About OMICS Group

OMICS Group International is an amalgamation of Open Access publications and worldwide international science conferences and events. Established in the year 2007 with the sole aim of making the information on Sciences and technology 'Open Access', OMICS Group publishes 400 online open access scholarly journals in all aspects of Science, Engineering, Management and Technology journals. OMICS Group has been instrumental in taking the knowledge on Science & technology to the doorsteps of ordinary men and women. Research Scholars, Students, Libraries, Educational Institutions, Research centers and the industry are main stakeholders that benefitted greatly from this knowledge dissemination. OMICS Group also organizes 300 International conferences annually across the globe, where knowledge transfer takes place through debates, round table discussions, poster presentations, workshops, symposia and exhibitions.

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OMICS Group International is a pioneer and leading science event organizer, which publishes around 400 open access journals and conducts over 300 Medical, Clinical, Engineering, Life Sciences, Pharma scientific conferences all over the globe annually with the support of more than 1000 scientific associations and 30,000 editorial board members and 3.5 million followers to its credit.

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The Homeostatic Intracellular Repair Response (HIR^2) And Heart Surgery

3rd International Conference on Clinical and Experimental Cardiology

Hilton Chicago, Northbrook, USA, 2013

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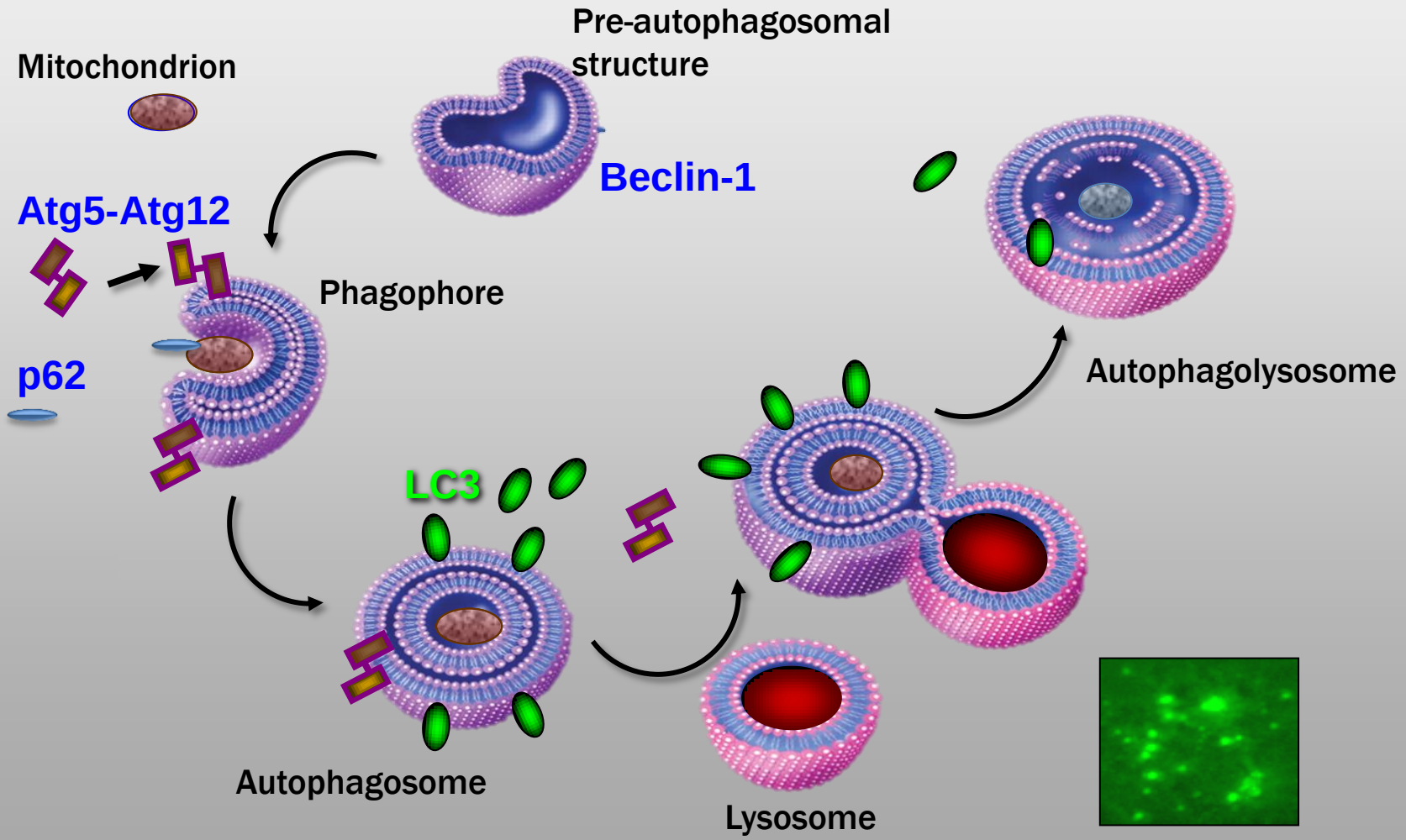
The Homeostatic Intracellular Repair Response (HIR^2)

- HIR^2 is a lysosomal adaptive response to stress
- Preclinical evidence indicates it is manifest in multiple organs
- In the heart it is a protective response to ischemia-reperfusion

Autophagy: A Survival Pathway



Modified from T. Shintani et al., Science 306, 990 -995 (2004)

Central Hypothesis

Autophagy is impaired in the setting of MetS and results in the loss of endogenous protection conferred by ischemic preconditioning (IPC)

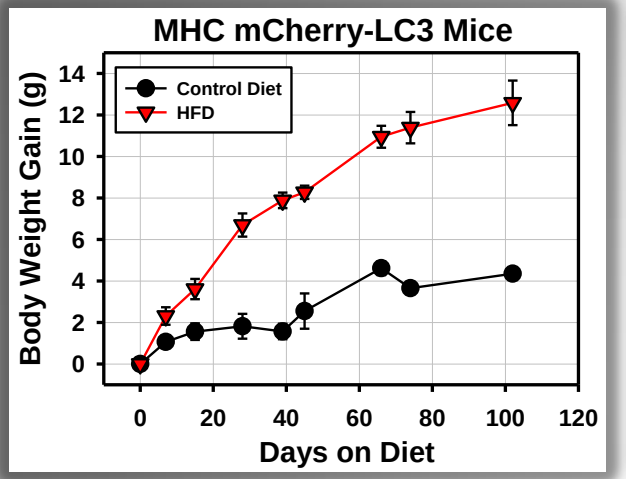
Metabolic Syndrome (MetS)

- Characterized by obesity, HC, dyslipidemia, and insulin resistance
- Increased risk of death from myocardial infarction and stroke
- Prevalence in the USA estimated at >30% of the population; >20% Japan (and rapidly increasing)

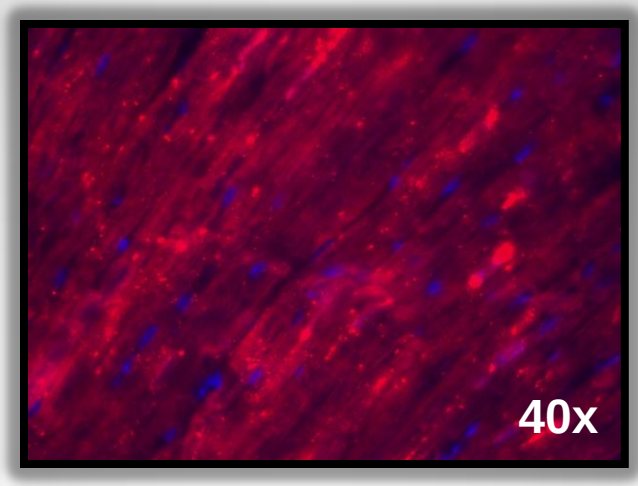
Methods

- Utilized 3 translational models of MetS
  - LC3-mCherry transgenic mice fed a high fat diet (HFD)
  - Genetic Zucker obese (ZO) rats
  - Yucatan pigs fed a high fat/high fructose diet (HF/HF)
- Assessed autophagy (puncta, Western blot)
- Measured infarct size (TTC) and response to ischemic preconditioning (IPC)

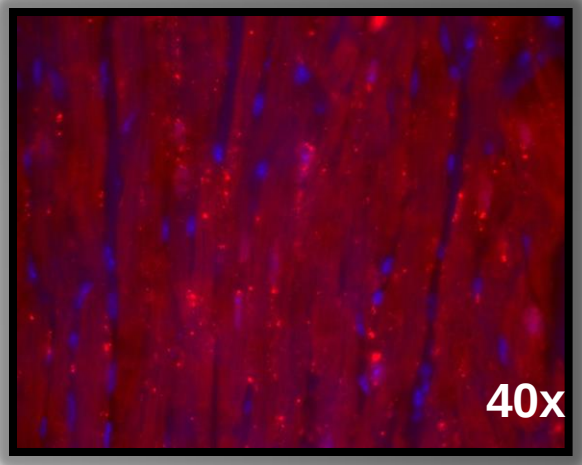
Fewer Cardiac Autophagosomes in DIO Mice

