

## Role of Sirtuin 1 in the phenotype and functions of dendritic cells in the context of transplantation of obese animals

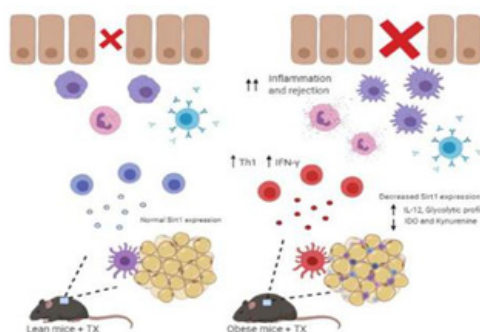
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### Abstract

Sirtuin 1 (SIRT1) is a class 3 Histone Deacetylase (HDAC3) that acts primarily by regulating T cell differentiation, proliferation and activation, therefore disabling transcriptions of genes in Dendritic Cells (DCs) that are important for T cell activation and differentiation of effector cells in graft rejection and in other chronic inflammatory processes like obesity. Therefore, our hypothesis that the obesity influences the differential expression of sirtuin 1 (SIRT1) in DCs, changing its phenotype and function, and thus T cell activation, exacerbating the allograft immune response. Thus, our goal was to specifically investigate the role of SIRT1 in the function, phenotype and the implications on DCs metabolism, and if it can affect T cell functions in the context of skin transplantation in obese animals. We saw the impact of absence of SIRT1 in the mitochondrial metabolism of DCs (by Seahorse technology) in animals with specific deletion of SIRT1 gene in DCs (CD11cCreSIRT1<sup>flox/flox</sup>). In addition, we observed after treatment with a SIRT1 agonist (resveratrol, 50 nM) in Bone Marrow-Derived DC (BMDCs) increase of protein expression of TGF- $\beta$ , IDO and the decreased of costimulatory molecules (CD40, CD80, CD86) with parallel induction of SIRT1. In a hyperlipid diet-induced obesity (HFD) mode plus transplantation, we observed that DCs from obese animals and with skin graft had the most lower SIRT1 expression and this led to a more pro-inflammatory profile as well as less glycolytic metabolic profile and relation with tryptophan metabolism, which is characteristic of a DC tolerance according to the literature. Based on the results obtained so far, we can suggest that increased expression of SIRT1 by resveratrol treatment leads to a more tolerogenic profile in BMDCs and DC, which may influence CD4+ T cell proliferation and polarization and consequently an improvement in the graft acceptance in obesity.



### Biography

Jean de Lima holds the title of Biotechnologist from the Pontifical Catholic University of Paraná (PUC-PR), where he worked with in vitro analysis of *Campomanesia xanthocarpa* extract in cell activation in HUVECs and THP-1 strains and is a collaborator to investigate biogenesis of circular RNA in humans. Currently, he is conducting an internship program at Lausanne University in Switzerland and is also active in humanitarian activities teaching guitar and informatics to special students.

### Publications

1. Fachi JL, Felipe JS, Pral LP, da Silva BK, Corrêa RO, de Andrade MCP, da Fonseca DM, Basso PJ, Câmara NOS, de Sales E Souza ÉL, Dos Santos Martins F, Guima SES, Thomas AM, Setubal JC, Magalhães YT, Forti FL, Candreva T, Rodrigues HG, de Jesus MB, Consonni SR, Farias ADS, VargaWeisz P, Vinolo MAR. Butyrate Protects Mice from *Clostridium difficile* Induced Colitis through an HIF-1-Dependent Mechanism. **Cell Rep.** 2019 Apr 16;27(3):750-761.e7. doi: 10.1016/j.celrep.2019.03.054.
2. Angela Castoldi; Vinicius Andrade-Oliveira; Pedro Manoel Moraes-Vieira; Niels Olsen Saraiva Câmara et al. Dectin-1 activation exacerbates obesity and insulin resistance in absence of MyD88. **Cell Rep.** 2017 Jun 13;19(11):2272-2288. doi: 10.1016/j.celrep.2017.05.059
3. Cuartero, Sergi; Weiss, Felix D.; Dharmalingam, Gopuraja; Guo, Ya; Ing Simmons, Elizabeth; Masella, Silvia; Robles-Rebollo, Irene; Xiao, Xiaolin; Wang, Yi-Fang; Barozzi, Iros; et al. Control of inducible gene expression links cohesin to hematopoietic progenitor self-renewal and differentiation. **Nature Immunology**, v. 19, n. 9, p. 932+, SEP 2018. Citações Web of Science: 14.
4. Moraes-Vieira, Pedro M. M.; Larocca, Rafael A.; Bassi, Enio J.; Peron, Jean Pierre S.; Andrade-Oliveira, Vinicius; Wasinski, Frederick; Araujo, Ronaldo; Thornley, Thomas; Quintana, Francisco J.; Basso, Alexandre S.; et al. Leptin deficiency impairs maturation of dendritic cells and enhances induction of regulatory T and Th17 cells. **European Journal of Immunology**, v. 44, n. 3, p. 794-806, MAR 2014. Citações Web of Science: 35. (09/50450-7, 08/58564-9, 08/55447-1)
5. Cunha, EBB; Silva, NF; De Lima, J; Serrato, JA; Viecili, PRN; Aita, CAM; Herai, RH. Leaf extracts of *Campomanesia 1 xanthocarpa* positively regulates atherosclerotic-related protein expression. **Phytomedicine**.