Autophagic cell death in the myocardium of mice subjected to ischemia followed by reperfusion

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Introduction: The extent of autophagy in the heart following myocardial infarction has not been well elucidated. We sought to determine the magnitude and temporal dependence of autophagic cell death in the myocardium of murine hearts following ischemia and reperfusion.

Methods: 10-12 week old transgenic GFP-LC3 mice on a C57Bl6 background were subjected to LAD ligation for 1 or 4 hours followed by 24 hours of reperfusion (1HTLR24H, 4HTLR24H) or to 24 hours of persistent ligation (24HPL). Their hearts were harvested, frozen, sectioned, and analyzed by fluorescence microscopy.

Results: Transgenic GFP-LC3 mice starved for 48 hours were used as a positive control for detection of GFP-LC3 dots. These mice exhibited (448 ± 87 dots per high power field (HPF), n = 3). GFP-LC3 mice that were subjected to sham surgery were used as negative controls (79 ± 35 dots per HPF, n = 3). There was a significant reduction in fluorescent dots in the border zones of mice subjected to ischemia followed by reperfusion and persistent ligation compared with mice subjected to sham surgery (31 ± 10, n =3 for 1HTLR24H, $p \leq 0.05$ and 9 ± 5, n =3 for 4HTLR24H, $p \leq 0.05$, 32 ± 9, n =3, $p \leq 0.05$ for 24HPL).

Conclusion: Autophagy in the border zone of ischemic myocardium decreases significantly early after myocardial infarction in mice. Autophagy is a method by which cells under stress protect themselves; thus, increasing autophagy in the border zone by a pharmacological intervention may be a target for diminution of infarct size after myocardial infarction.