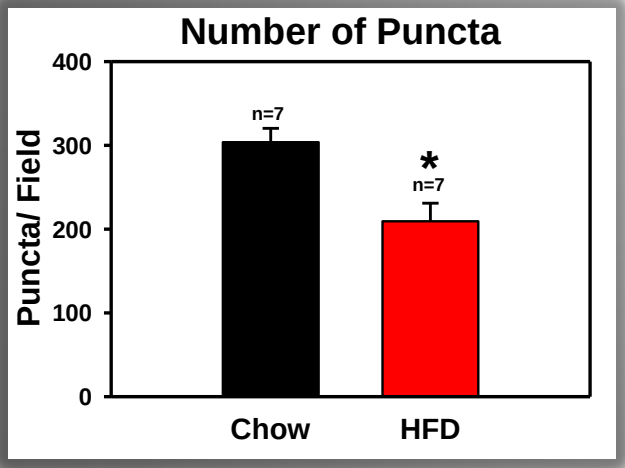


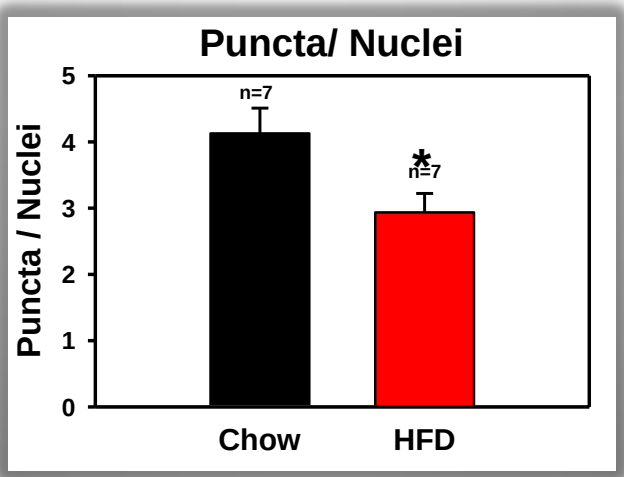
Normal Chow

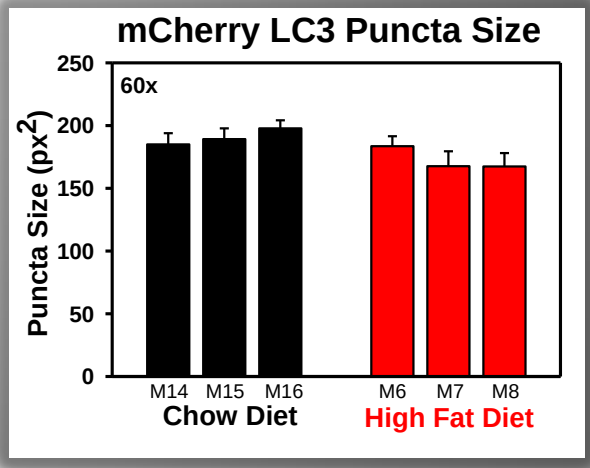


High Fat Diet

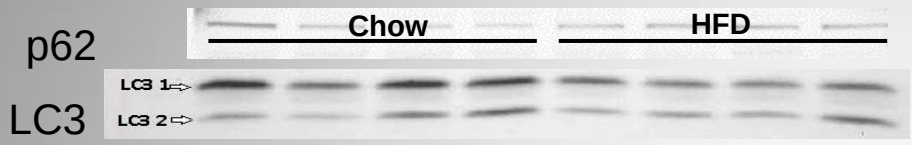


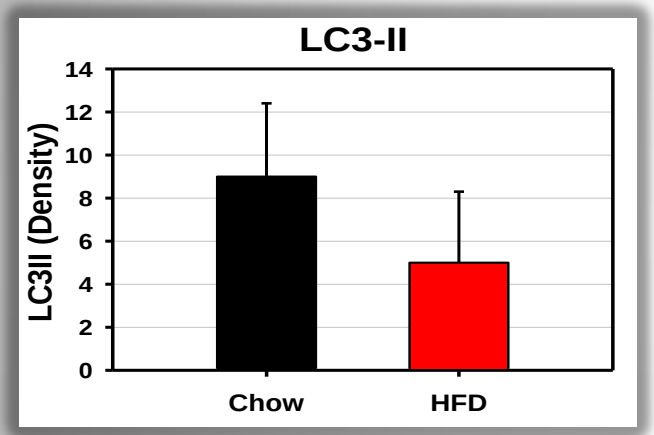


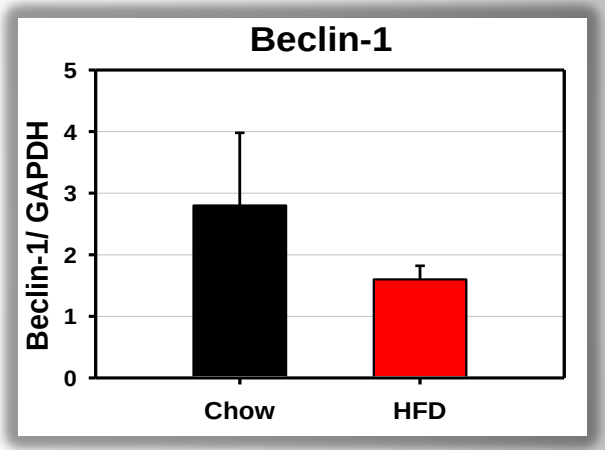


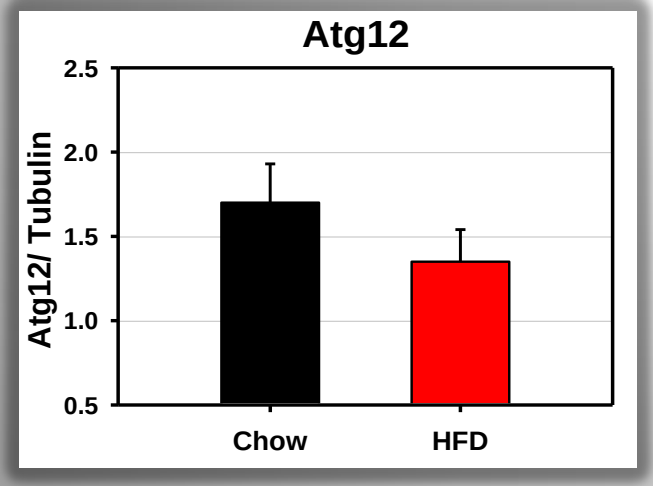


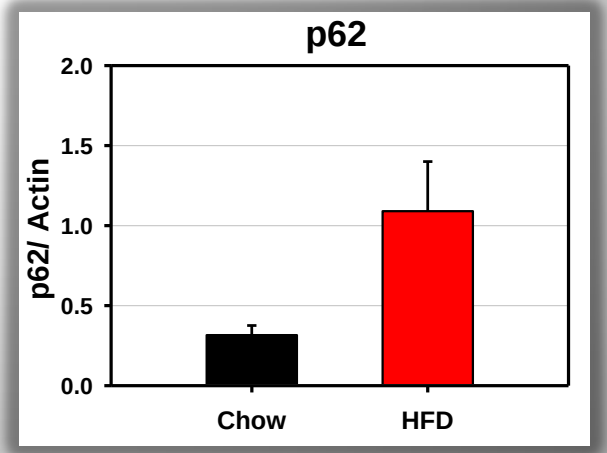
Autophagy is Decreased in DIO Mice



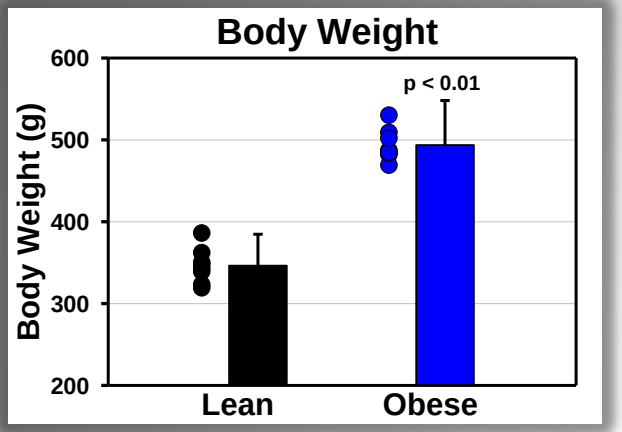


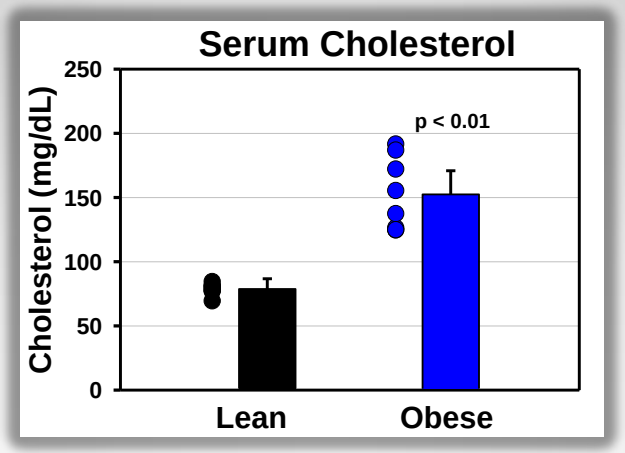


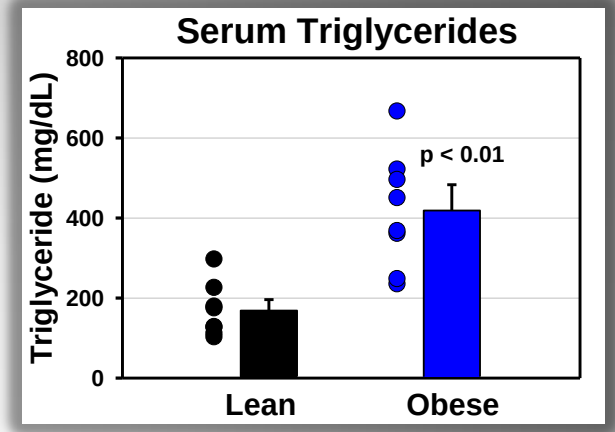


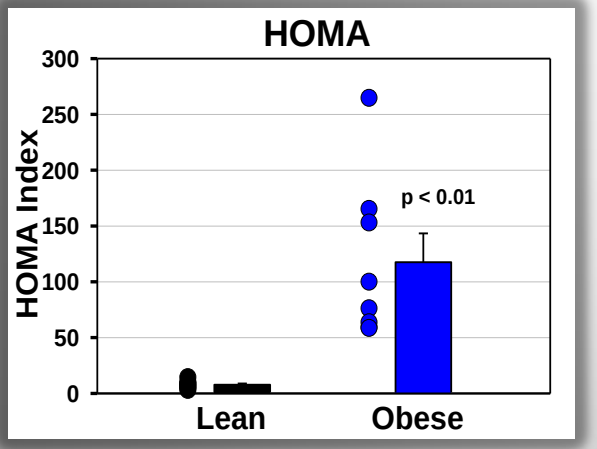


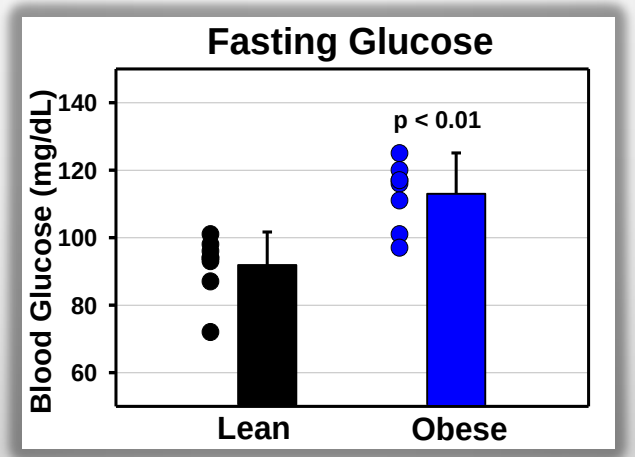
MetS in Zucker Obese Rats

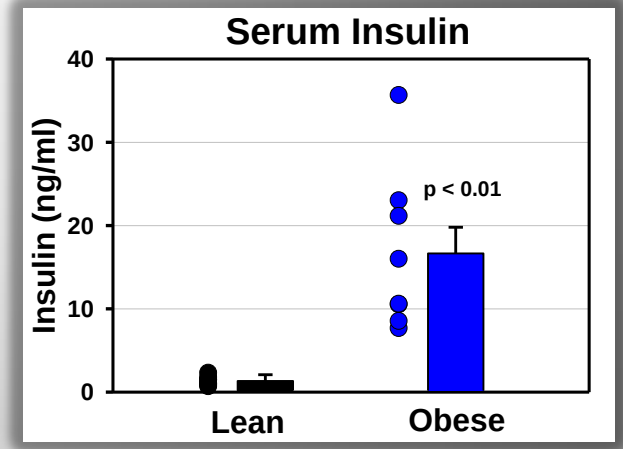




