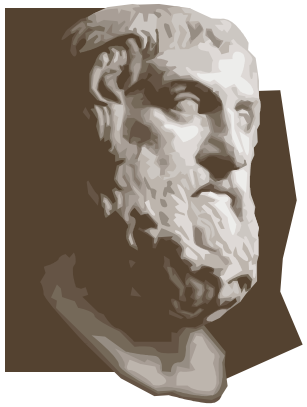
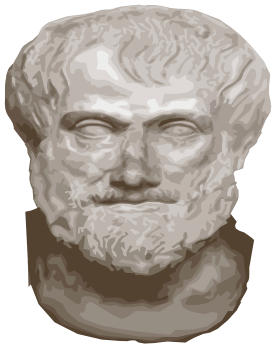
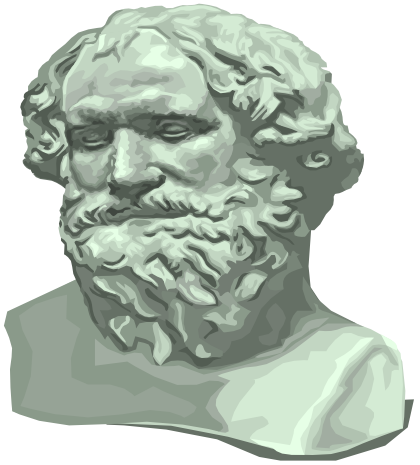
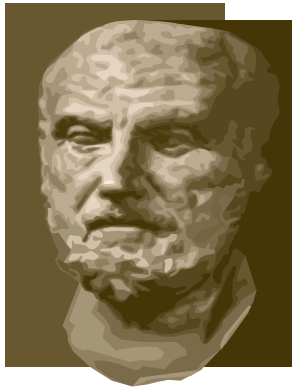
