatment with RAPA (0.15 pg/mL) ($p<0.05$). With regard to cytokine dosage in the lymph node samples, the T1DM group infected with Sb treated with RAPA (340.52 pg/mL) showed a higher concentration of TNF-α compared to the CT (16.37 pg/mL) and T1DM groups with (1.42 pg/mL) and without treatment with RAPA (0.82 pg/mL) ($p<0.05$), and the CT group infected with Sb treated with RAPA (33.76 pg/mL) showed a higher concentration of IL-2 compared to the T1DM group treated (0.32 pg/mL) ($p<0.05$). **Conclusions:** Regarding the count of colony forming units, mice treated with RAPA have a smaller spread of the fungus to the liver and brain. Taking the results together, RAPA treatment might prolong the life of infected mice with T1DM when compared with their respective control, and the 14-day Sb infection period showed a Th1 response profile, with macrophage activation. **Financing:** FAPESP; CAPES; CNPq **Keywords:** diabetes; infection; sporotrichosis; autophagy; rapamycin