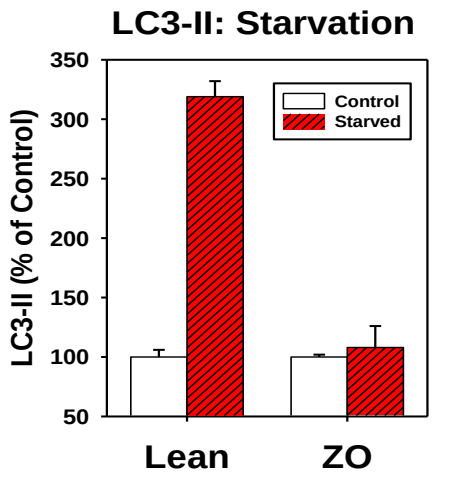


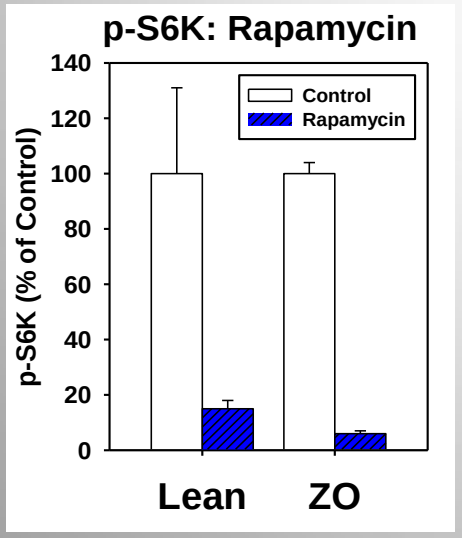


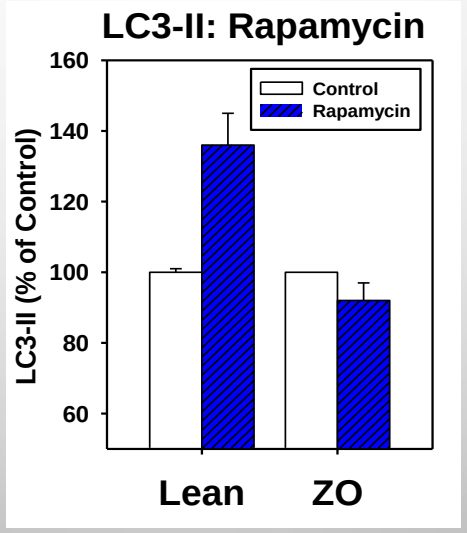


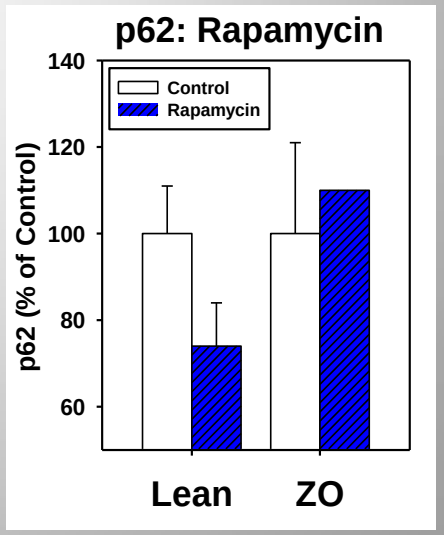


Impaired Autophagy in Adult Myocytes from ZO Rats with MetS

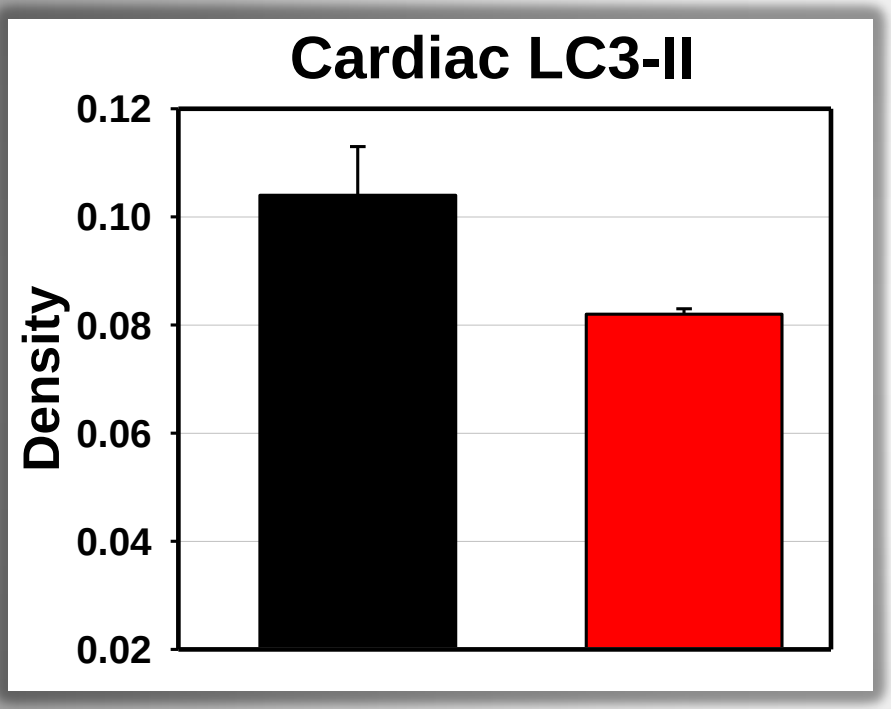


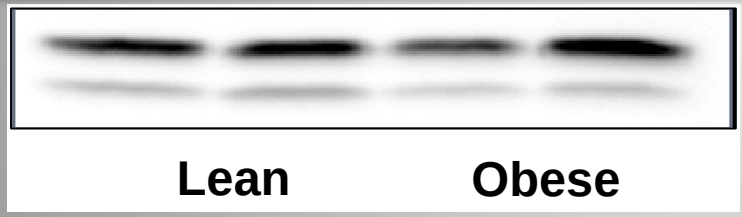


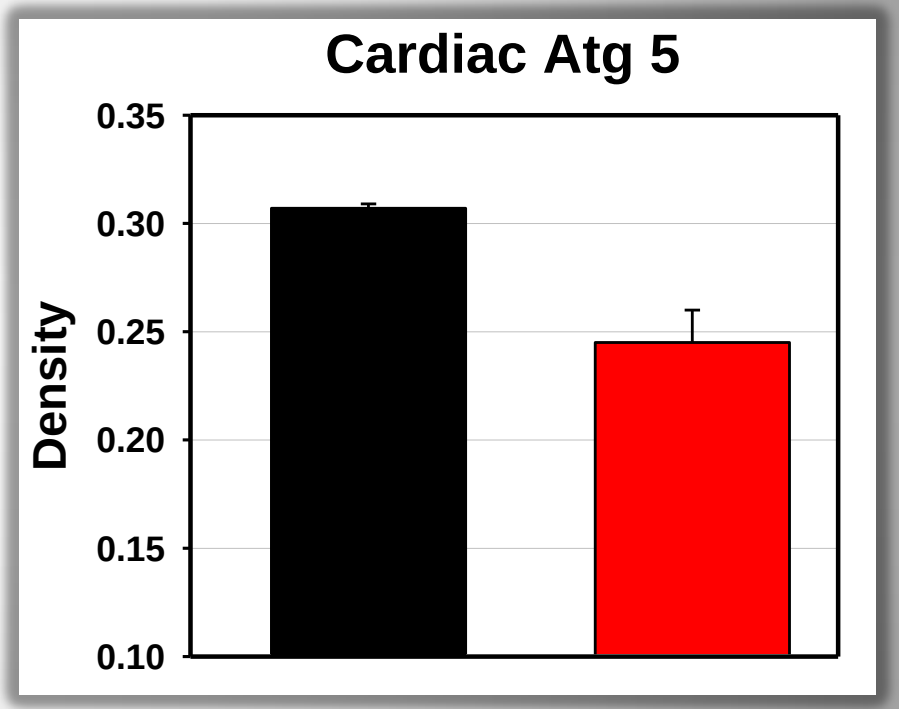




Autophagy is Reduced in in ZO Rats with MetS

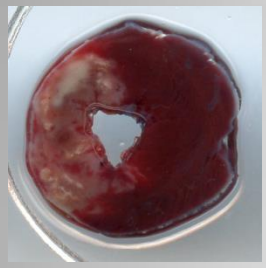


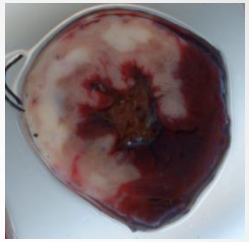


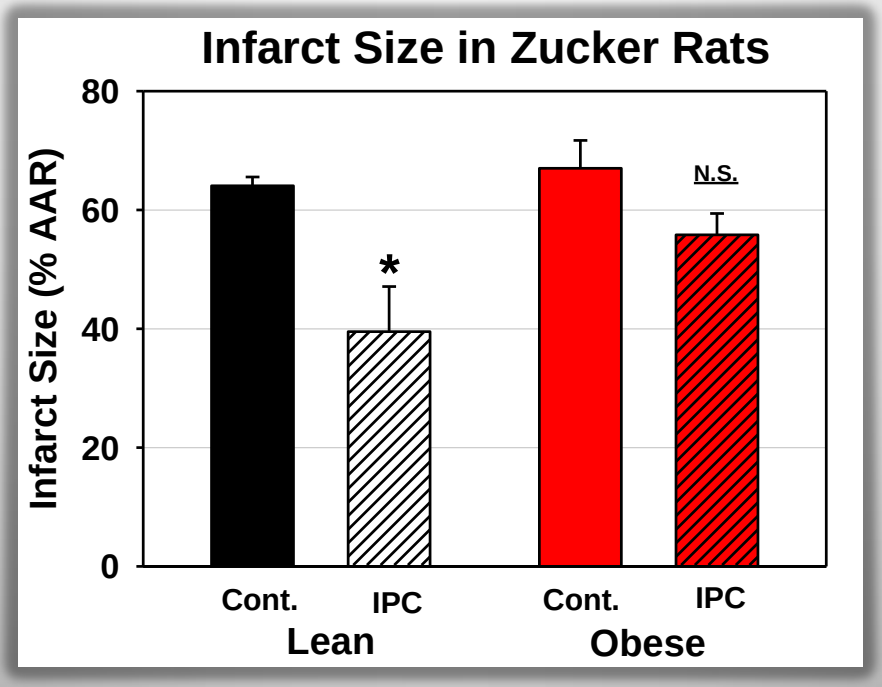


Impaired Pre-conditioning in Zucker Obese Rats with MetS

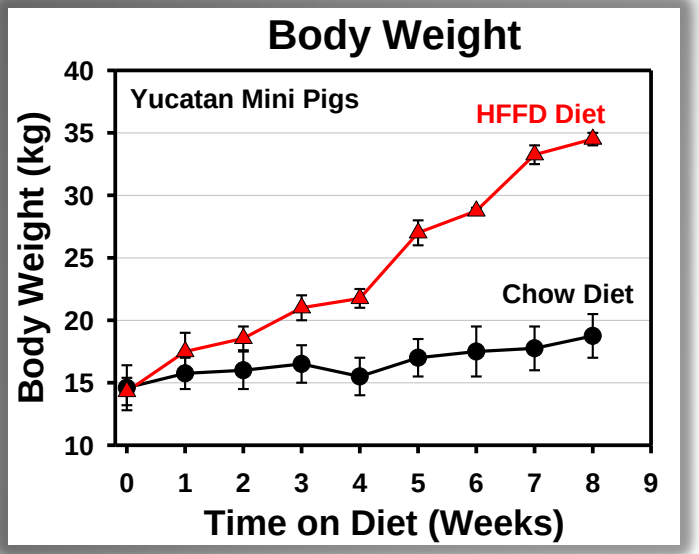
Lean Cont. **Lean IPC** **Obese Cont.** **Obese IPC**

