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# **UVRAG and Rubicon Regulate Cardiac Autophagy and Function**

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**Macroautophagy (Autophagy) is a evolutionarily conserved pathway that degrades cytoplasmic components in lysosomes.**

# Physiological Functions of Cardiac Autophagy

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- Basal autophagy is required for the maintenance of homeostasis in the heart.
- Provision of nutrient during catabolism
- Generation of ATP in starved cells
- Removal of damaged organelles and protein aggregates
- Degradation of misfolded proteins
- Dysregulated autophagy contributes to many forms of heart diseases.

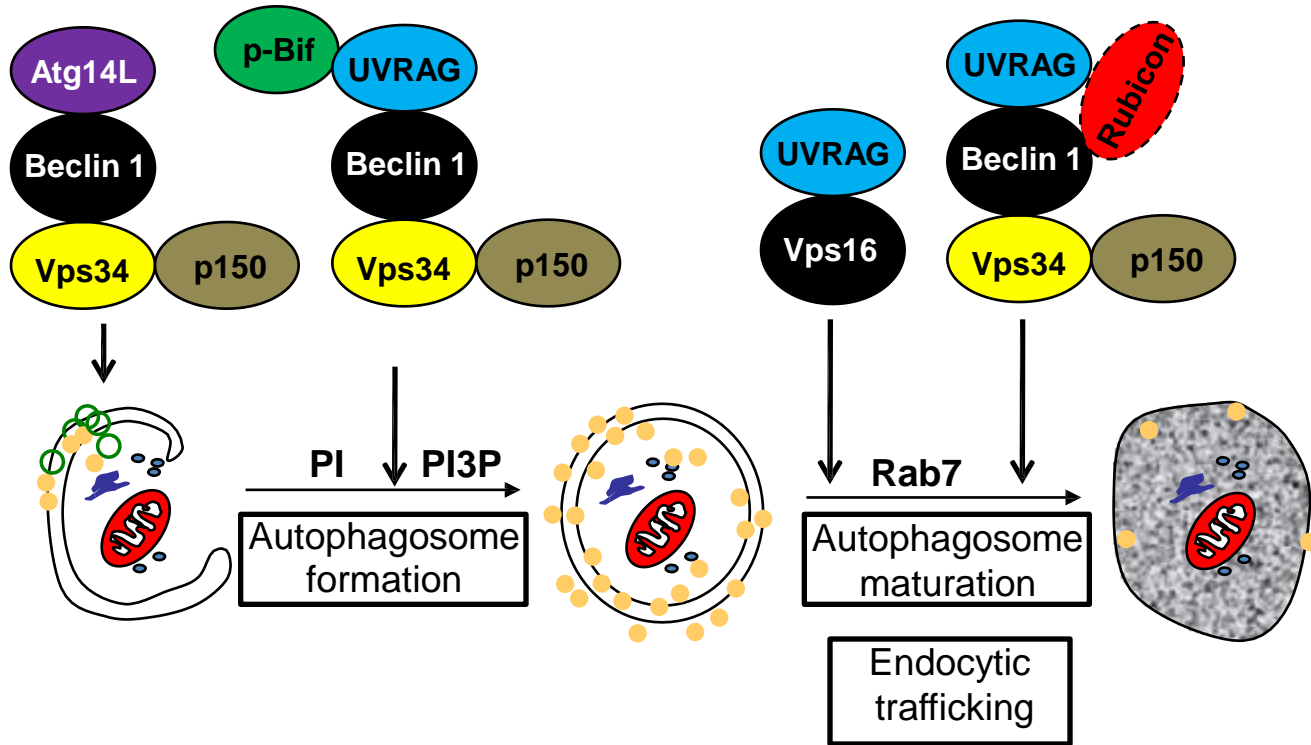
# UVRAG

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- UVRAG: The ultraviolet (UV) radiation resistance-associated gene.
  - Homologue of yeast Vps38.
  - Partially complement UV sensitivity in xeroderma pigmentosum (XP) cells.

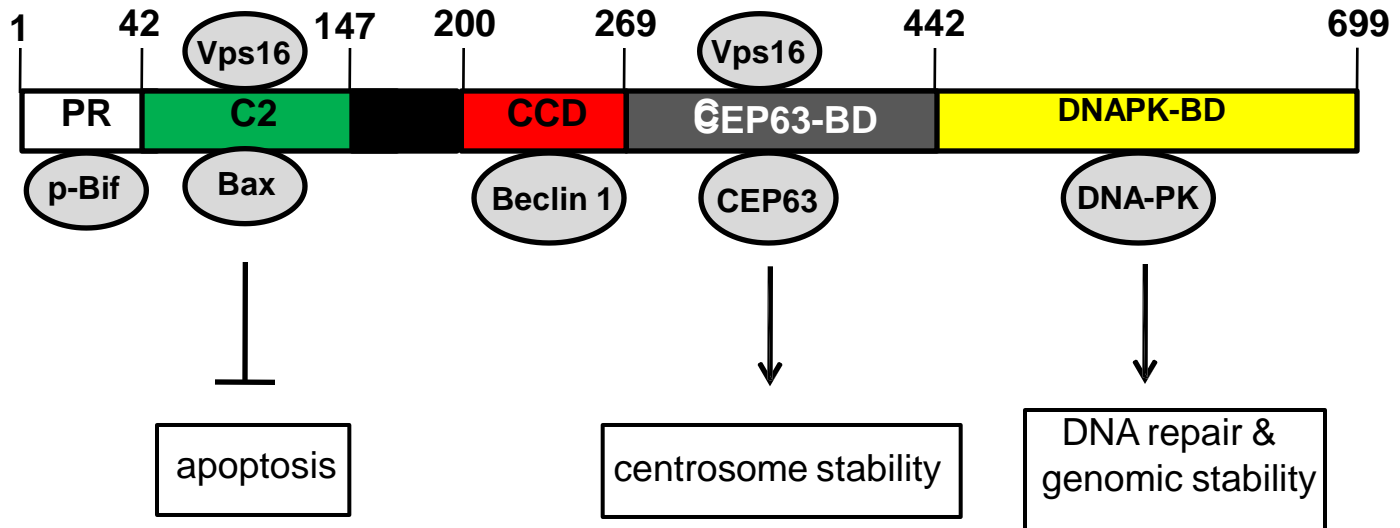
Monoallelically deleted in colon cancer, breast cancer and gastric cancer.
  - Tumor suppressor.

