



## ALDEHYDE DEHYDROGENASE 2 AS A NEW TARGET FOR TREATMENT OF PERIPHERAL ARTERY DISEASE

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Aldehyde dehydrogenase 2 (ALDH2) has recently emerged as a key enzyme in the maintenance of cellular homeostasis, since it efficiently eliminates toxic aldehydes (i.e., 4-HNE and acetaldehyde) by catalyzing their oxidation to nonreactive acids. We recently demonstrated that improving ALDH2 activity protects against cardiac diseases. Here, we characterized the role of ALDH2 during peripheral artery disease (PAD) progression in a mouse model of femoral artery ligation. Our results show that this animal model presents 70% blood flow reduction at the first day after surgery and presents clinical signs of PAD during the progression of disease. Moreover, PAD mice presented a reduction in both skeletal muscle cross-sectional area (50%) and contractility properties (35%) compared to sham group at day 28 after surgery. These changes were accompanied by 75% reduction in voluntary locomotor activity and 50% reduction in ALDH2 enzymatic activation profile in plantaris muscle. Finally, as a proof of concept, mice ALDH2 knock-in showed a reduction of 60% at voluntary locomotor activity after PAD surgery along with a reduction of 25% in ex vivo muscle contractile function when compared to PAD control group. Thus, we demonstrated that this experimental model was able to mimic the PAD and that the progression of the disease is characterized by a reduction in ALDH2 activation, since ALDH2 knock-in animals are more susceptible to the development of PAD. These findings are extremely promising and indicate ALDH2 as a possible therapeutic target in the treatment of PAD.

Key words: aldehyde dehydrogenase 2, peripheral artery disease, skeletal muscle CNPq and FAPESP