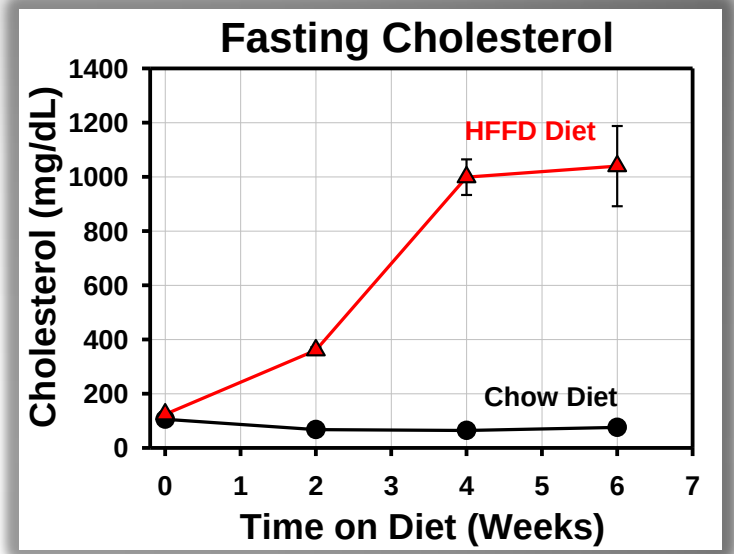


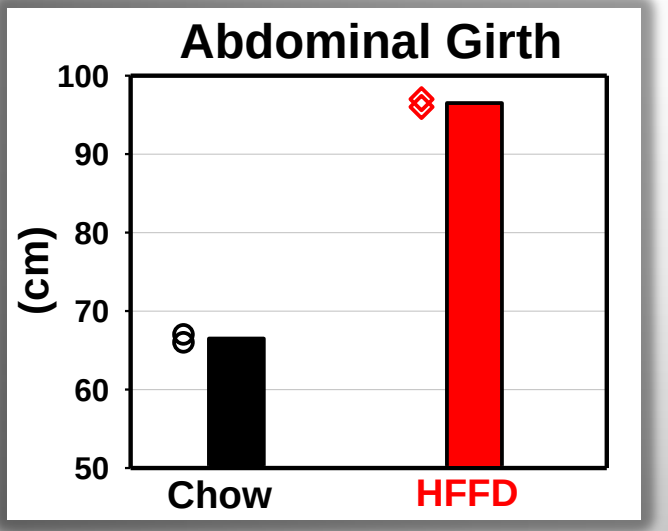


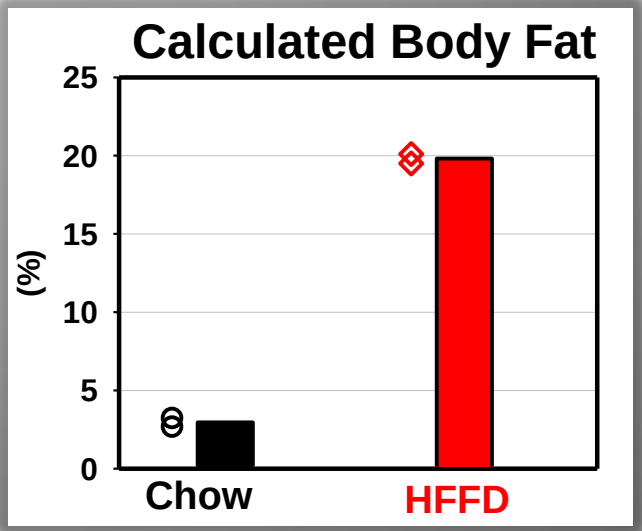



Obesity and Hypercholesterolemia in High Fat/ Fructose Fed Yucatan Pigs

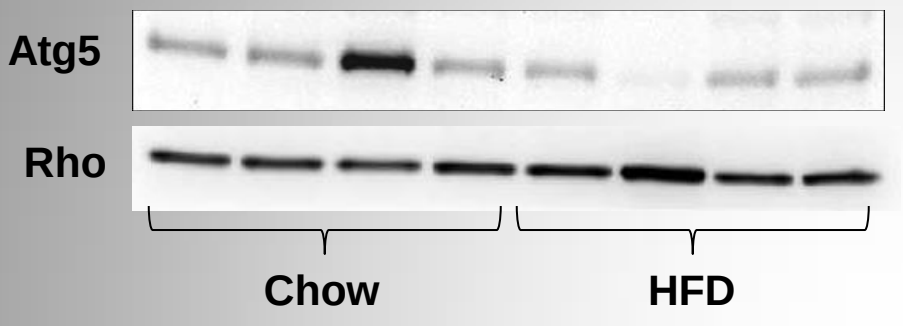


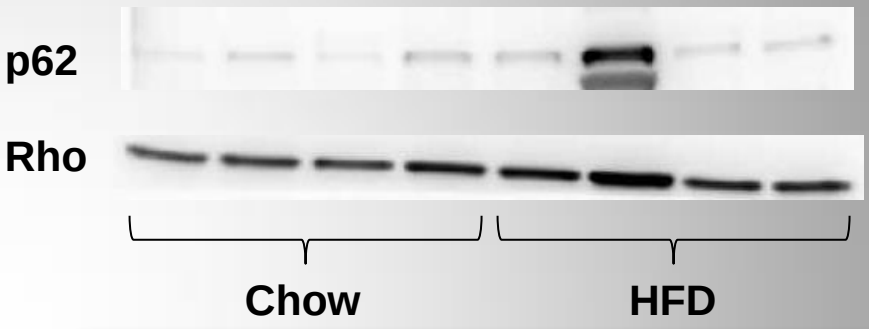


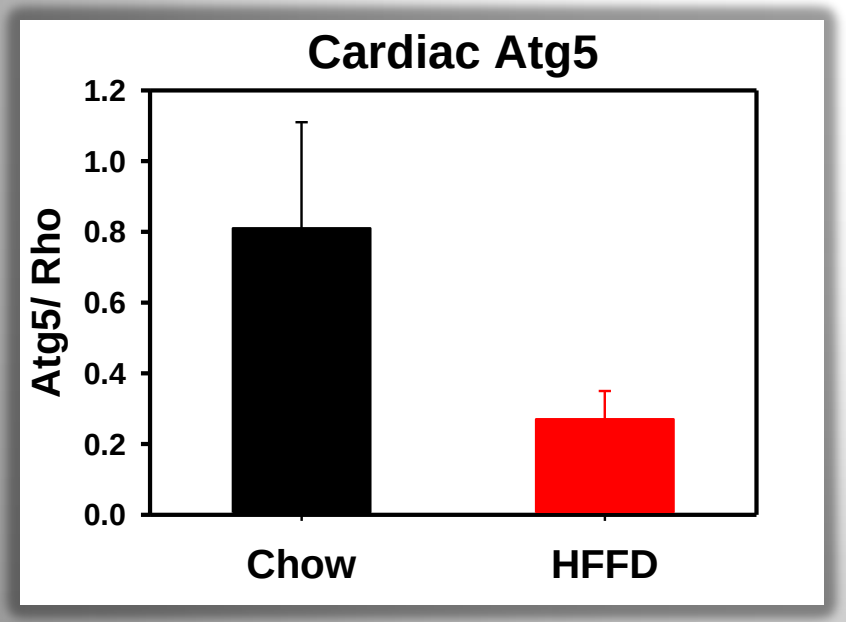


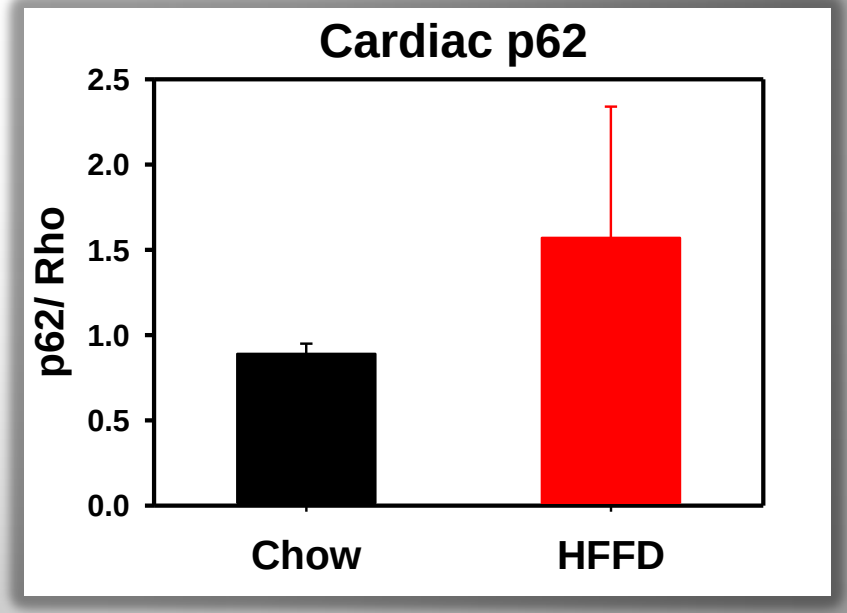


Depressed Autophagy in Obese Yucatan Pigs

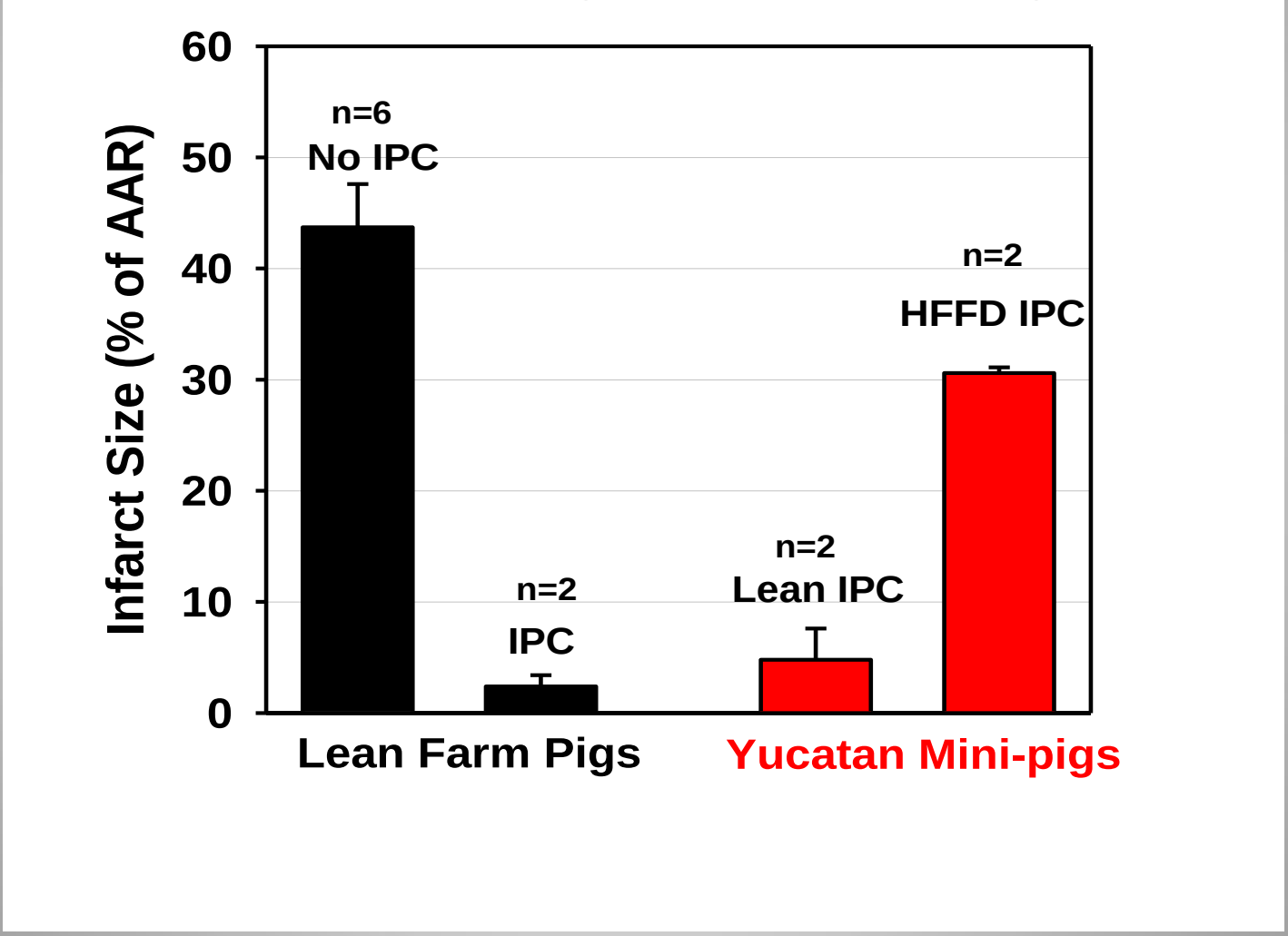








Impaired Preconditioning in Obese Swine with MetS



Summary

Animal models of metabolic syndrome show impaired autophagy and loss of cardioprotection