# Regulation of Autophagy and Endocytic Trafficking by UVRAG and Rubicon



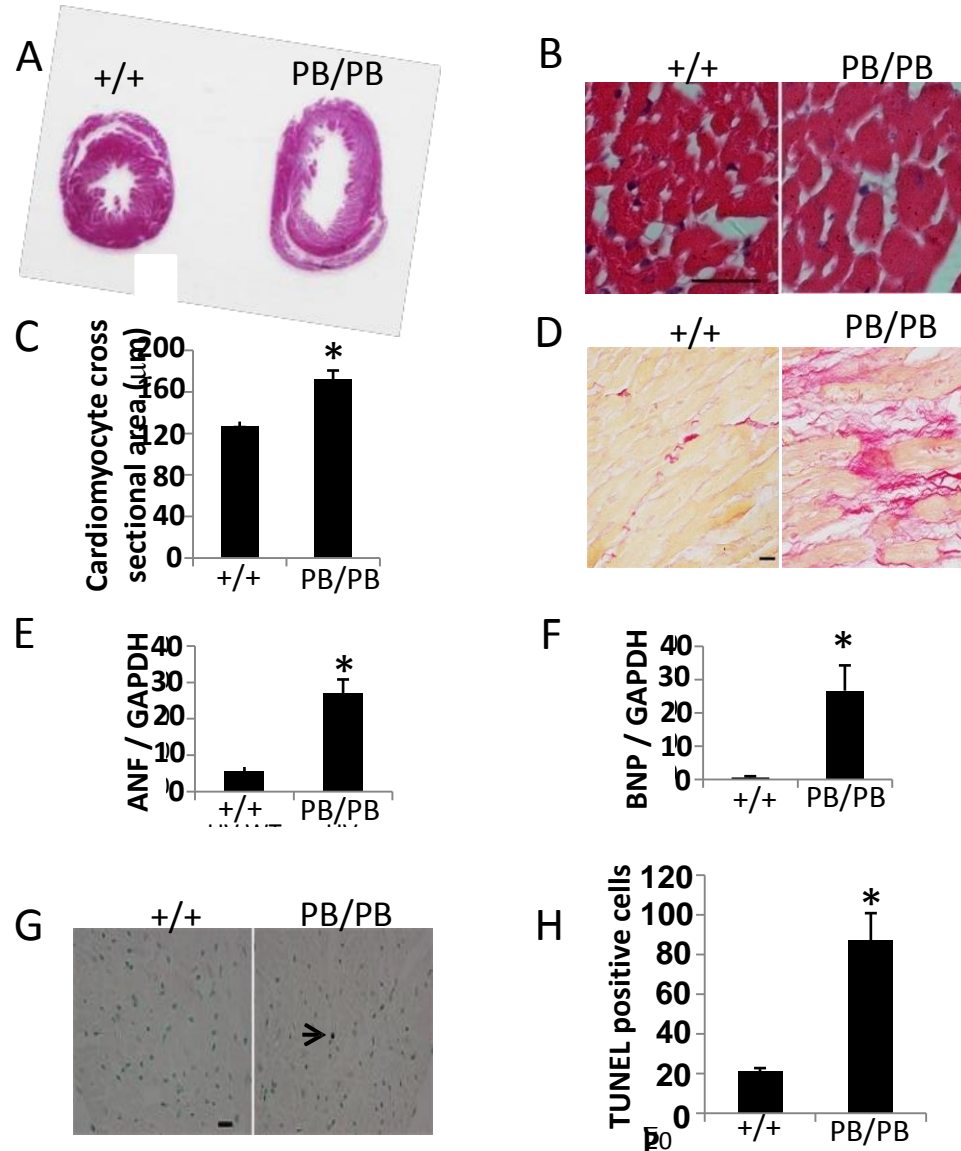
# UVRAG Complexes

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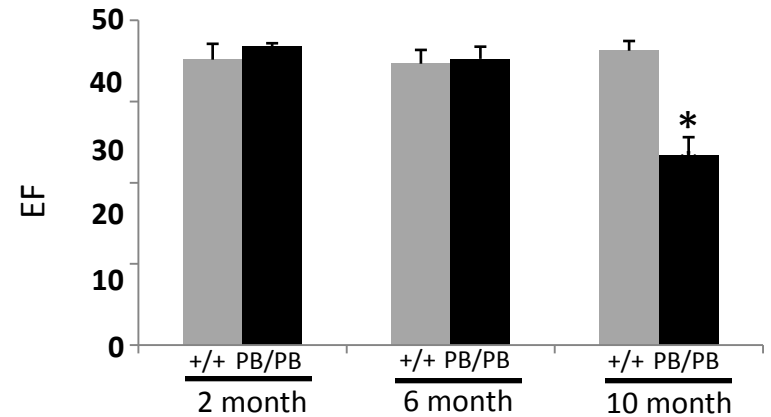