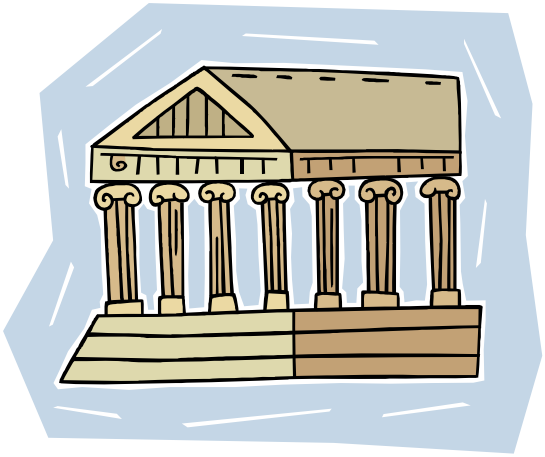
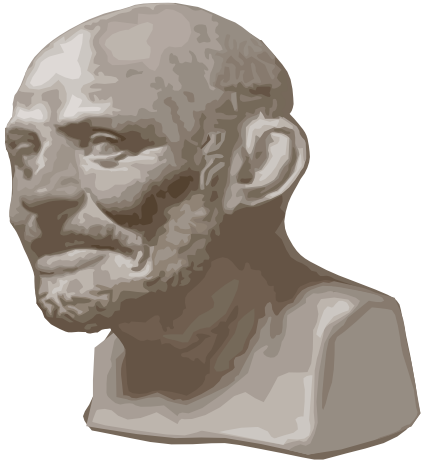
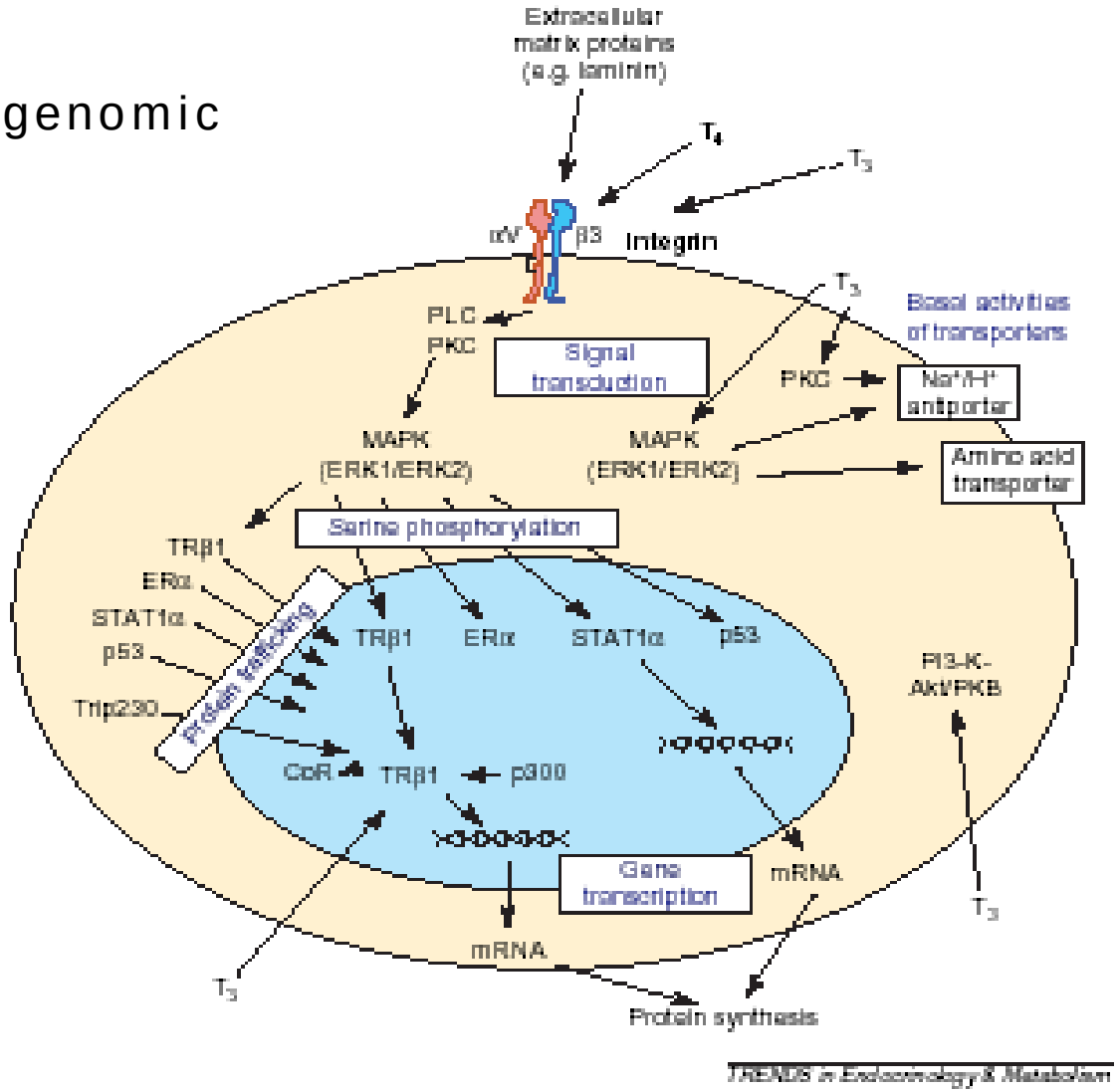
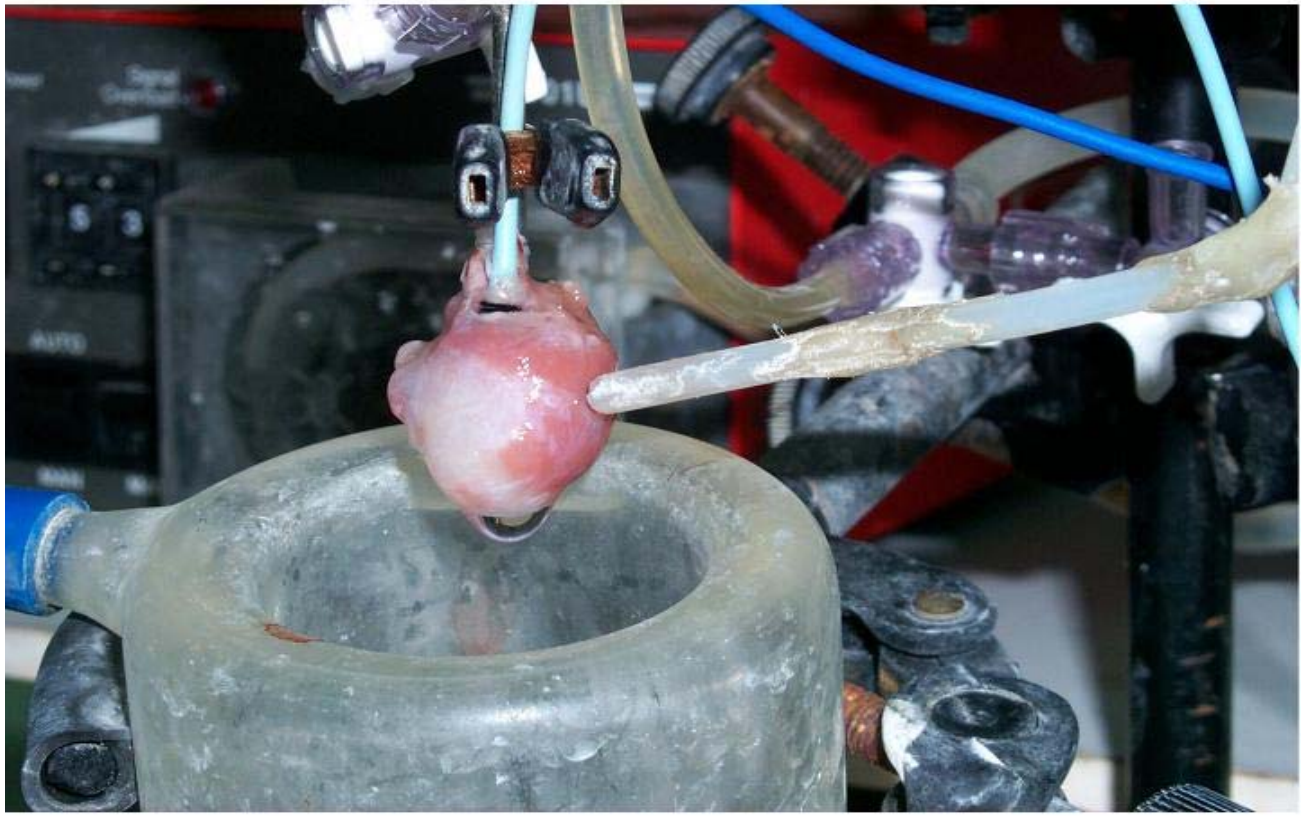