But do we know about autophagy and cardioprotection in the human heart?

Autophagy in the Human Heart

- Upregulated autophagy in failing heart decreased after mechanical unloading
  - Kassiotis et al. *Circulation* 2009
- Impaired autophagy associated with postoperative atrial fibrillation
  - Garcia et al. *J Thorac Cardiovasc Surg* 2011

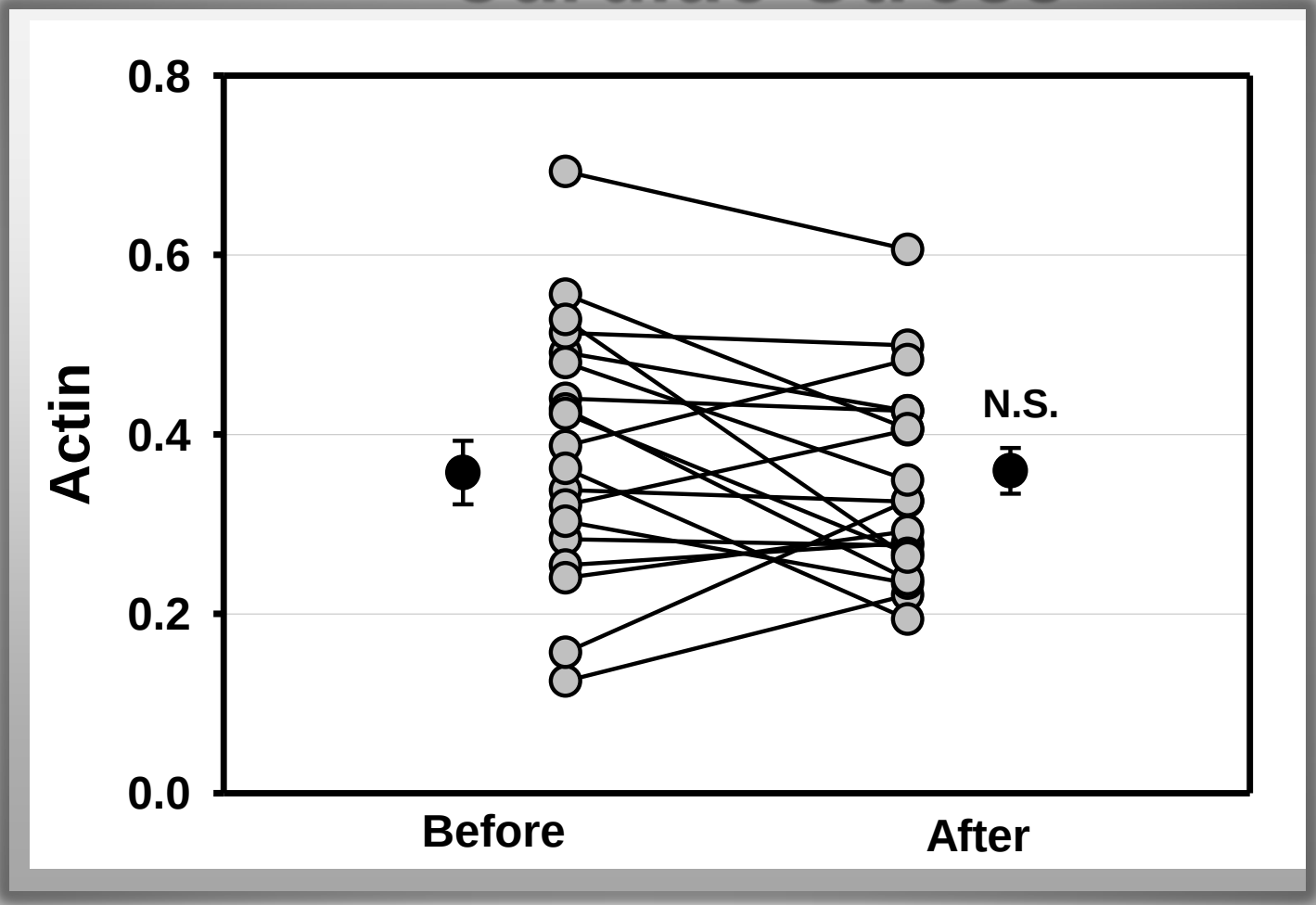
Methods (1)

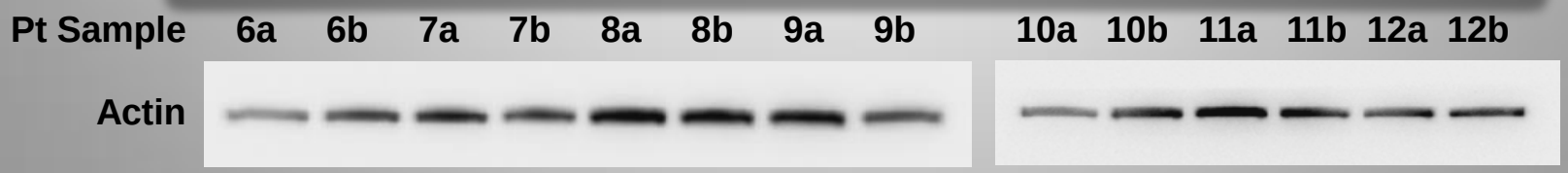
- 19 patients (38 samples) undergoing cardiac surgery
- Right atrial tissue (200-400 mg) obtained before cross-clamping the aorta and after its removal
- Western blotting used to measure autophagy proteins (Beclin-1, Atg5-12, SQSTM1/p62)