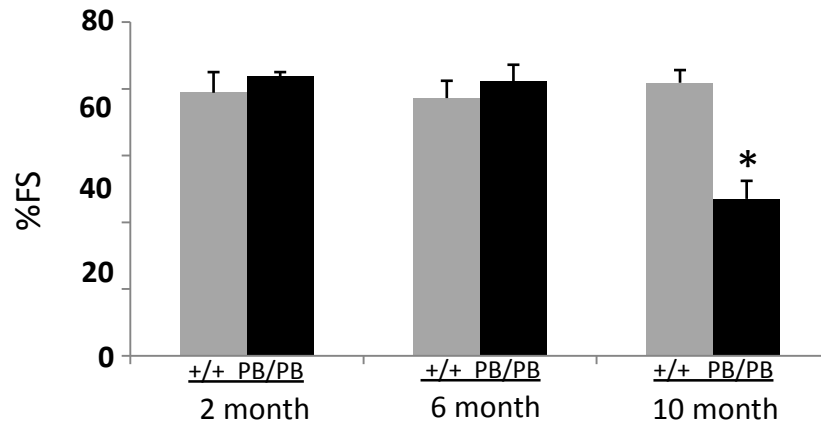
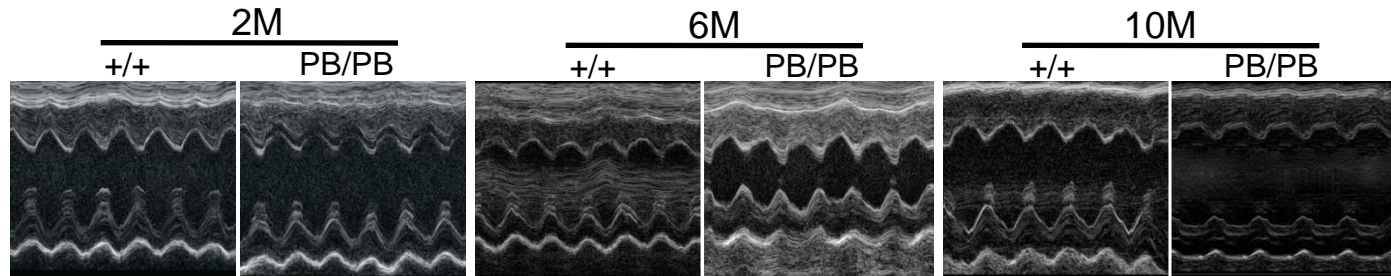




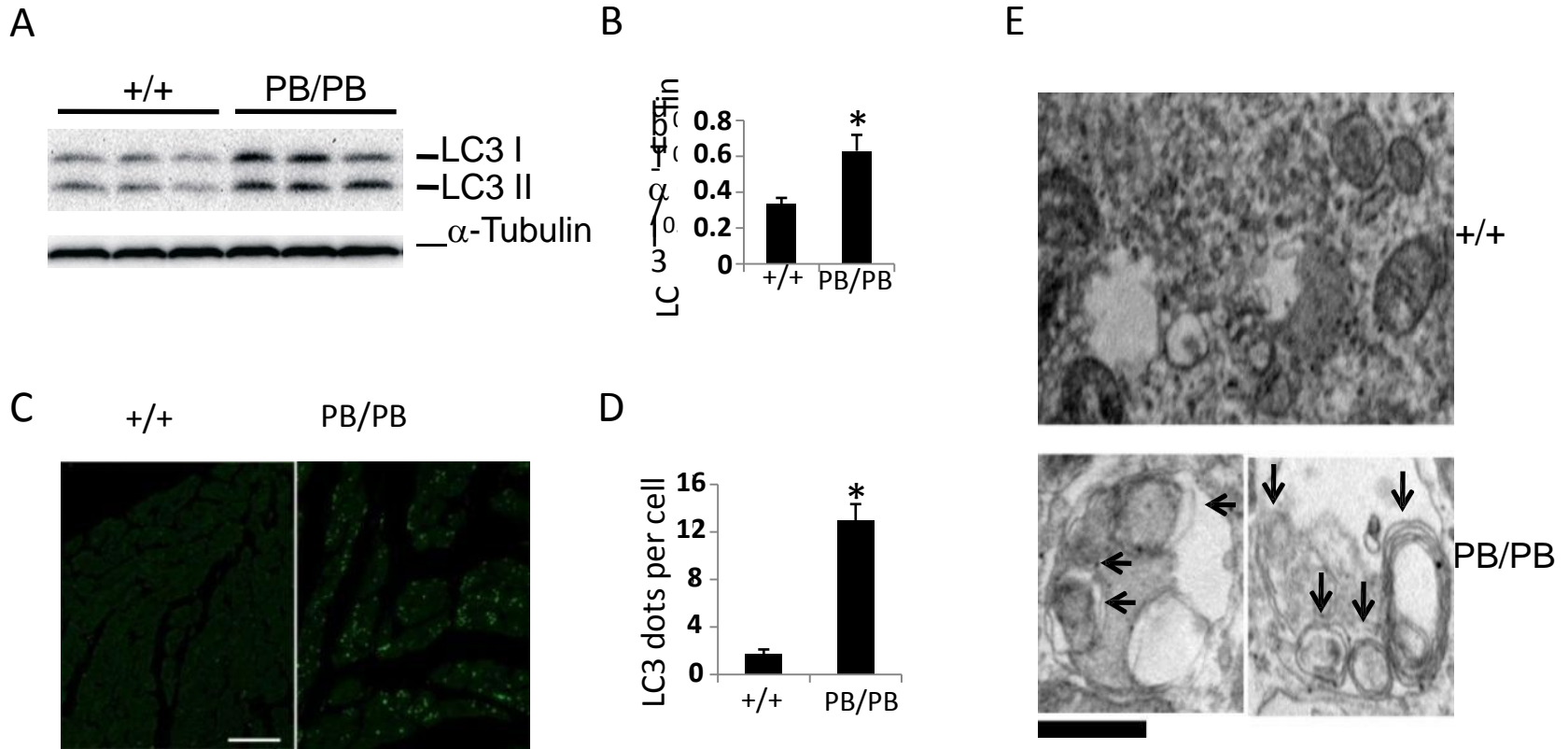
# UVRAG-deficient Mice Develop Age-related Cardiomyopathy



