Simvastatin promotes expression of the Notch1 pathway in endothelial cells infected with *Trypanosoma cruzi*: implications for a potential beneficial effect of statins in the chronic infection

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Chagas disease is an ailment that inflicts about 7 million people in Latin America y many people worldwide due to migration. The leading cause of death due to the *Trypanosoma cruzi* infection is a chronic cardiomyopathy that manifests more early than other, ischemic, atherosclerotic cardiomyopathies. The primary cause of the disease is the persistence of the parasite and the consequent inflammation produced, which is permanent but of low grade. Part of this process is the activation of endothelium that participates in the recruitment of inflammatory and immunologic cells. Aside, there is a robust fibrotic input and cardiomyocyte death. Previously we reported about the influence of simvastatin, via the pro-resolutive lipid 15-epi-lipoxin A4, on decreasing cell adhesion molecules in endothelial cells. Considering the role of the Notch pathway in decreasing the fibrotic response after an ischemic cardiac attack, we examine if there is a relationship between *T. cruzi* infection, simvastatin treatment and the activation of the Notch pathway. HUVEC or EAhy.926 endothelial cells were infected with *T. cruzi* during 16 hours and treated with 500 nM simvastatin during 6 hours. This strategy demonstrated increased exposition of Notch1 on the cell surface, increased presence in the nucleus of the intracellular fragment of Notch, NICD; and, modification in the expression of downstream proteins such as Hey and Jagged1. The activity of Notch was also increased by the administration of 15-epi-lipoxin A4, even in the presence of 5-lipoxygenase inhibitors or its receptor (FPR2/ALX) antagonist, BOC-1. Thus, simvastatin may modulate the activity of Notch1 pathway in endothelial cells infected with *T. cruzi*, which in the in vivo context, might have therapeutic implications to decrease cardiac remodeling in the early stages of Chagas cardiomyopathy.

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