**LYSOSOMAL CYSTEINE PROTEASES AND DISTURBANCES OF THEIR REGULATION IN ATHEROSCLEROSIS**

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**Objectives**. Hyperlipidaemia increases the risk of myocardial infarction and stroke.

**Background**. The poloxamer 407 (P-407)-induced hyperlipidemic mouse model represents a convenient, inexpensive, and well-documented mouse model with which to study cardiovascular heart disease arising from dyslipidemia and atherosclerosis. Methods. Mice were administered P-407, a well-documented general lipase inhibitor, for 1 month as an i.p. injection at a dose of 300 mg/kg twice per week. The specific activities of cathepsin B (EC 3.4.22.1) and cathepsin L (EC 3.4.22.15) were determined according to Barrett and Kirschke (1981). The expression of lysosomal acid lipase (LAL), a lipase inhibited by P-407, was quantified using RT-qPCR.

**Results**. Similar to humans, the onset of atherosclerosis in P-407-treated mice was characterized by a steady increase in serum low-density, intermediate-density and very-low-density lipoprotein (VLDL) fractions, as well as VLDL subfractions.

P-407-treated mice revealed significant hyperlipidemia, moderately elevated blood pressure, general lipidosis in liver cells, increased cysteine protease activity in heart tissue, and contractile-type changes in cardiomyocytes.

The specific activity of cathepsin B in liver tissue increased modestly 24 h after stopping P-407 treatment for 1 month. The specific activity of cathepsin B and cathepsin L in heart tissue remained significantly (p < 0.01) elevated relative to control for as long as 24 h after the last dose of P-407 and returned to normal (control) values by day 4 following discontinuation of P-407 treatment.

**Conclusion**. We demonstrated that an increase in the activity of cathepsins B and L in heart tissue was positively correlated with morphological changes observed in contractile-type cardiomyocytes.