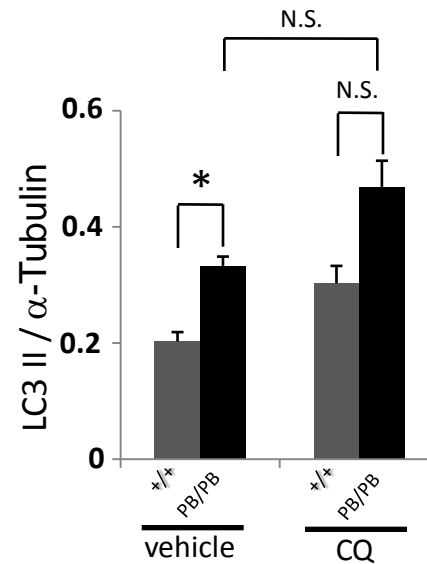
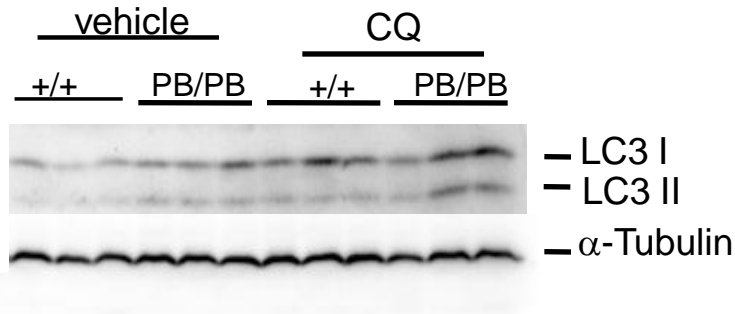
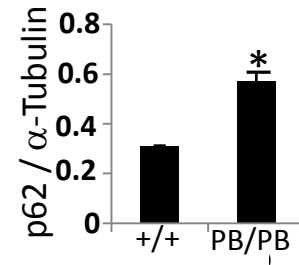
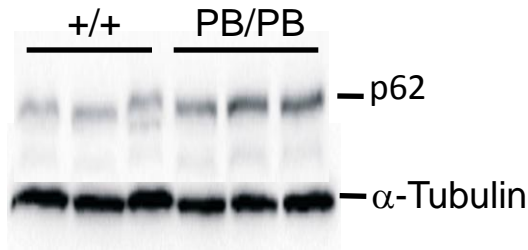
# Cardiac Function is Compromised in UVRAG-deficient mice



# Autophagosome is Accumulated in UVRAG-deficient Heart

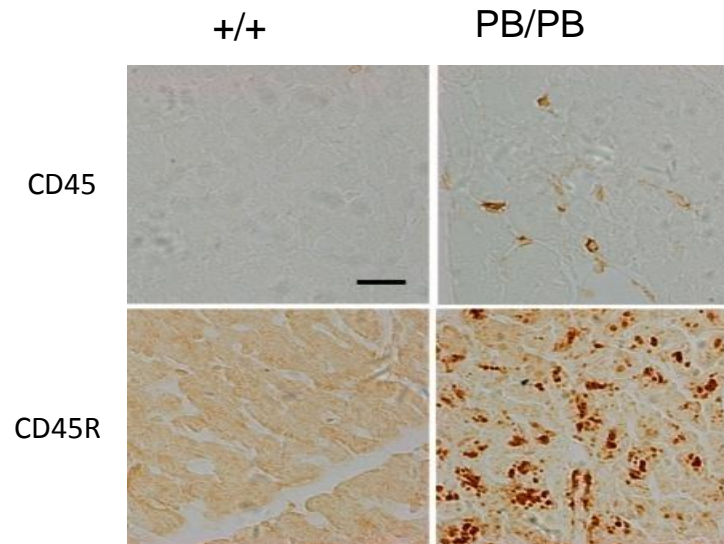
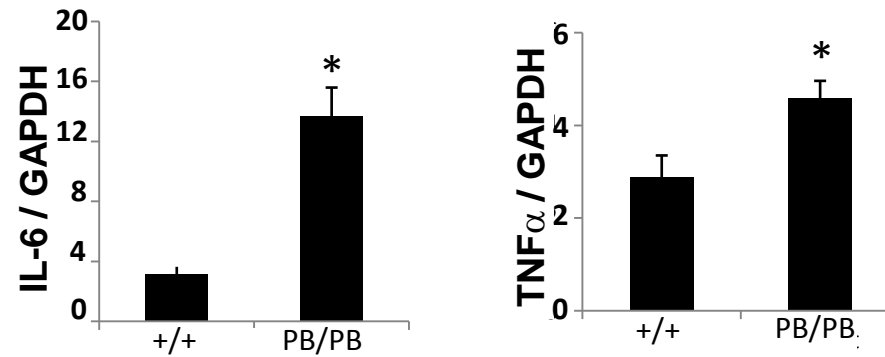


# UVRAG Deficiency Enhances Autophagic Flux in the heart



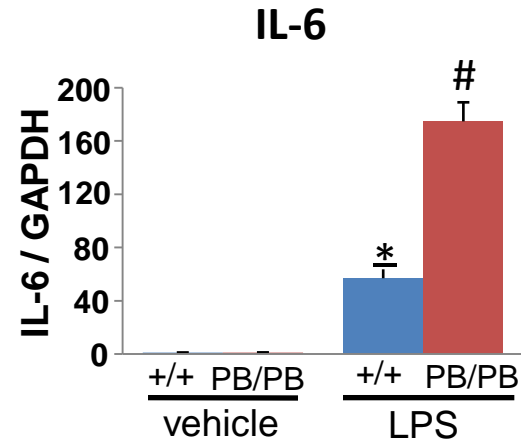
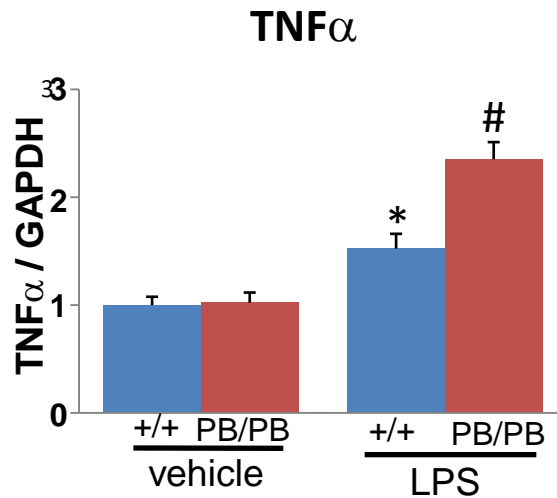
# Inflammatory Cytokine Expression is Up-regulated in UVRAG-deficient Heart