University of Athens

C Pantos/ DV Cokkinos

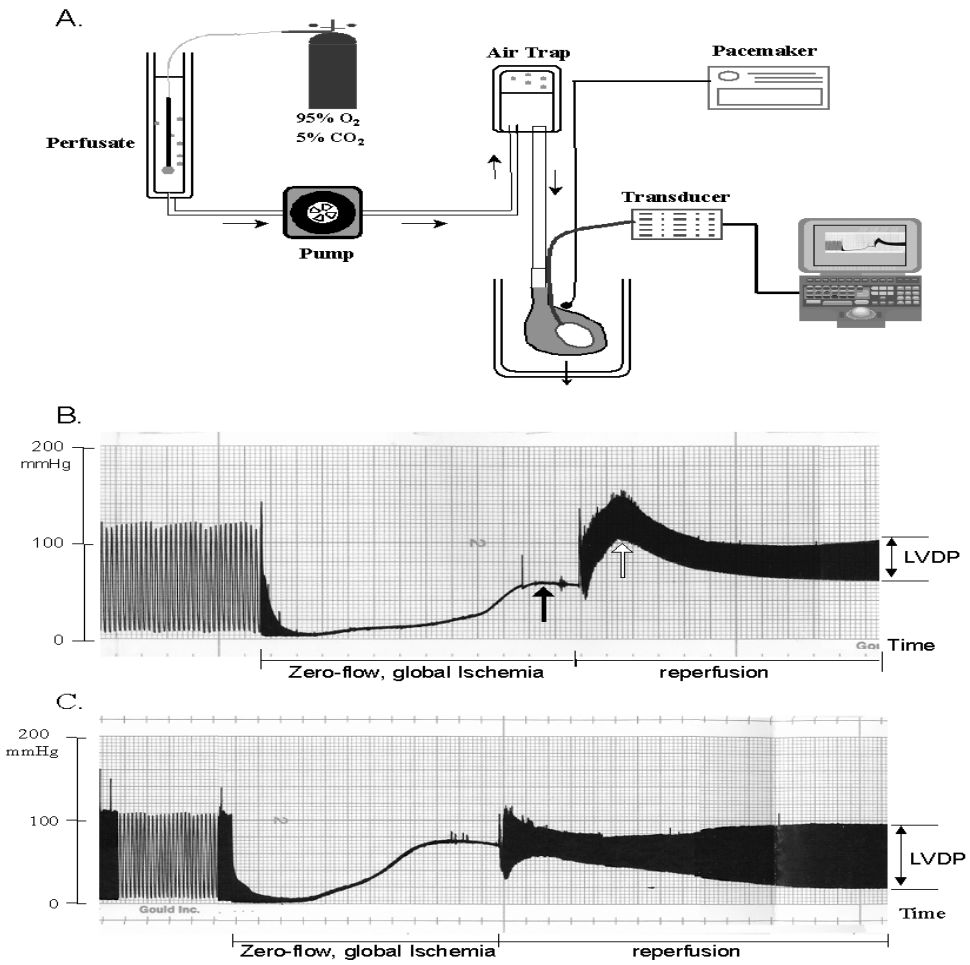
TH –non genomic action





TH can modulate myocardial injury via non genomic action

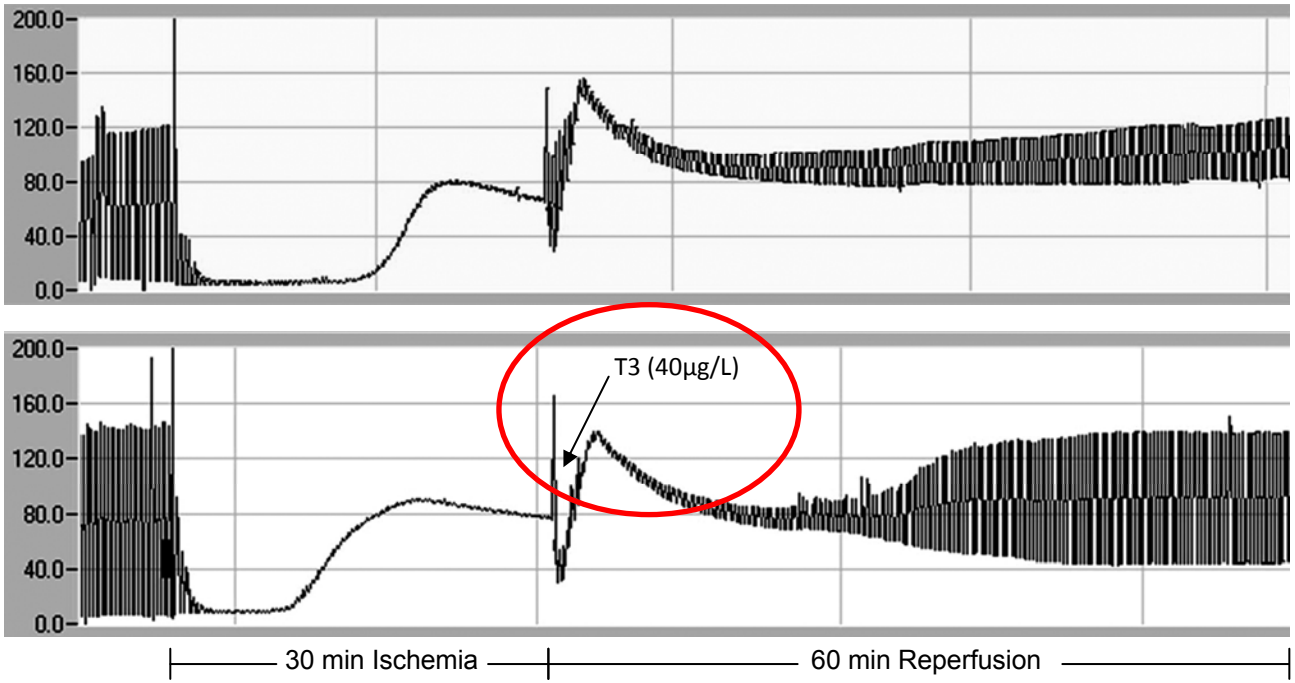
Studies in Isolated rat heart preparations – experimental model of ischaemia-reperfusion



DV Cokkinos, C Pantos , G Heusch, H Taegtmeyer (Eds), Myocardial ischemia : From mechanisms to therapeutic potentials, Springer , 2006

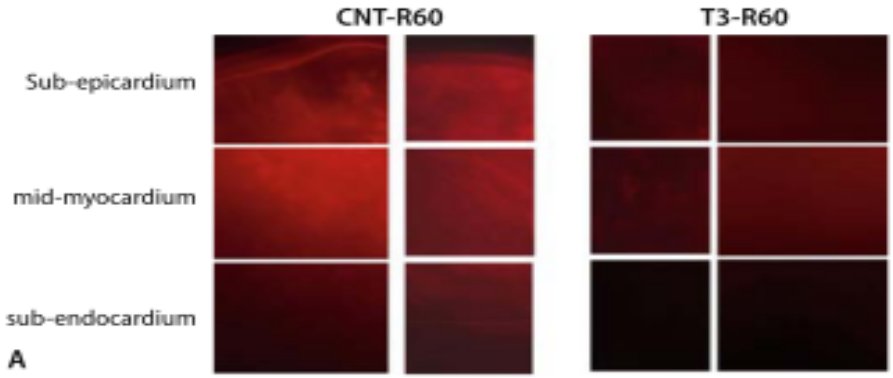
TH can modulate myocardial injury via non genomic action

LVDP (mmHg)



Pantos et al 2009, Basic Res Cardiol , 2009

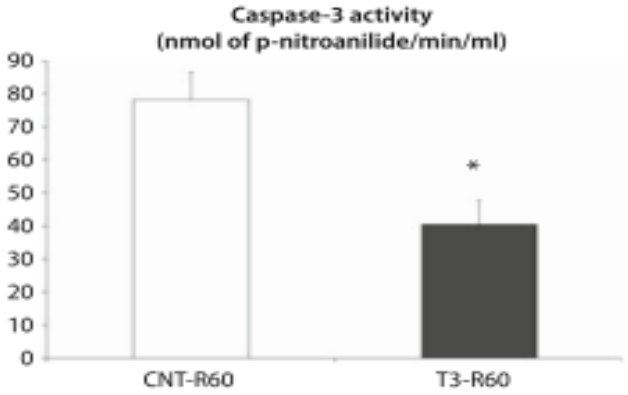
TH limits apoptosis



A

B

	CNT-R60	T3-R60	Mann-Whitney (P)
Sub-epicardium	28.2 (3.2)	12.5 (1.8)	0.003
mid-myocardium	33.3 (3.7)	14.6 (2.1)	0.002
Sub-endocardium	17.3 (1.4)	8.6 (1.3)	0.004



