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Autophagic process is sexually different in VSMCs from human male and female neonates

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Sex has largely been neglected in cellular studies. Autophagy is a sophisticatedly regulated homeostatic mechanism, which ensures cell's constituent turnover. Under physiological conditions, autophagy levels are usually low (constitutive autophagy), but can be induced by numerous cellular stresses such as starvation. The influence of sex on autophagy has been studied either in vitro or in vivo, and previous our findings demonstrated the existence of sex differences in rat heart and HUVECs. Vascular smooth muscle cells (VSMCs) are a good experimental model for studying the physiopathology of the cardiovascular system, in which autophagy plays an important physiological role. Therefore, we investigated the occurrence of sexual dimorphism in constitutive and starvation-induced autophagy between the VSMCs obtained from human umbilical cord arteries (HUASMCs) of male (MHUASMCs) and female (FHUASMCs) neonates.

HUASMCs were isolated from the umbilical cord of healthy and normal weight male and female neonates. The expression of oestrogen receptor (ER-α and ER-β) and the primary molecules involved in autophagic process [the mammalian target of rapamycin (mTOR), beclin-1 and microtubule-associated protein 1 light chain 3 (LC3)] were analysed by western blotting. Both cell types expressed both isoforms of the oestrogen receptor (ER): ER-β was higher expressed in the MHUASMCs than the FHUASMCs while ER-α was similarly expressed in both sexes. The level of constitutive autophagy, measured as LC3II/I ratio was higher in FHUASMCs than in MHUASMCs, while male cells had an higher expression of Beclin-1, indicating that constitutive autophagy was at least partly beclin-1-independent. mTOR activity, a regulator of autophagy, did not vary between the sexes, indicating that the observed differences could not be attributed to this central pathway. Starvation promoted autophagy in both MHUASMCs and FHUASMCs, but the increase was more pronounced in FHUASMCs.

Our results show that sex-differences start in utero and are parameter-specific, suggesting that HUASMCs of both sexes are necessary in in vitro studies to elevate the quality and translational value of research results. The observed differences in the autophagic process could help to emeliorate our knowledge on sex-differences observed in cardiovascular diseases.

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Keywords

Sex differences; HUASMCs; autophagy.