The Role of Growth Factor Proteins in Cardiac Hypertrophy observed in Neonatal Cardiomyocytes

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Introduction

What is Cardiac Hypertrophy?

- Enlargement of myocardial cells
  - heart’s response to increased biomechanical stress due to intrinsic and extrinsic stimuli

- Genetic Disorder
  - familial hypertrophic cardiomyopathy (weakening of the heart muscle)
  - autosomal dominant trait

- Acquired
  - arterial hypertension, coronary artery disease, valvular heart disease, aortic stenosis
  - risk factors include obesity, history of heart attack

Introduction (cont...)  

Maladaptive?

➢ Physiologic vs. Pathological Hypertrophy

- Similarities: greater cell size, protein synthesis, and more structured sarcomere
- Difference: apoptotic activity
- Better distinction necessary
Lab Objective

- To understand the key pathways involved in cardiac hypertrophy leading to apoptosis in the rat model with the intention to develop treatment and preventative measures against heart failure in human subjects.
Cardiac Hypertrophy Signaling Pathway
Research Objectives

- To quantitatively identify and compare the level of protein activity produced with different combinations of growth factor in neonatal cardiomyocytes
  - Insulin Growth Factor 1 (IGF-1)
    - hypertrophic agent
  - Protein Kinase B (Akt)
    - antiapoptotic
  - Phosphoinositide 3-kinase (PI3K)
    - activates Akt
Procedural Approach

- Heart Extraction
- Cell Isolation
- Protein Isolation
- BCA Procedure
- Western Blot Procedure
- Reblot Procedure
Results
Results (cont…)

Phospho Akt/Total Akt

- Control
- IGF1 10-7
- IGF1 10-8
- EGFP
- AdAkt
- BD110

Phospho Akt/Total Akt
Implications

- IGF-1 increases the activity of Akt in a dose-dependent manner.

- Adenoviral transfection with Ad-Akt does not increase the activity of quiescent neonatal cardiomyocytes.

- Activation of up-stream PI 3-kinase by Ad-BD110 transfection, a constitutively active PI 3K, enhances the Akt activity in neonatal cardiomyocytes.
Conclusion

- Activation of PI 3K may play a crucial role in the activation of Akt-dependent anti-apoptotic pathways.

- IGF-1 known anti-apoptotic effects may be mediated through PI 3K/Akt activation.
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