C

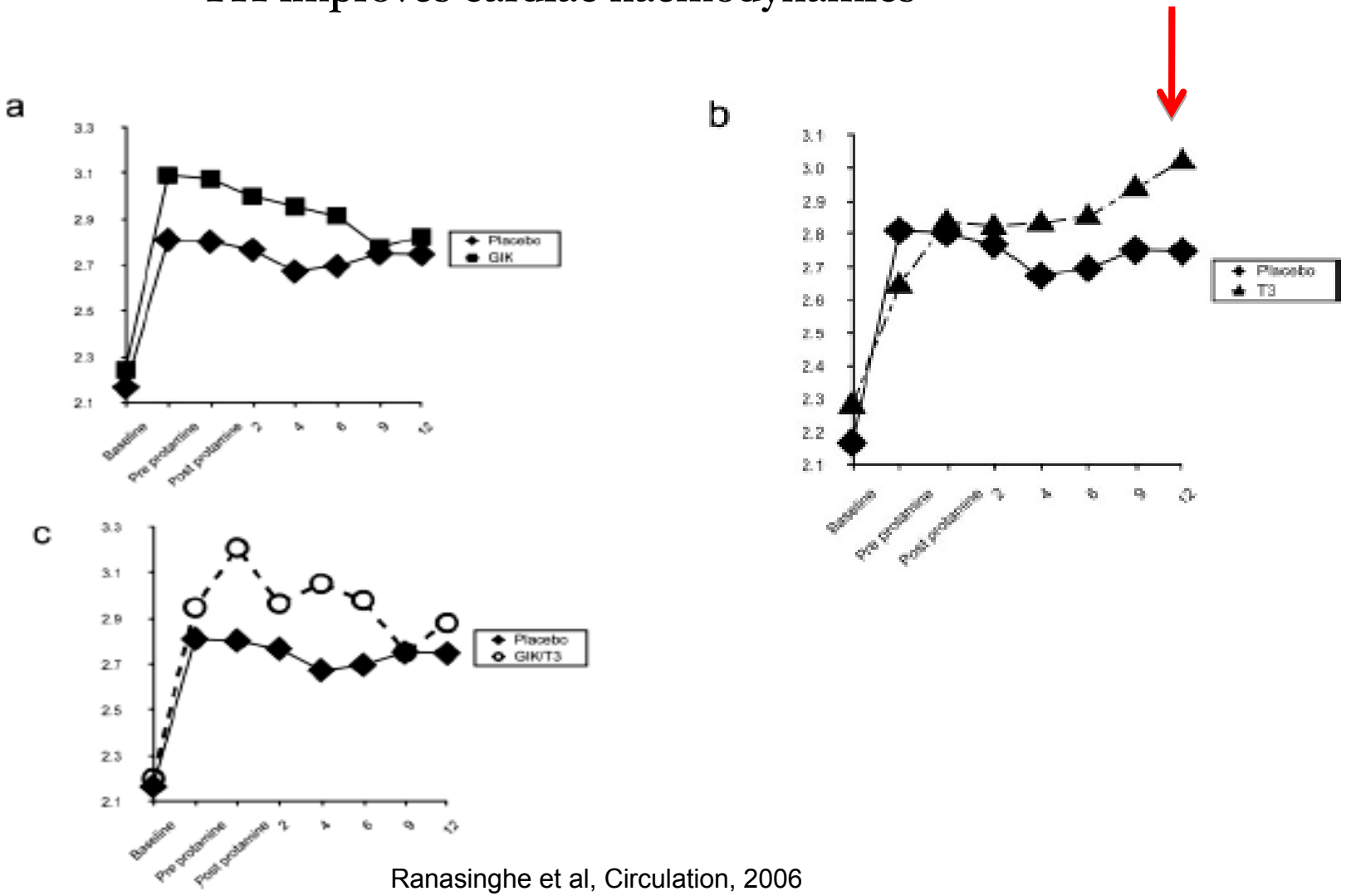
Pantos et al 2009, Basic Res Cardiol , 2009

Translational implications of non genomic action of TH

Glucose-Insulin-Potassium and Tri-Iodothyronine Individually Improve Hemodynamic Performance and Are Associated With Reduced Troponin I Release After On-Pump Coronary Artery Bypass Grafting

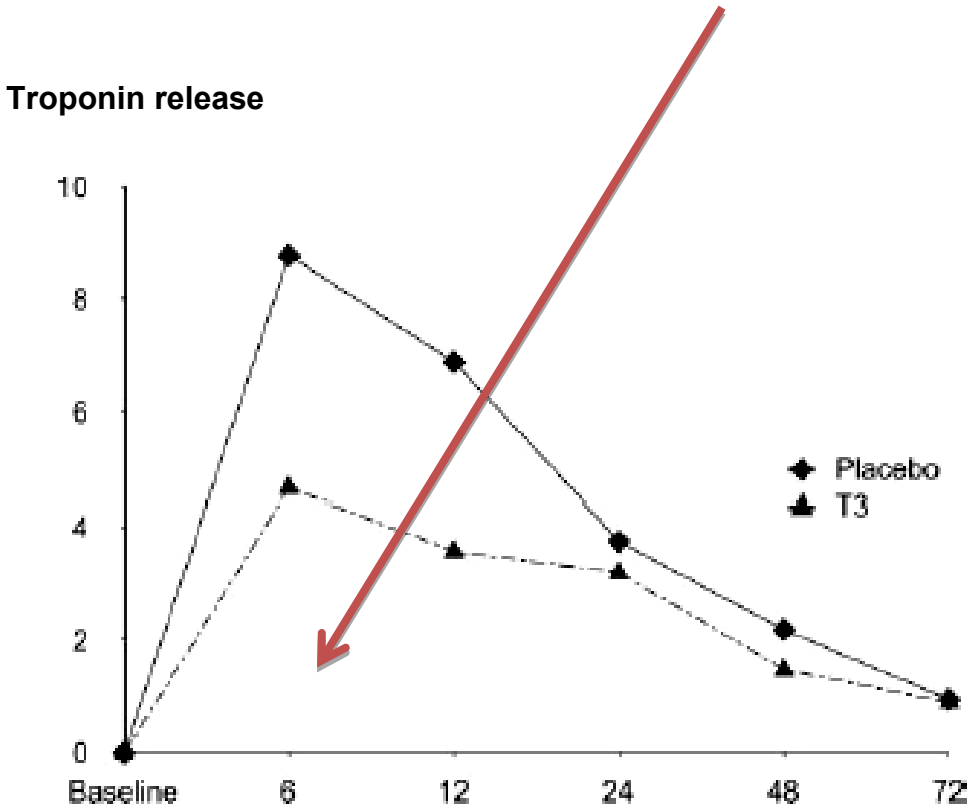
Aaron M. Ranasinghe, MB, MRCS; David W. Quinn, BSc, FRCS; Domenico Pagano, MD, FESC, FRCS; Nicola Edwards, MB, MRCP; Muzzafar Farooqui, MB, FRCA; Timothy R. Graham, MB, FRCS; Bruce E. Keogh, MD, FRCS; Jorge Mascaro, MD, FRCS; David W. Riddington, MB, FRCA; Stephen J. Rooney, MB, FRCS; John N. Townend, MD, FRCP; Ian C. Wilson, MD, FRCS; Robert S. Bonser, MD, FRCP, FRCS

