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14.005 **Evaluation of the Effect of Autophagy Flux Control by Rapamycin and Hydroxychloroquine in the Senescent Phenotype of Hepatocytes and Adipocytes in Mouse Model.** De Queiroz LAD[1], Barros RS[1], Bustia SX[1],Pantoja KC[1], Migliorini S[1], Rodrigues SF[2], Guimarães JPT[3],Scoggin S[3], Moustaid-Moussa N[3], Martins JO[1] [1]USP, Dept of Clinical and Toxicological Analyses; [2]USP, Dept of Pharmacology; [3]TTU Lubbock, Dept of Nutritional Sciences, & Obesity Research Institute

Introduction: Aging is a natural and multifactorial process characterized by the gradual loss of physiological integrity. In this context, the intracellular degradation promoted by autophagy plays a central role in cellular homeostasis, and consequently in the aging process. Our goal is to investigate the relationship between the control of autophagic flux, increased by rapamycin (RAPA) or reduced by hydroxychloroquine (HCQ), in the regulation of the senescent phenotype in Senescence-Accelerated Mouse Prone (SAM- P)8 and Senescence-Accelerated Mouse Resistant (SAM-R)1. **Material and Methods:** 12 weeks male and female SAM-P8 and SAM-R1 were oral treated with RAPA (0.78µg/Kg every 5 days) or HCQ (50mg/kg/daily) or vehicle (water as control) for 6 months. We conducted gene expression for autophagy, senescence, energetic metabolism, and inflammation in liver and White Adipose Tissue (WAT). **Results:** Male SAM-R1 HCQ showed upregulation ($p<0.05$) in galactosidase beta (gbl)1, GATA Binding Protein (GATA)4, mammalian target of rapamycin (mTOR), microtubule-associated proteins 1A/1B light chain (LC)3B, interleukin (IL)1β, and peroxisome proliferator-activated receptor gamma coactivator (PGC)-1α, compared to the male SAM-R1 control group, with no significant differences among all other groups in liver, and for Rapamycin-insensitive companion of mTOR (RICTOR), neighbor of Brca (breast cancer)1 - (NBR)1, Ubiquitin-binding protein p62 (p62), tumor protein p53 (p53), IL-6, and PGC-1α in WAT. **Conclusions:** No effects of RAPA were detected in live or WAT. However, male SAMR1 were more sensitive to HCQ and had higher hepatocytes and adipocyte mRNA levels for senescence (glb1, GATA-4, p53), autophagy (mTOR, RICTOR, LC3B, NBR1, p62), inflammation (IL-1β, IL-6), and metabolic marker (PGC-1α). These results demonstrate that HCQ targets autophagy pathways. Moreover, increased expression of senescence markers demonstrated a direct relationship between these two phenomena, with a potential sexual dimorphism in response to HCQ in SAM-R1 lineage. **Financing:** FAPESP; CAPES; CNPq **Keywords:** Aging; Autophagy, Rapamycin; Hydroxychloroquine