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# UVRAG Deficiency Enhances Pro-inflammatory Cytokine Expression in the Heart Following LPS Treatment

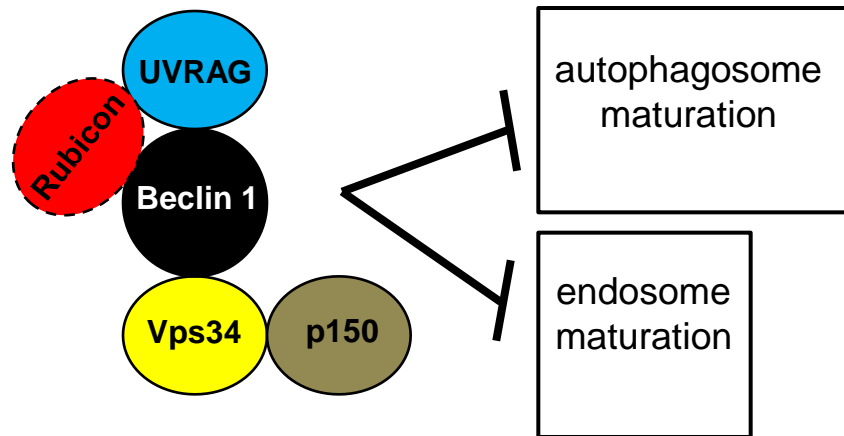
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# Rubicon

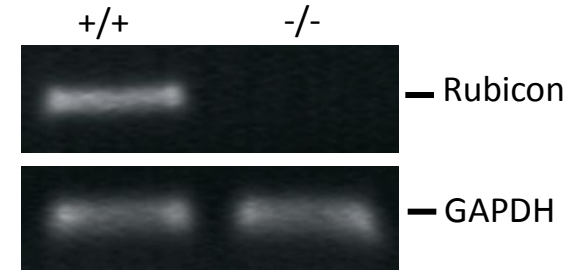
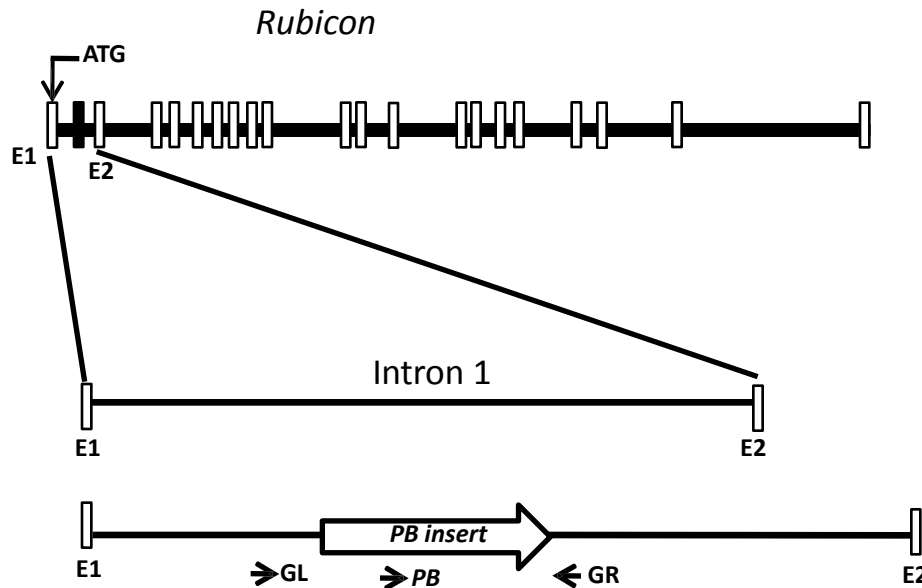
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- Rubicon: RUN domain protein as Beclin-1-interacting and cysteine-rich containing.



What is the physiological function of Rubicon in the heart?

