

# SCIENTIFIC REPORTS



OPEN

## Amiodarone as an autophagy promoter reduces liver injury and enhances liver regeneration and survival in mice after partial hepatectomy

Received: 27 May 2015  
Accepted: 05 October 2015  
Published: 30 October 2015

Chih-Wen Lin<sup>1,2,3,4</sup>, Yaw-Sen Chen<sup>4,5</sup>, Chih-Che Lin<sup>8</sup>, Yun-Ju Chen<sup>6,7</sup>, Gin-Ho Lo<sup>2,4</sup>, Po-Huang Lee<sup>4,5</sup>, Po-Lin Kuo<sup>1</sup>, Chia-Yen Dai<sup>1,9,10</sup>, Jee-Fu Huang<sup>1,9</sup>, Wang-Long Chung<sup>1,9</sup> & Ming-Lung Yu<sup>1,9,10,11</sup>

The deregulation of autophagy is involved in liver regeneration. Here, we investigated the role of autophagy in the regulation of liver regeneration after partial hepatectomy (PHx) and the development of pharmacological interventions for improved liver regeneration after PHx. We show that autophagy was activated in the early stages of liver regeneration following 70% PHx *in vivo*. Moreover, amiodarone was associated with a significant enhancement of autophagy, liver growth, and hepatocyte proliferation, along with reduced liver injury and the termination of liver regeneration due to decreased transforming growth factor- $\beta$ 1 expression after 70% PHx. The promotion of autophagy appeared to selectively increase the removal of damaged mitochondria. We also found that Atg7 knockdown or pretreatment with chloroquine aggravated the liver injury associated with 70% PHx and reduced liver growth and hepatocyte proliferation. Finally, amiodarone improved liver regeneration, survival, and liver injury after 90% PHx. In conclusion, our results indicate that autophagy plays an important role in mouse liver regeneration and that modulating autophagy with amiodarone may be an effective method of improving liver regeneration, increasing survival, and ameliorating liver injury following PHx.

The liver is an organ that has a remarkable capacity for self-regeneration<sup>1,2</sup>. Liver regeneration in rodents that have had 70% of their liver removed in a partial hepatectomy (PHx) has become a useful model for studying regenerative organ growth. Hepatocytes that are typically in a quiescent phase enter the

<sup>1</sup>Graduate Institute of Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung. <sup>2</sup>Division of Gastroenterology and Hepatology, Department of Medicine, E-Da Hospital, I-Shou University, Kaohsiung. <sup>3</sup>Health Examination Center, E-Da Hospital, I-Shou University, Kaohsiung. <sup>4</sup>School of Medicine, College of Medicine, I-Shou University, Kaohsiung. <sup>5</sup>Department of Surgery, E-Da Hospital, I-Shou University, Kaohsiung. <sup>6</sup>Department of Medical Research, E-Da Hospital, I-Shou University, Kaohsiung. <sup>7</sup>Department of Biological Science & Technology, I-Shou University, Kaohsiung. <sup>8</sup>Department of Surgery, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Kaohsiung. <sup>9</sup>Hepatobiliary Division, Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung. <sup>10</sup>Faculty of Medicine, College of Medicine, and Center for Infectious Disease and Cancer Research, and Center for Lipid and Glycomedicine Research, Kaohsiung Medical University, Kaohsiung. <sup>11</sup>Institute of Biomedical Sciences, National Sun Yat-Sen University, Kaohsiung, Taiwan. Correspondence and requests for materials should be addressed to M.-L.Y. (email: fish6069@gmail.com)