Methods (2)

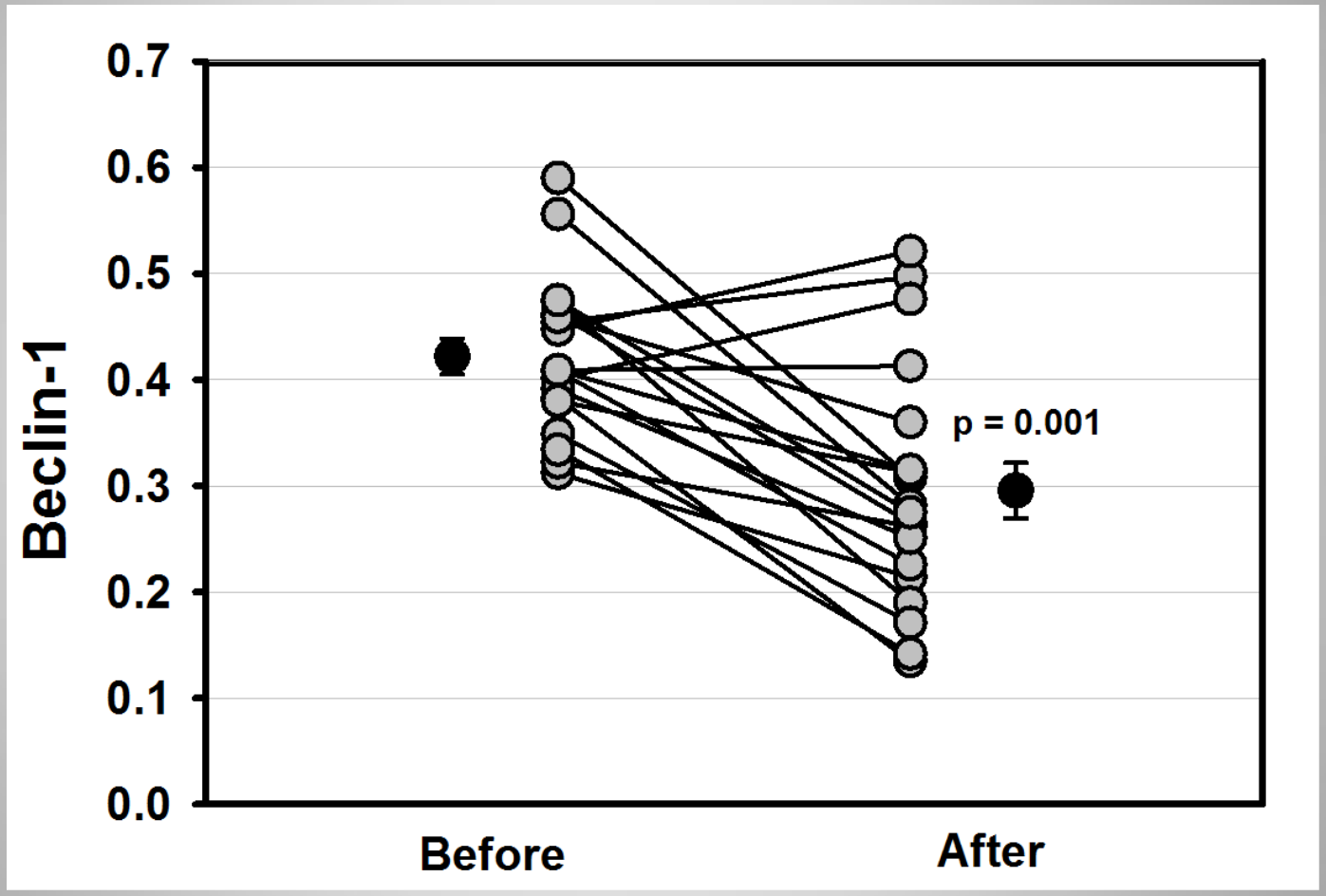
- The perioperative autophagic response was correlated with the morbidity and mortality risk calculated from STS Adult Cardiac Surgery Database