TH improves cardiac haemodynamics



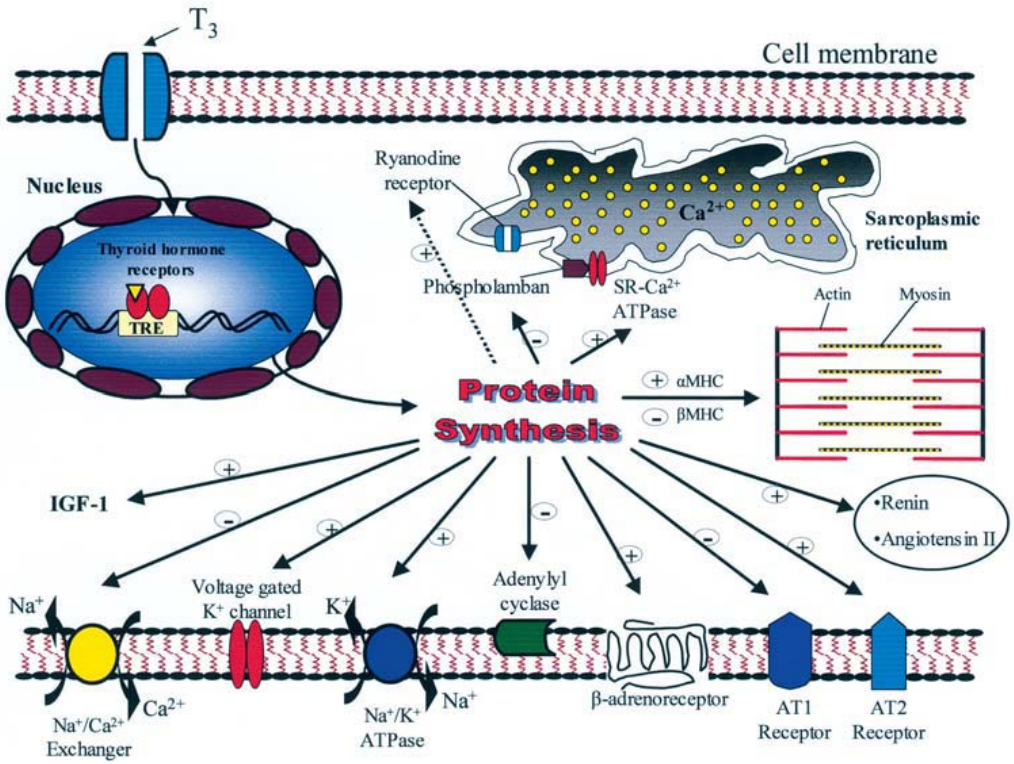
Ranasinghe et al, Circulation, 2006

TH limits the extent of myocardial injury



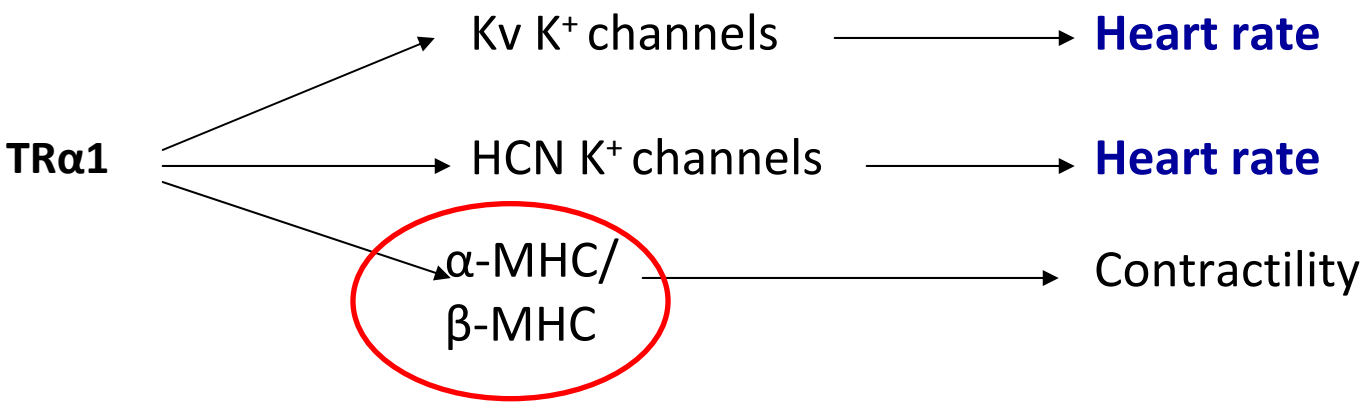
Ranasinghe et al, Circulation, 2006

TH- genomic action



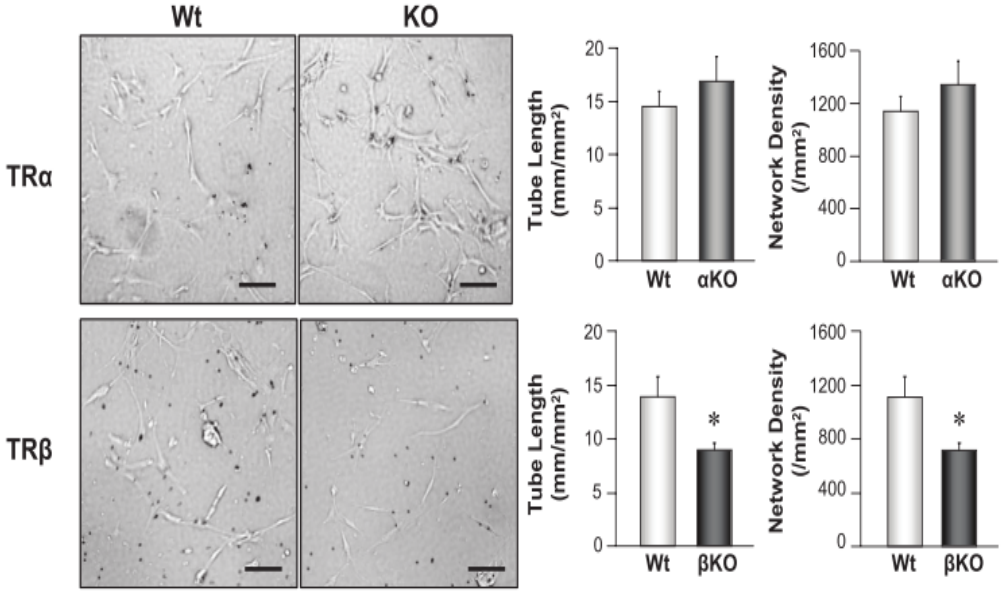
Pantos C ……. Cokkinos DV, Basic Res Cardiol, 2003

TH genomic action – TH nuclear receptors (TRs)