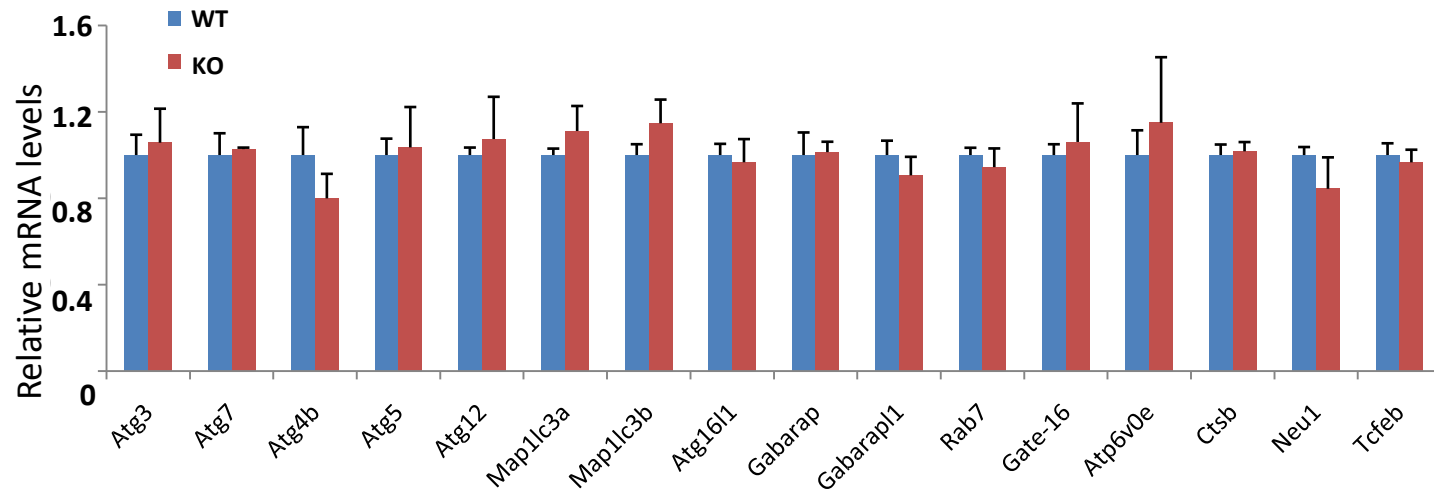
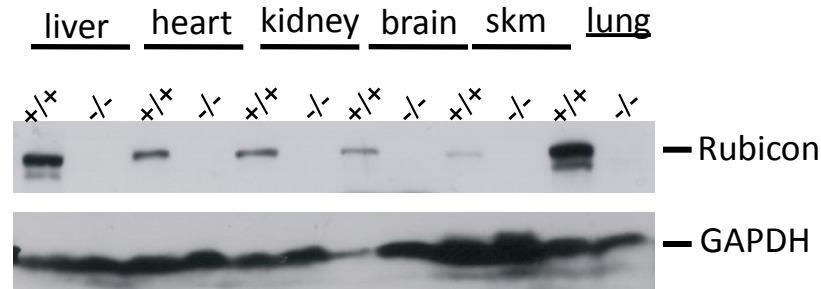
# Genetic Characterization of Rubicon Knockout (KO) Mice



+/+	PB/+	PB/PB	Total
80	150	70	300

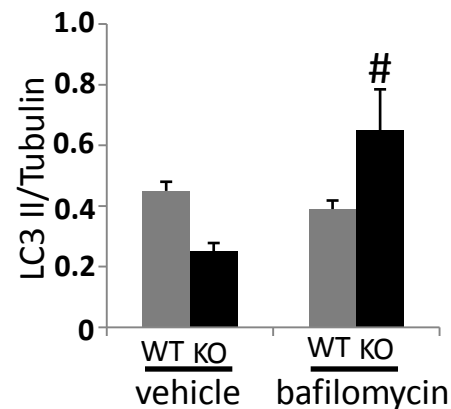
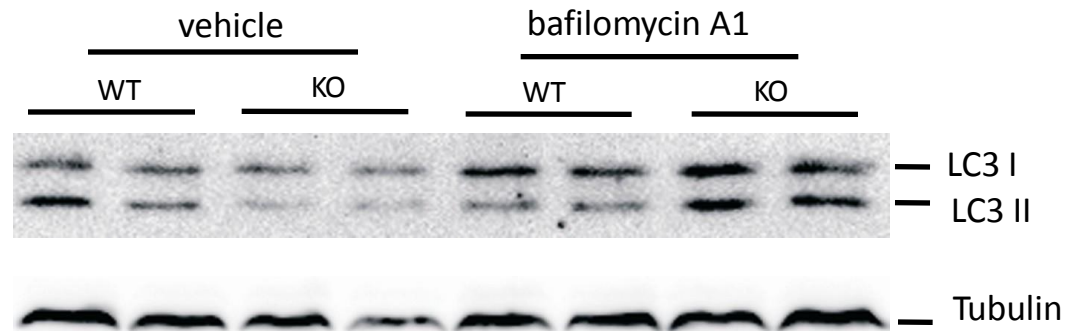