Actin Levels Are Unaffected By Cardiac Stress

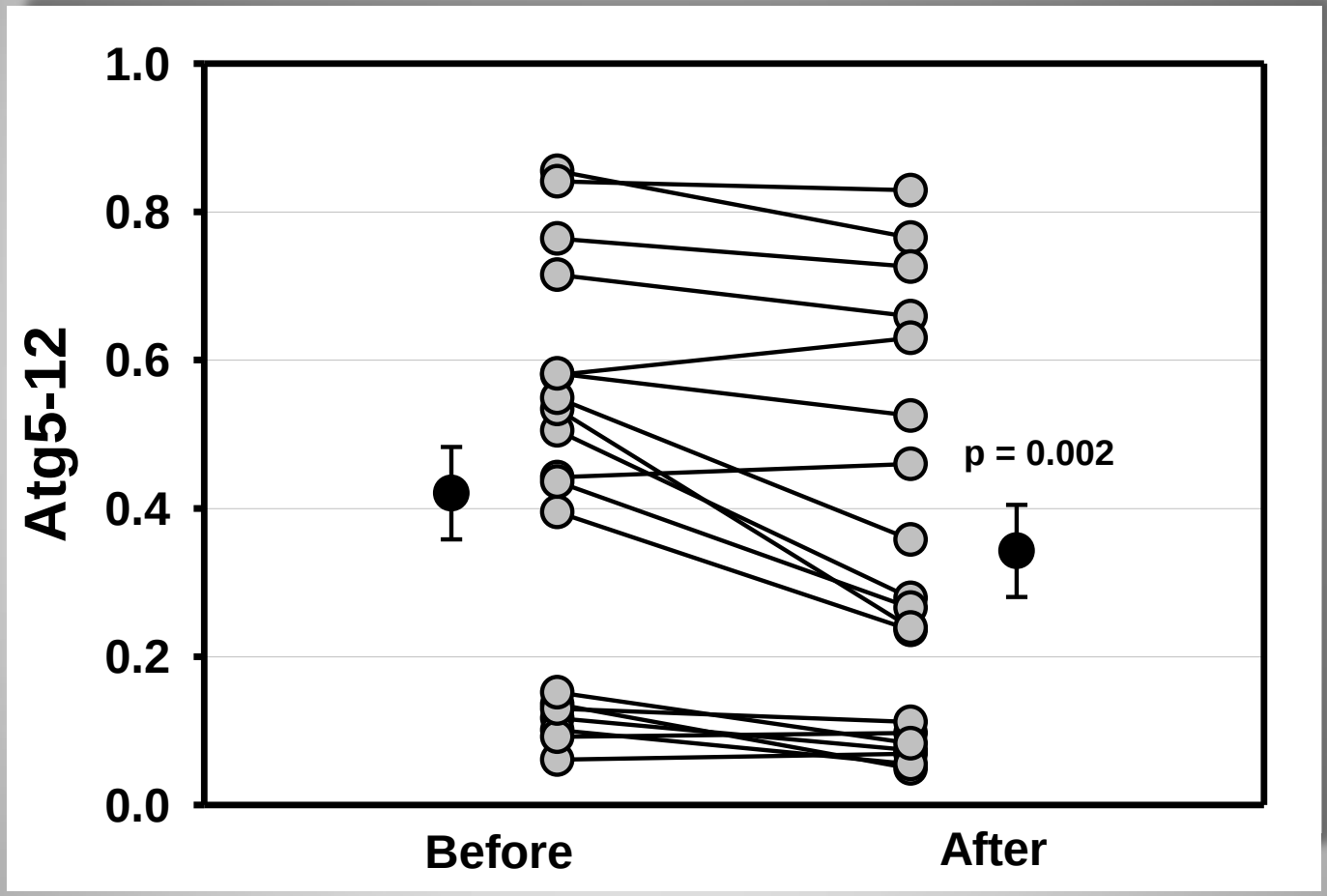


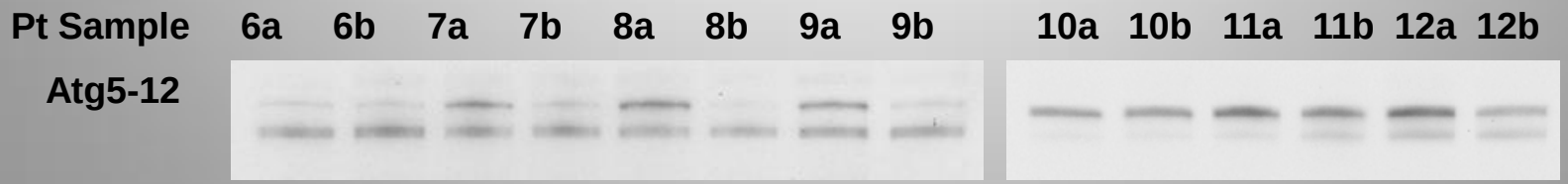


Cardiac Stress Is Associated with Decreased Levels of Beclin -1

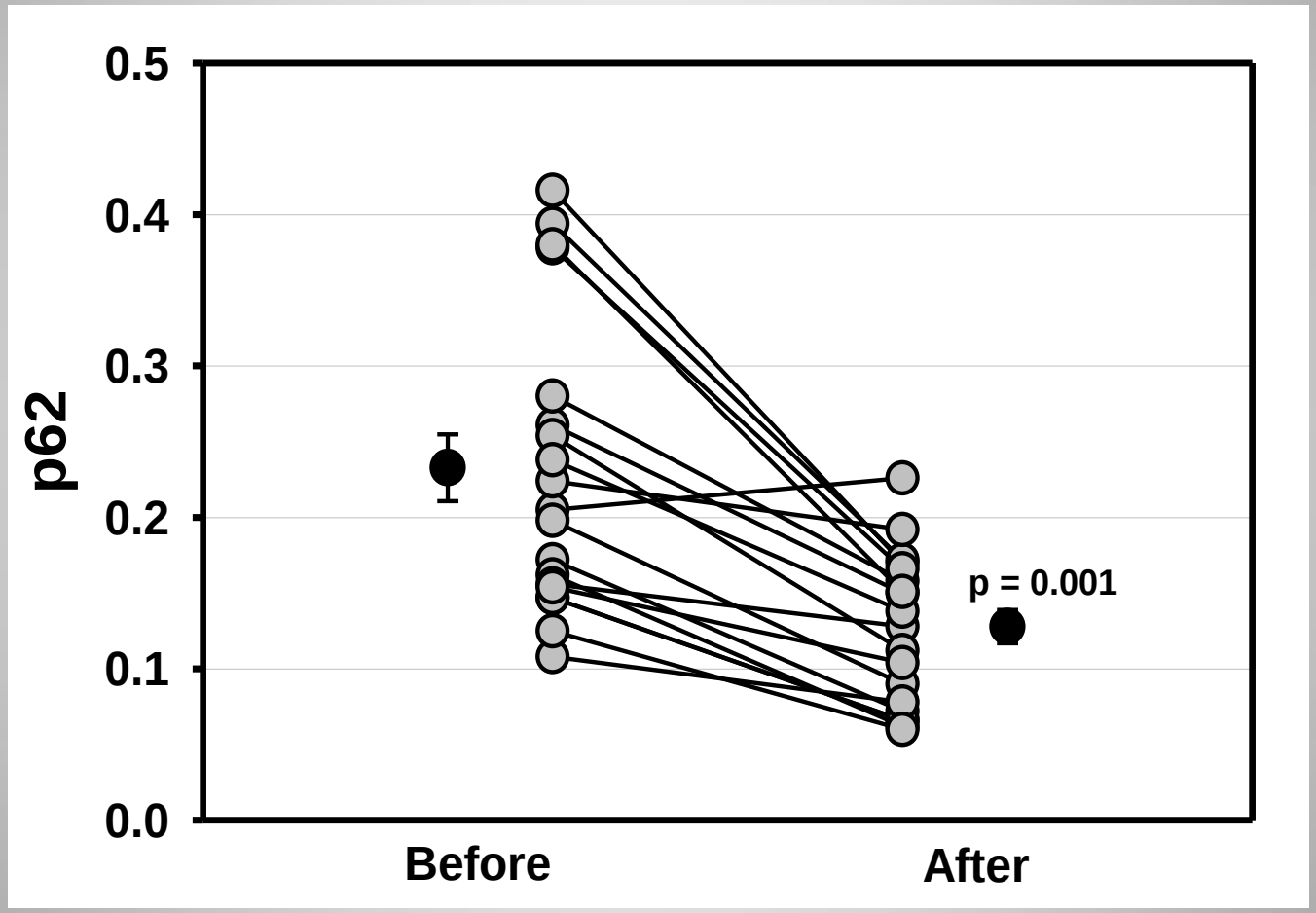


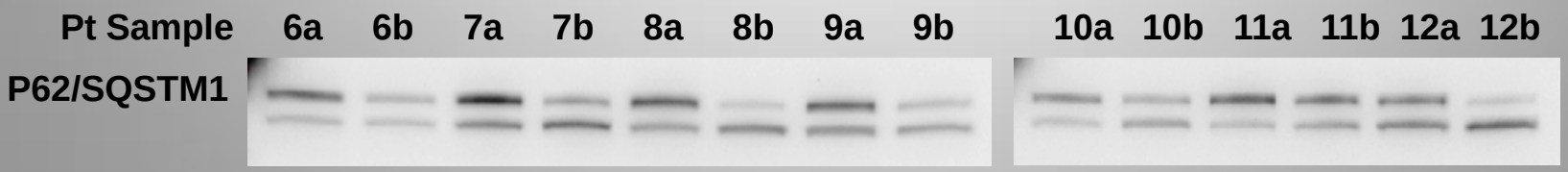
Cardiac Stress Is Associated with Decreased Levels of Atg5-12



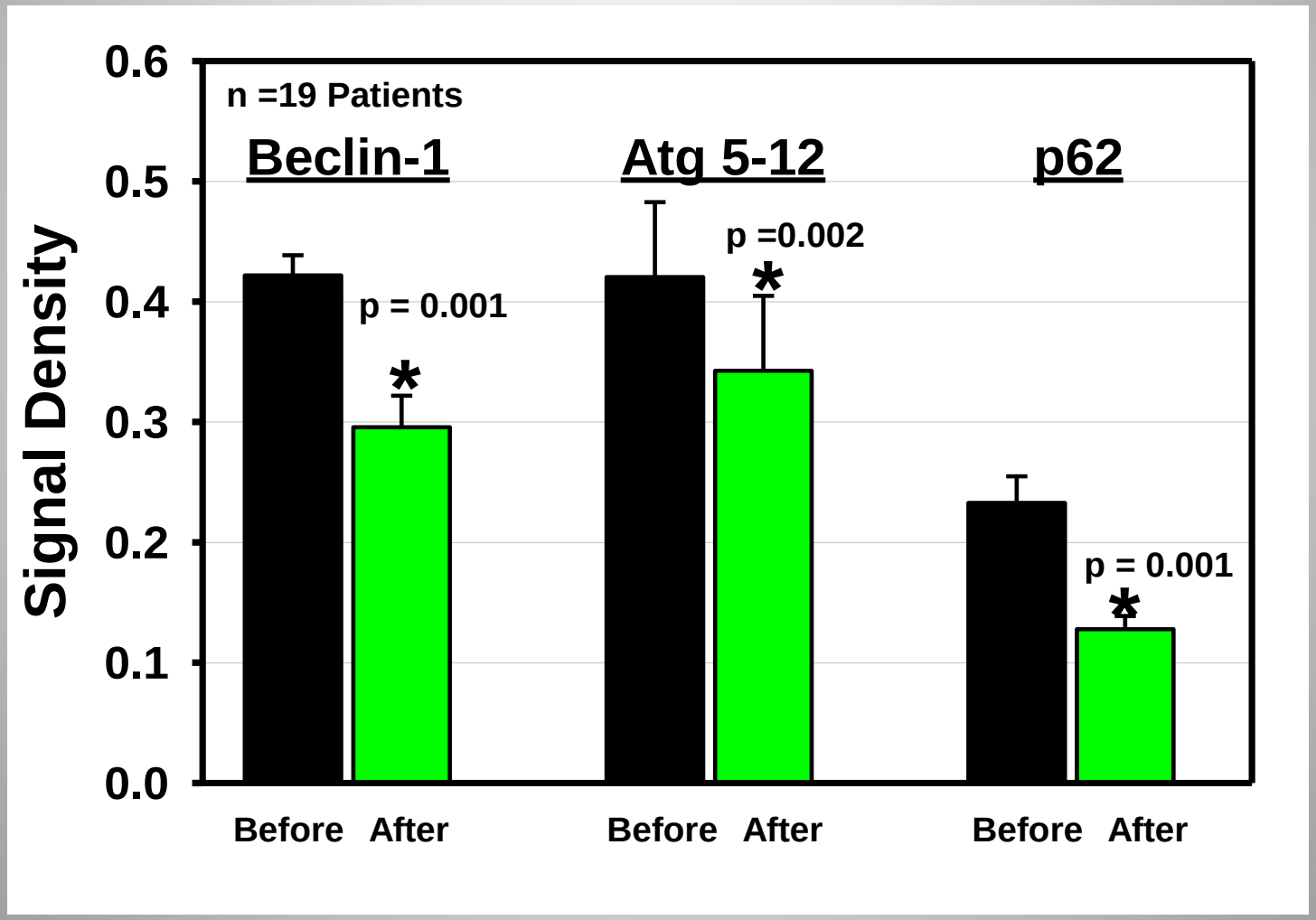


Cardiac Stress Is Associated with Decreased Levels of p62

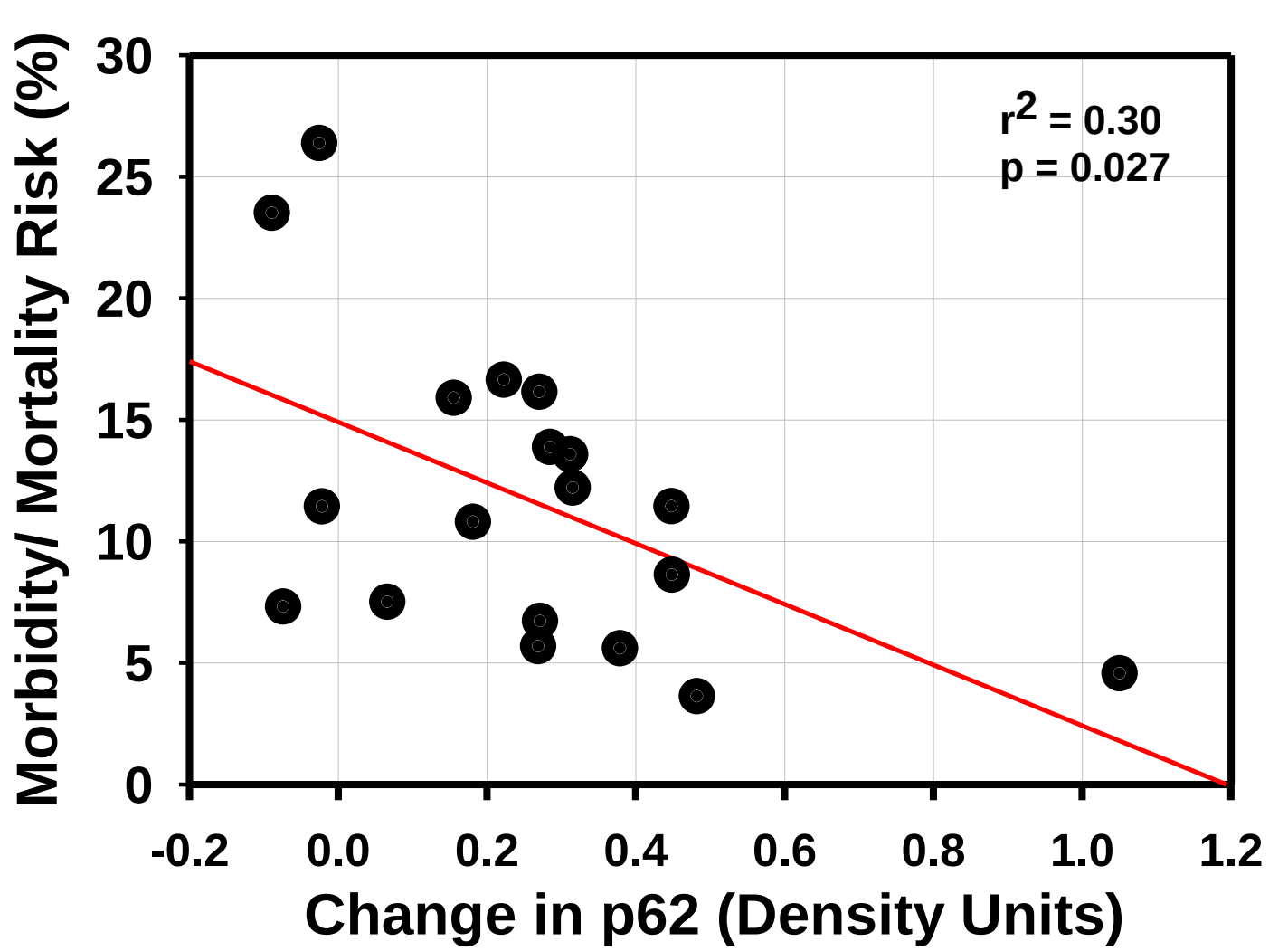




Cardiac Stress Depletes Key Autophagy Proteins



Operative Risk Correlates with Changes in Autophagy



Summary

- Preclinical studies support concept that autophagy is cardioprotective and is impaired in MetS
- Cardiac surgery and its attendant ischemia is accompanied by accelerated autophagic flux
- The magnitude of flux increase is inversely correlated with risk