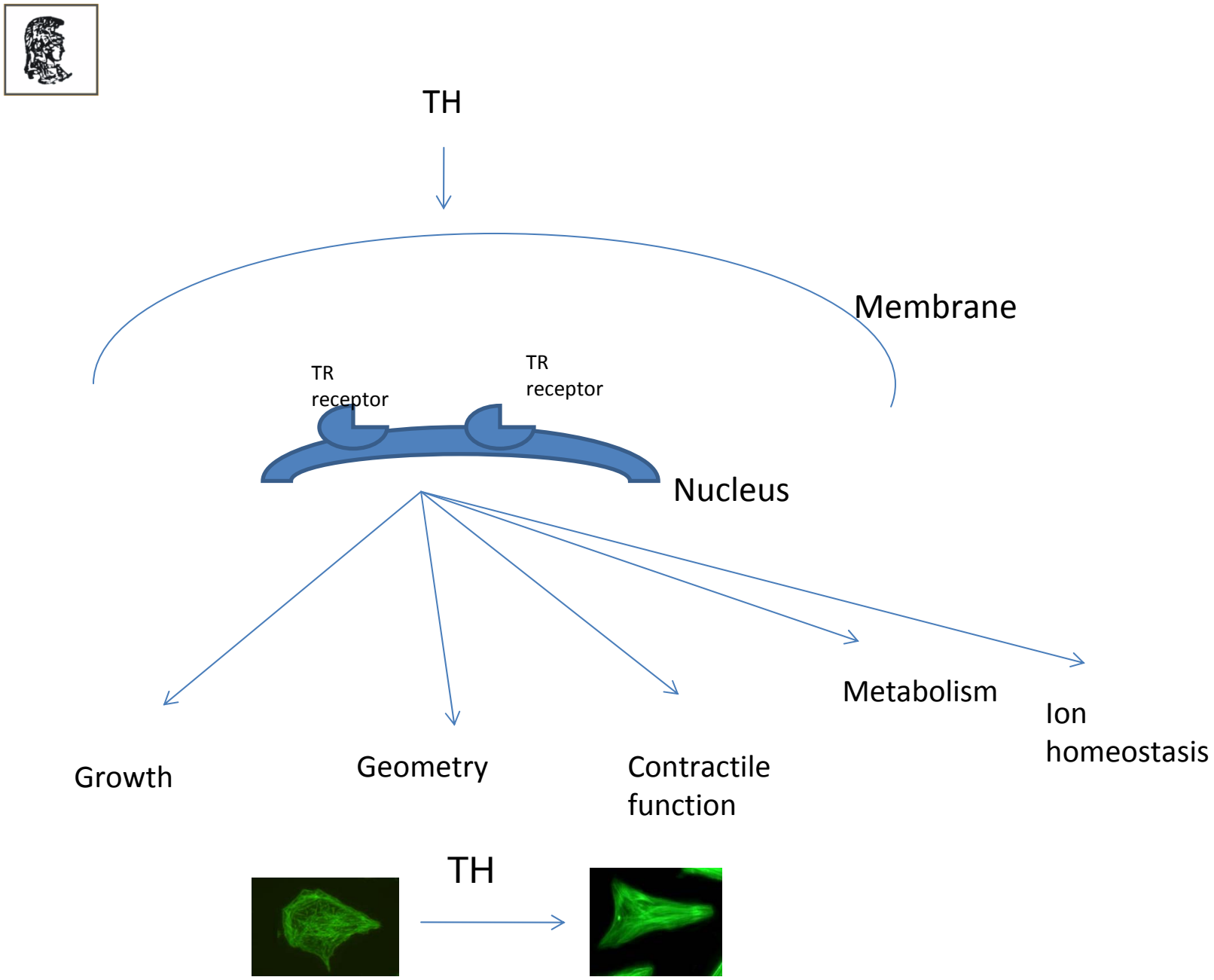


Mol Endocrinol , 2005

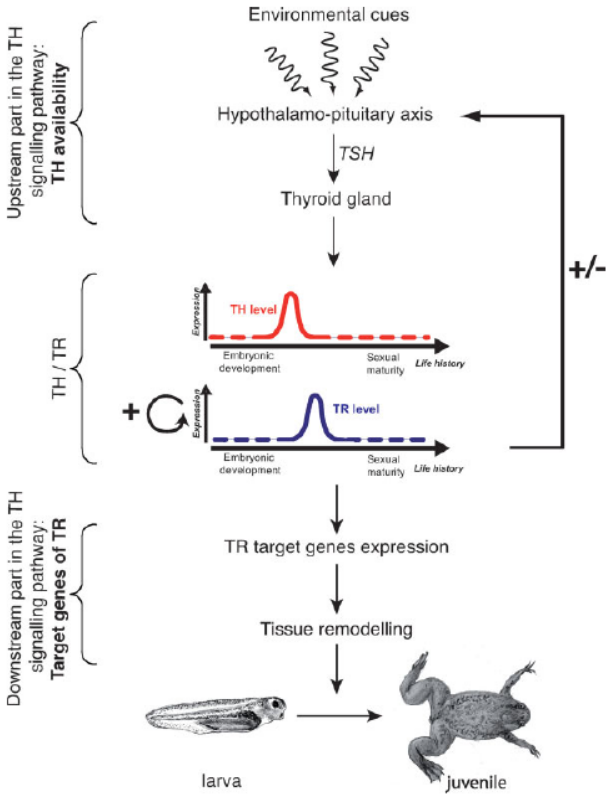
TR β angiogenesis



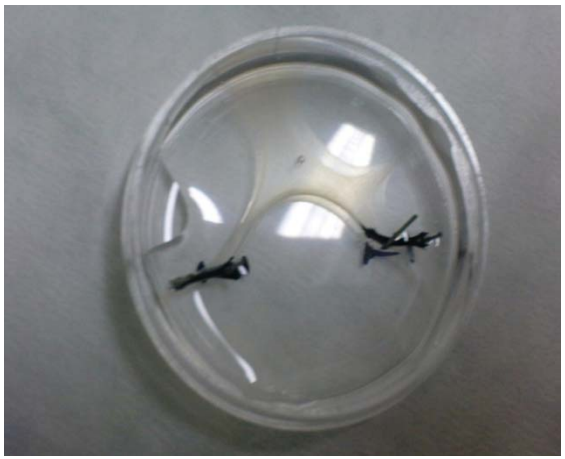
Makino A, Endocrinology, 2009


TH
Membrane
TR receptor
TR receptor
Nucleus
Growth
Geometry
Contractile function
Metabolism
Ion homeostasis
TH