# Genetic Characterization of Rubicon Knockout (KO) Mice



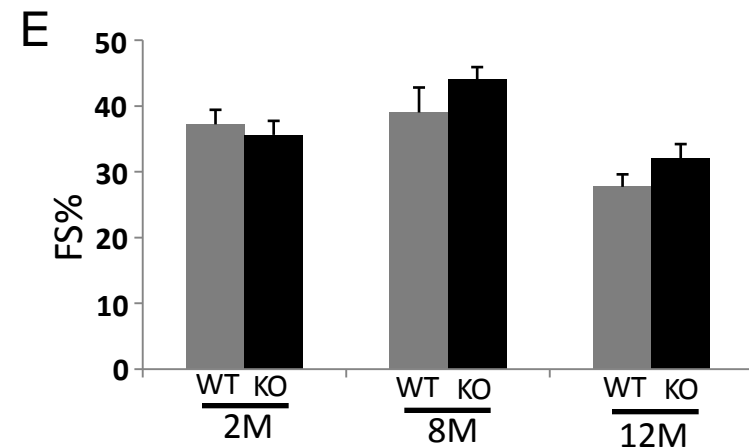
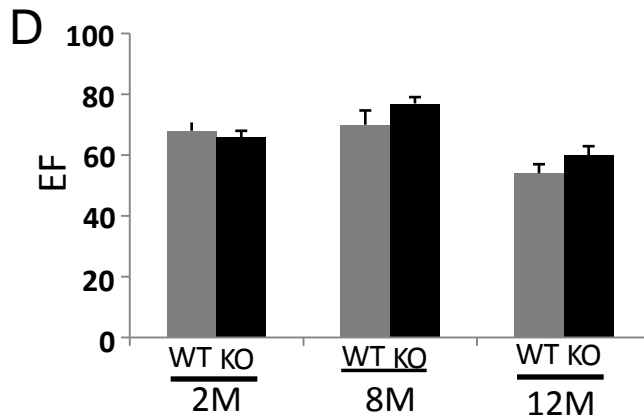
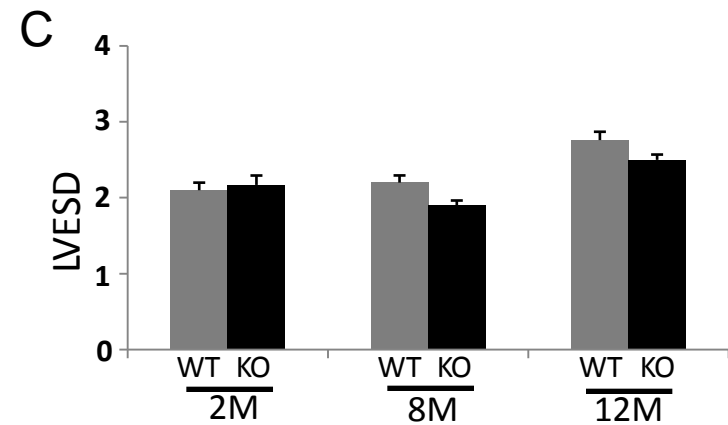
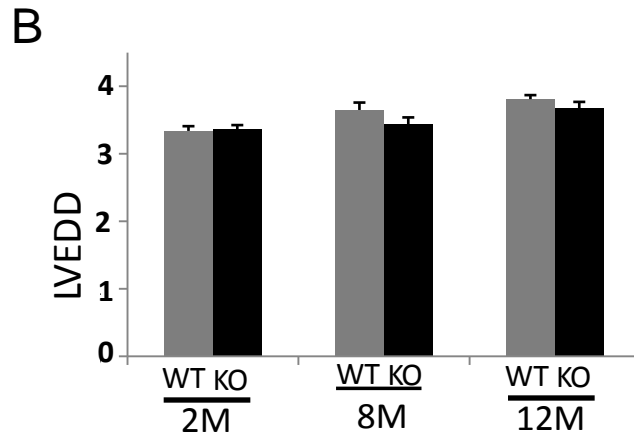
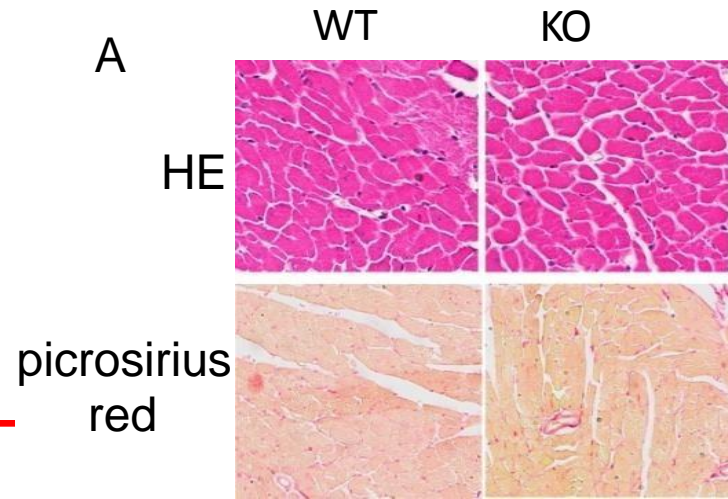
# Autophagic Flux is Enhanced in Rubicon KO Mouse Hearts

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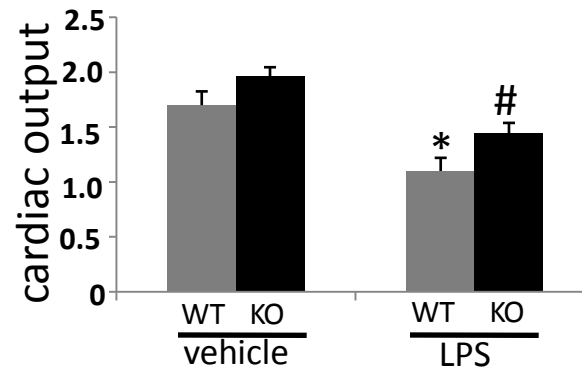
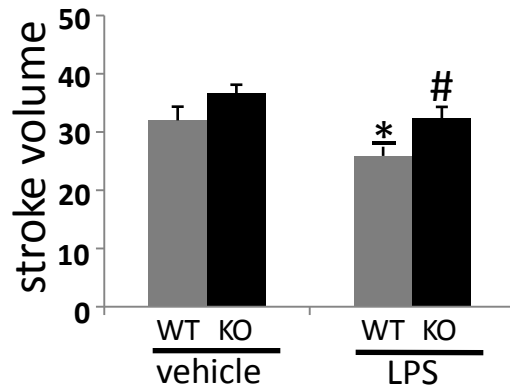
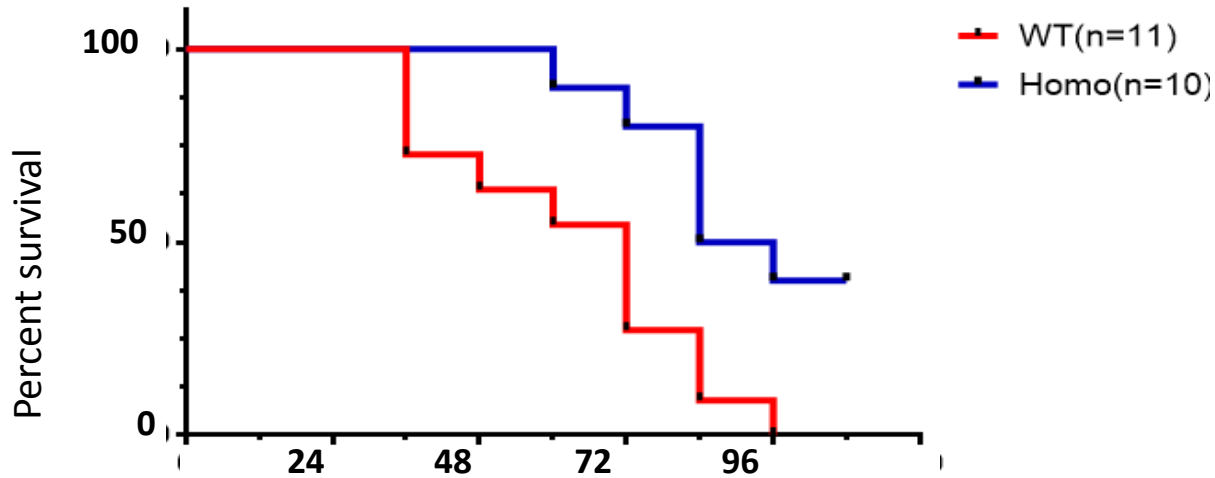