Conclusion

- Studies evaluating the role of autophagy in setting of I/R are feasible in humans
- Enhancement of autophagy represents a new clinical approach to myocardial protection during heart surgery

Preparing for OMICS 2013

Acknowledgements

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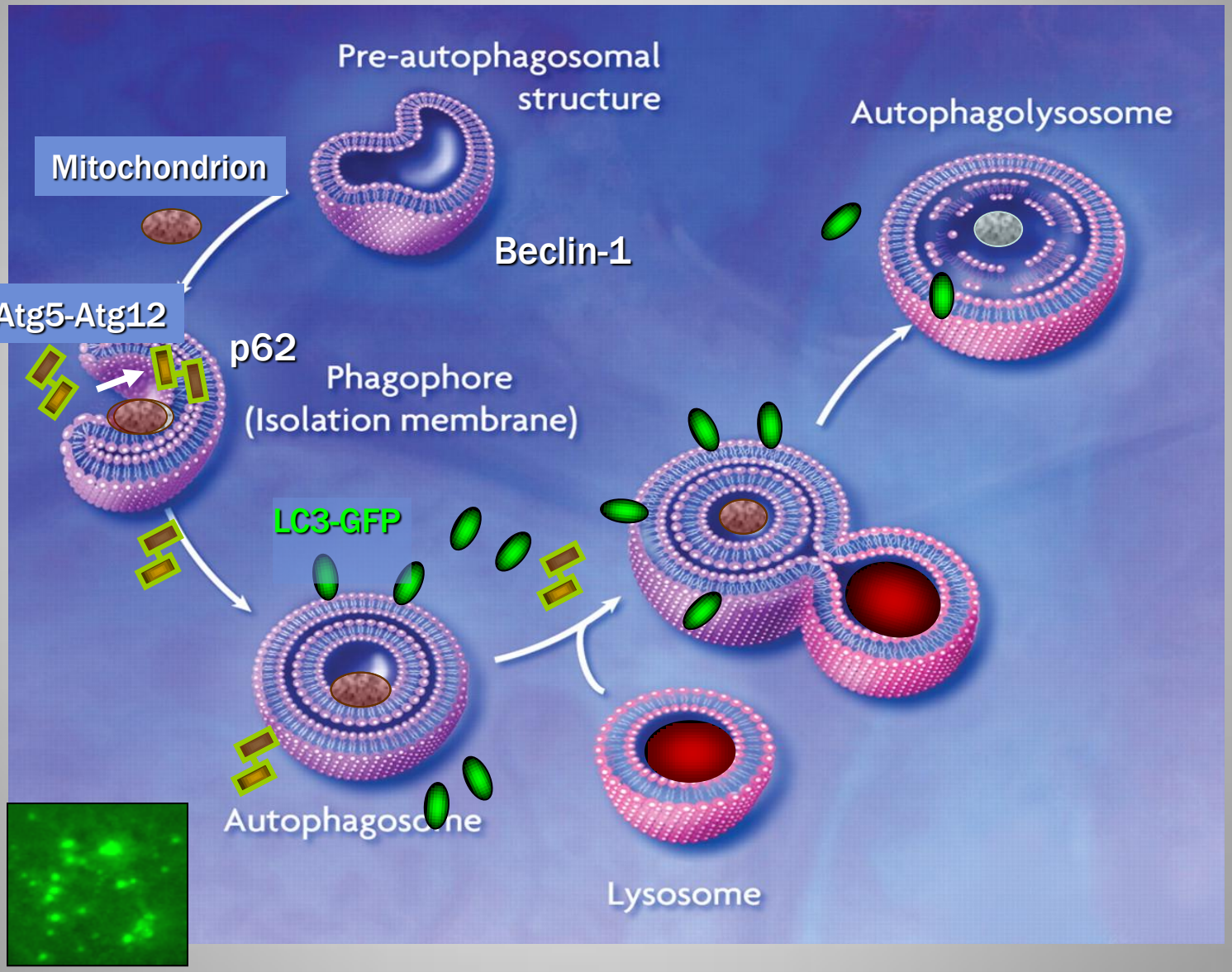
  - Zoltan Giricz
  - Allen Andres
- Students
  - Nandini Ravindran
  - Carlos Bazan

Mechanism is Adaptive Autophagy



Modified from T. Shintani et al., Science 306, 990 -995 (2004)

Conclusion

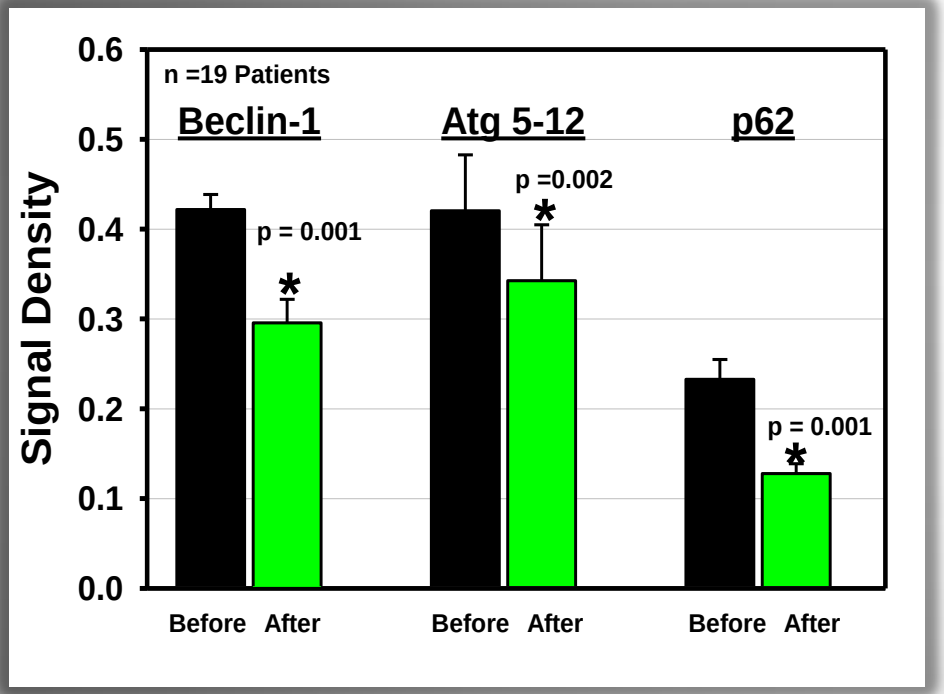
- The findings suggest that the future of better cardioprotection lies with our ability to enhance this important adaptive response to ischemic stress

The Homeostatic Intracellular Repair Response (HIR^2)

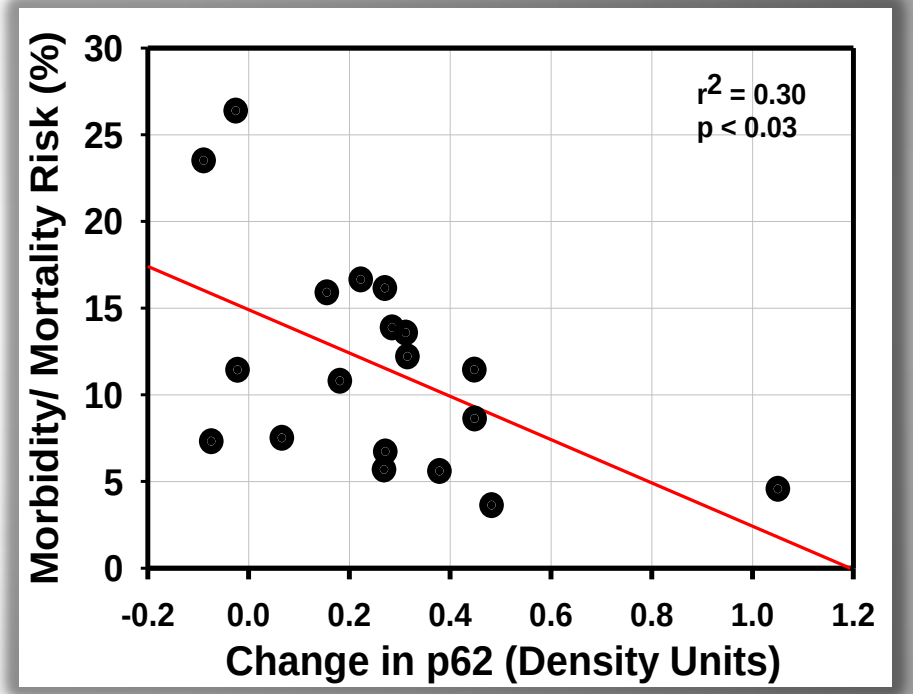
- HIR^2 is a lysosomal adaptive response to stress
- Represents a new approach to myocardial protection
- Preclinical evidence indicates it is manifest in multiple organs and is cardioprotective

Increased Autophagic Flux is Associated with Reduced M/M Risk

Autophagy Proteins



Calculated M/M Risk vs. p62



Summary

- Autophagy flux is inversely correlated with operative risk
- Autophagy in humans is an endogenous self protective response

Thanks' for your kind attention!!!!!!

Let Us Meet Again

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