Nature has already ‘used’ TH for tissue remodeling

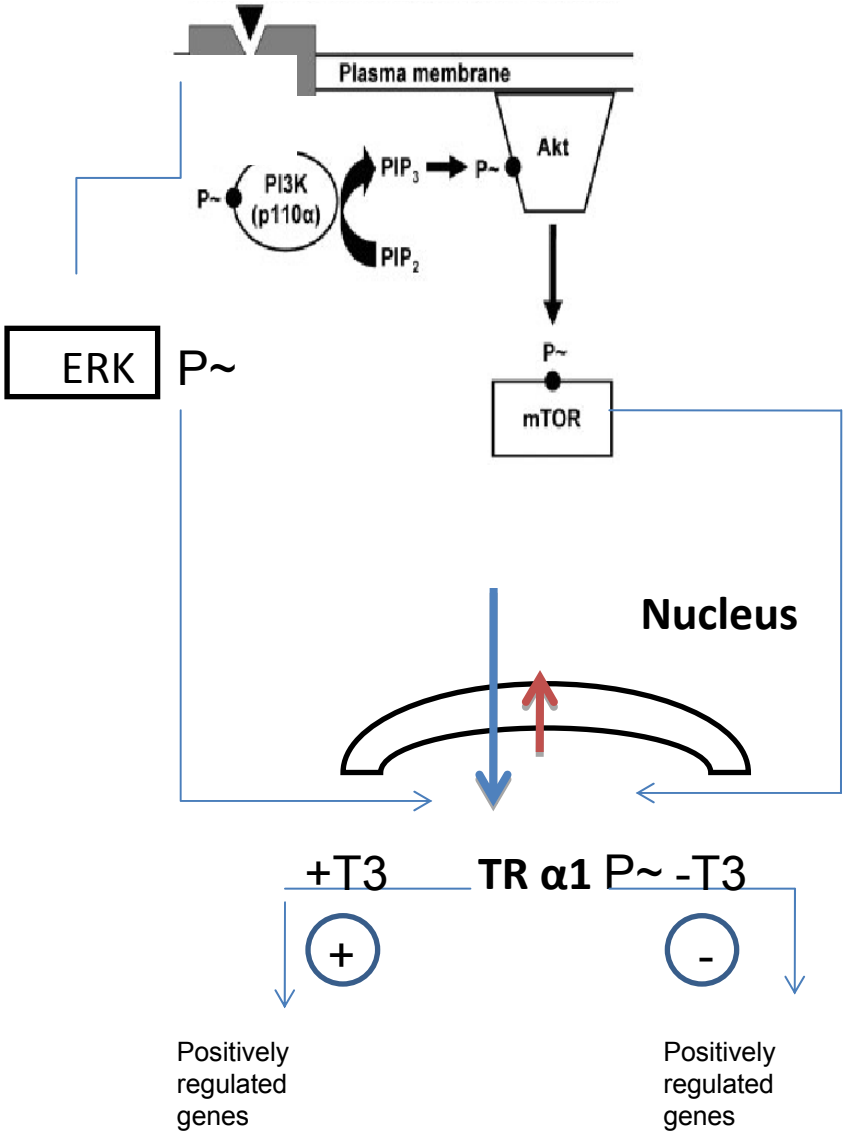


TH and bioengineering



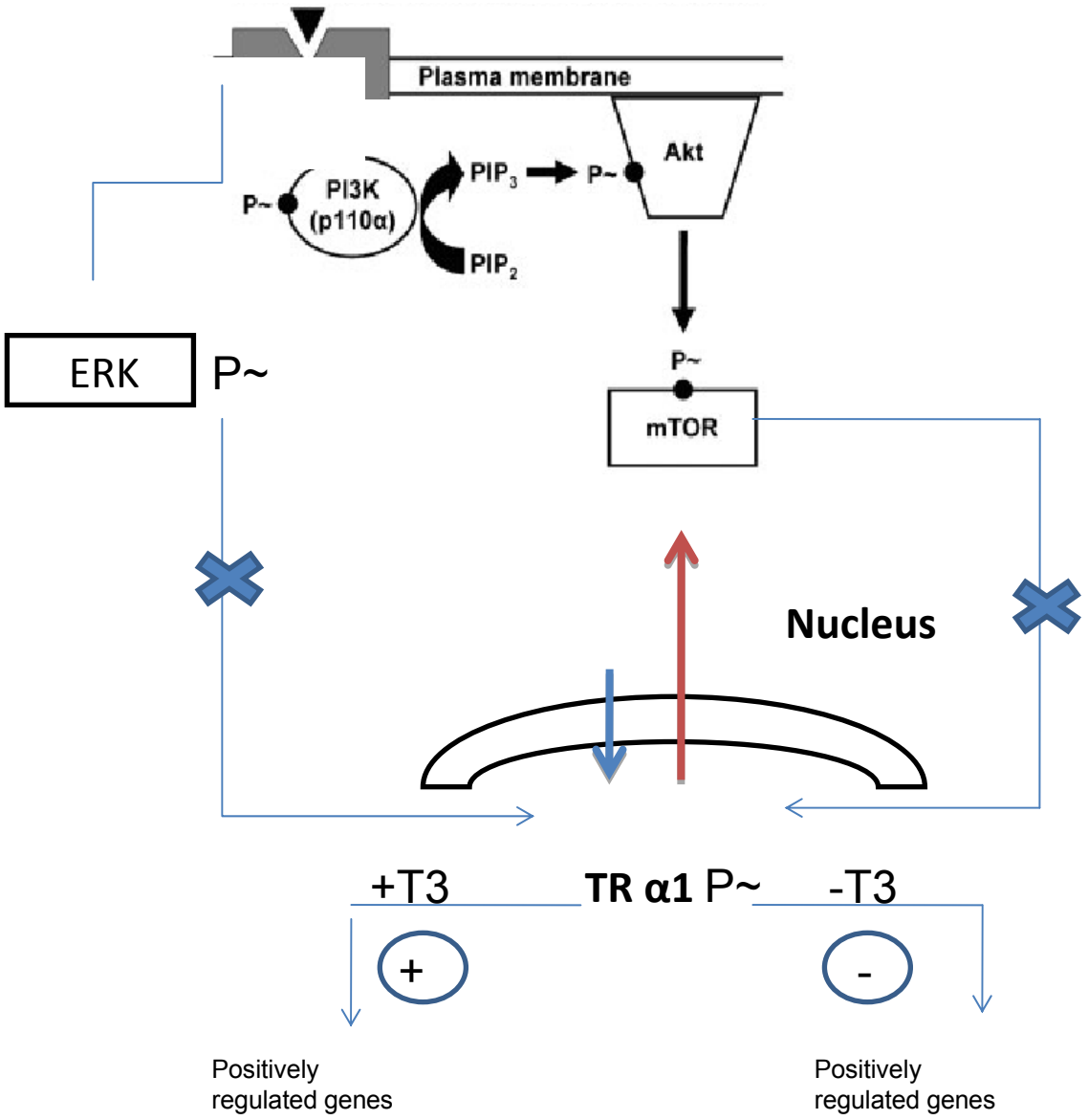
Thyroid hormone is a regulator of stress response

