ABSTRACT

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Doctoral Degree Program: Pharmacology and Toxicology

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Title of Doctoral Thesis: Possible changes of endoglin expression in endothelial cells

Endoglin (Eng) is a co-receptor for ligands of the Transforming Growth Factor β superfamily. Multiple studies have demonstrated that Eng is associated with metabolic syndrome-related pathological conditions, such as hypercholesterolemia, hyperglycemia, hypertension, or obesity. However, the exact role of Eng in these pathologies is still unknown. Therefore, the main purpose of this thesis was to elucidate and summarize the role of membrane and soluble Eng in the selected pathologies associated with metabolic syndrome.

We demonstrated that soluble Eng (sEng) levels, together with plasma lipids and markers of inflammation, were reduced after every lipoprotein apheresis in patients with familial hypercholesterolemia. This result, in combination with knowledge acquired by the review article, indicates that increased sEng levels are associated with cardiometabolic disorders. Regarding the role of membrane Eng, we showed that blockage of Eng expression by TRC105 results in a decrease in hypercholesterolemia- and hyperglycemia-induced Eng expression, followed by inhibition of Eng-mediated signaling and reduced adhesion and transendothelial migration of monocytes. This suggests that the interaction between membrane Eng and monocytes, responsible for adhesion and transendothelial migration of monocytes, might be the potential pharmacological target in diseases associated with elevated levels of glucose and/or cholesterol.

In conclusion, this doctoral thesis helped to extend the knowledge regarding the role of Eng in metabolic syndrome-related disorders. We suggest that sEng can be considered a biomarker of cardiometabolic diseases and that lowering its levels should be considered in patients who are prone to develop these diseases. However, the membrane Eng role is still not fully elucidated, and more studies are necessary to understand all the mechanisms involved in its regulation and function.