In conclusion, our results suggest a potential role of PAI-1 as an enzyme involved in the shedding of TNF and its receptors (TNFRs).

We also observed that PAI-1 expression in LoVo cells moderately inhibited Furin-dependent maturation of proADAM-17/TACE, an enzyme involved in the shedding of TNF and its receptors (TNFRs). As a result, the Furin-activated cleavage of TNF and both TNFRs by ADAM-17 was significantly reduced by PAI-1 expression.

In conclusion, our results suggest a potential role of PAI-1 as a Furin inhibitor, which could give to PAI-1 a causative role in MS by regulating both insulin and TNF pathways.

Cardiac energy metabolism is a determinant of the response to hypertrophic stimuli. We investigated how energy metabolism responds to physiological or pathological stimuli leading to comparable levels of hypertrophy. We compared the cardiac energetic status in models of hypertrophy induced by physiological stimuli like pregnancy (18-19 days of gestation) or exercise training (8-weeks treadmill) and by hypertension (spontaneously hypertensive rats, SHR) in 15 weeks-old female rats, all leading to a 10% cardiac hypertrophy. Late stage of compensated hypertrophy was also studied in 25 weeks-old SHR (35% of hypertrophy).

Markers of cardiac remodelling did not follow a unique pattern of expression: in trained rats, only atrial natriuretic factor was increased and in gravid rats, calcineurin activation was reduced while β-MHC expression was enhanced. All these markers were clearly up-regulated in 25-weeks-old SHR. Respiration of permeabilized cardiac fibers revealed a 17% increase in oxidative capacity in trained rats only. Citrate synthase, complex I or cytochrome oxidase activity, and expression of the master regulator of mitochondrial biogenesis, PGC-1α, were not changed suggesting that compensated hypertrophy does not involve mitochondrial biogenesis alterations. Mitochondrial fatty acid utilization tended to increase in trained rats and decreased by 14% in early SHR. No change in PPARα expression but significant decrease in MCAD and CPT1 expression were observed in pregnancy, while these 3 markers of β-oxidation were up-regulated after training.

Taken together, these results show that there is not an univocal pattern of cardiac adaptations in response to physiological or pathological hypertrophic stimuli but that rather the pattern, intensity and nature of the stimuli play an important role in determining adaptation of energy metabolism to increased workload.

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