# Rubicon KO Mice Have Normal Cardiac Morphology and Function

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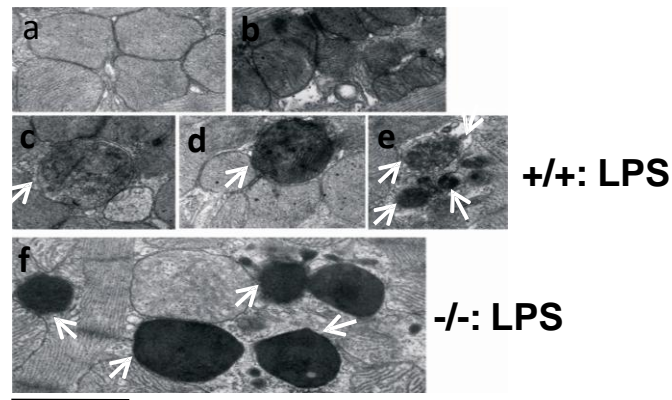
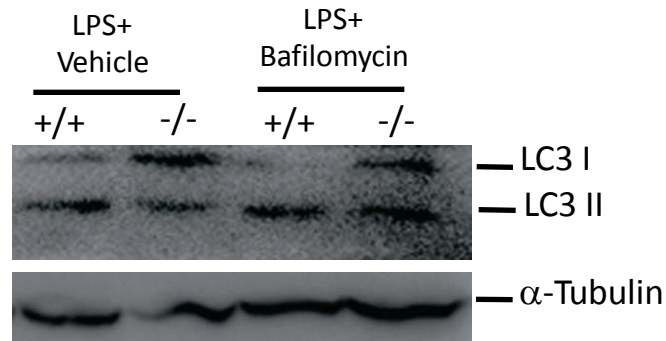


# Rubicon Deficiency Attenuates LPS-induced Lethality and Cardiac Dysfunction

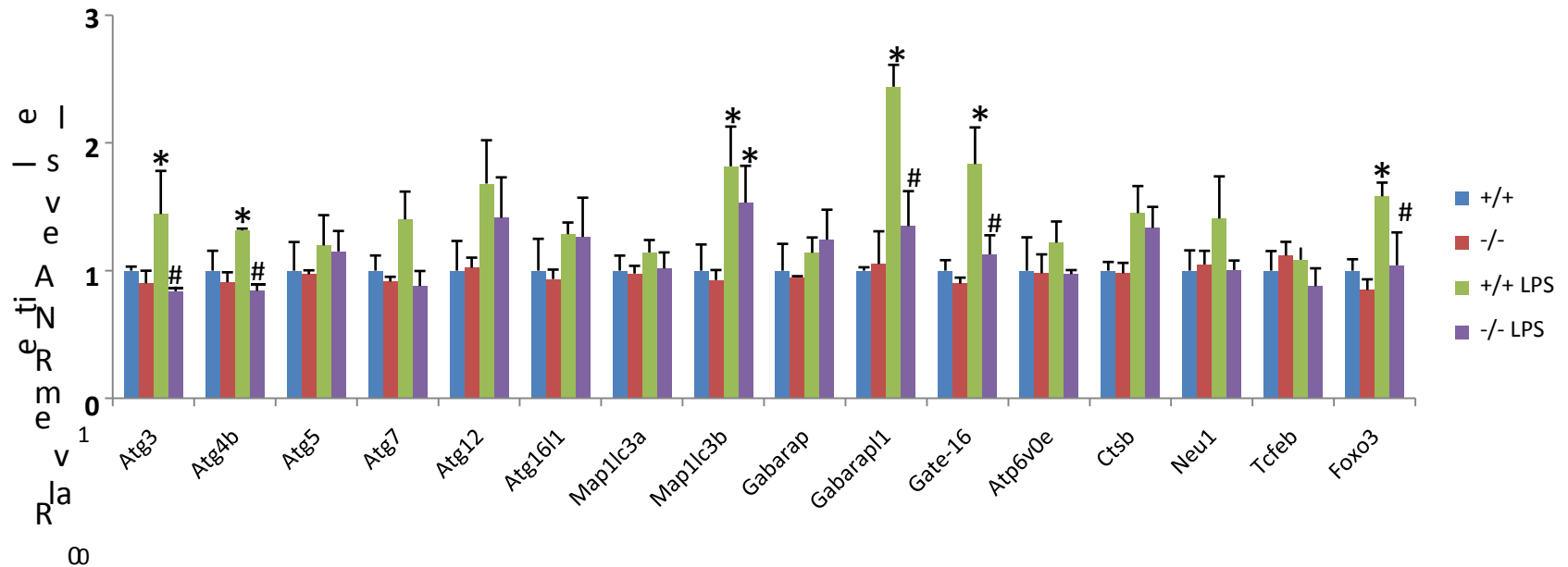


# Rubicon Deficiency Enhances Autophagic Flux in the Hearts

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# Analysis of Transcripts of Autophagy-related Genes in the Heart



# Summary

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- UVRAG deficiency impairs autophagic flux while Rubicon deficiency enhances autophagic flux in the heart.
- UVRAG deficiency leads to cardiomyopathy accompanied by compromised cardiac function.
- Inflammatory response is enhanced in UVRAG-deficient hearts.
- Rubicon deficiency attenuates LPS-induced lethality and cardiac dysfunction, which is associated with enhanced autophagic flux in the heart.

# Conclusion

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UVRAG plays an essential role in autophagy and maintenance of cardiac function.

Loss of Rubicon enhances autophagic flux in the heart with no obvious impact on cardiac morphology and function at baseline, but confers protection against LPS-induced lethality and cardiac dysfunction.



# Acknowledgements

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



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