**Cholesteryl ester transfer protein (CETP) expression induces contrasting effects on endothelium-dependent relaxation in males and females.**

Lazaro, CM. ¹; Victorio, JA. ¹; Davel, AP. ¹; Oliveira, HCF. ¹

 1 Department of Structural and Functional Biology, Biology Institute, University of Campinas - UNICAMP, Campinas, SP, Brazil.

**Introduction:** The cholesteryl ester transfer protein (CETP) main function is to transfer the cholesterol from HDL to lipoproteins containing apolipoprotein B which decreases HDL-cholesterol levels. Therefore, CETP has been considered pro-atherogenic. CETP inhibitors, by enhancing HDL levels, have emerged as a potential coadjutant therapy for dyslipidemias but revealed unexpected adverse effects related to cardiovascular diseases and it has been postulated that CETP could have direct effects on vascular cells. Furthermore, CETP may have sex-dependent metabolic effects on obesity and insulin sensitivity, although literature show conflicting results. Here, we hypothesized that CETP may play a sex-dependent role on vascular function. We analyzed the influence of human CETP expression on aortic contraction and endothelial relaxing function in males and females. **Methodology:** We use transgenic male and female mice (4–6-month-old) expressing human CETP (hCETP) and their respective nontransgenic (NTg) controls (CEUA 5353-1/2019). Thoracic aorta was isolated and dose-response curves to acetylcholine (ACh) in the presence and absence of nitric oxide synthase inhibitor L-NAME (300 μM) and to phenylephrine were performed. Potency (LogEC50) and maximal response (Rmax) to agonists were calculated and data analyzed by 2-way ANOVA (P<0.05). **Results:** Endothelium-dependent relaxation curve to ACh was shifted to right in aorta from hCETP male compared to male NTg (LogEC50: hCETP= -7.05±0.33 vs. NTg= -7.57±0.53 \*) with no change in Rmax. In contrast, there was a greater relaxation response to ACh in aorta from hCETP femaIe mice compared to NTg females (Rmax: hCETP= 80.05±6.76% vs. NTg= 72.07±6.87%\*) with no changes in the potency. Phenylephrine induced contraction was not affected in female hCETP mice. **Conclusion:** the results demonstrated that while human CETP expression impairs endothelial function in males, it increases endothelium-dependent relaxation in females, suggesting a sexual dimorphism in endothelial function induced by the presence of CETP.

Keywords: CETP; Vascular Reactivity; Endothelium; Sexual Dimorphism.

Financial Support: FAPESP.