PE, α1 adrenergic pro-growth stimuli

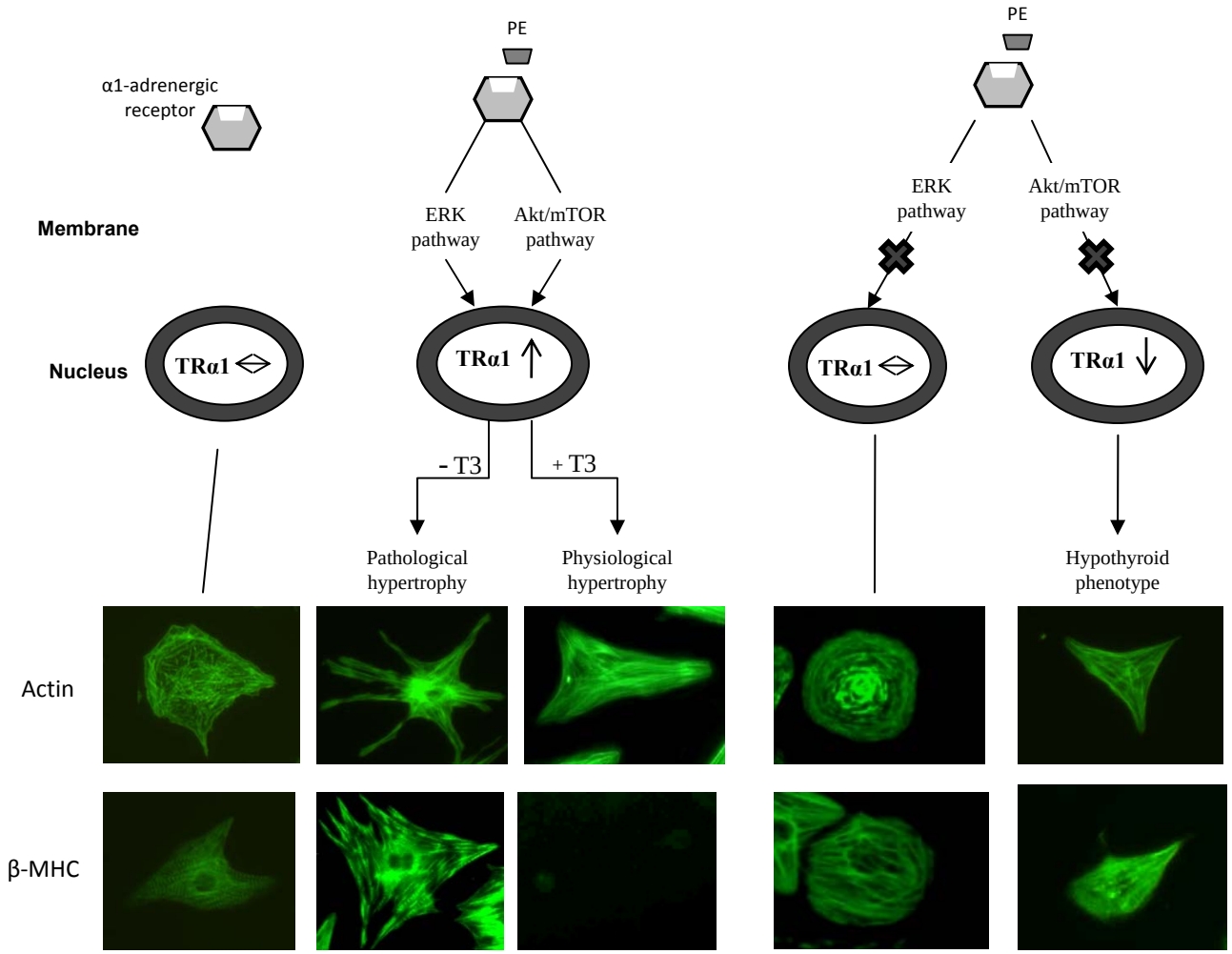


Thyroid hormone is a regulator of stress response

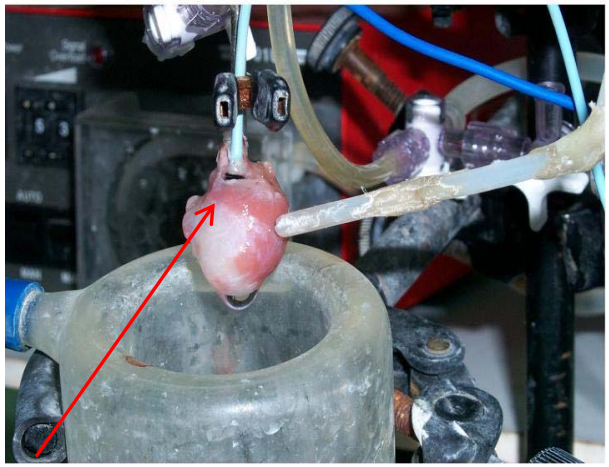
PE, α1 adrenergic pro-growth stimuli



Thyroid hormone is a regulator of stress response



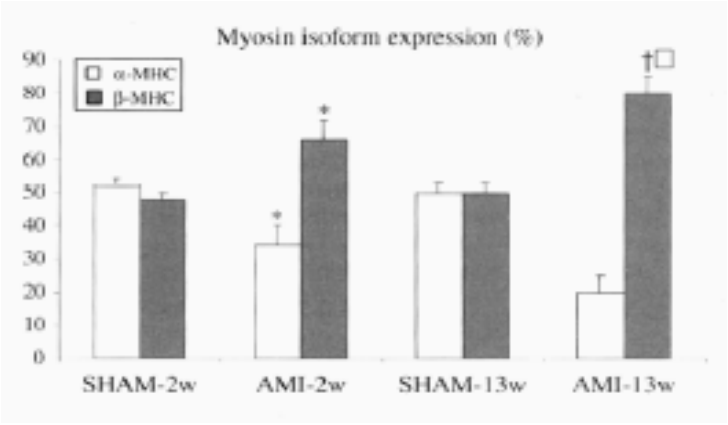
Postischemic LV remodeling : The concept of fetal repogramming



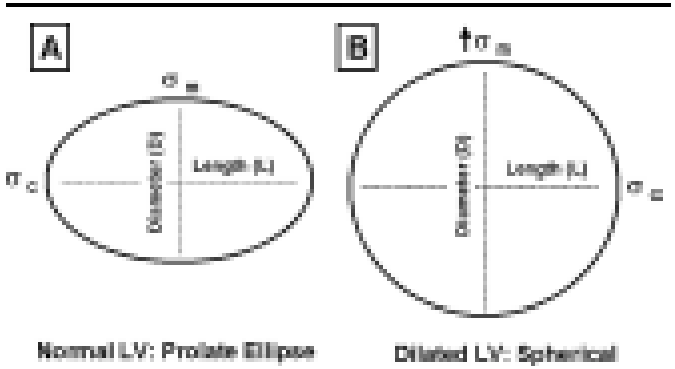
Ligation of coronary artery- acute MI in rats

Viable hypertrophic myocardium

Scar tissue

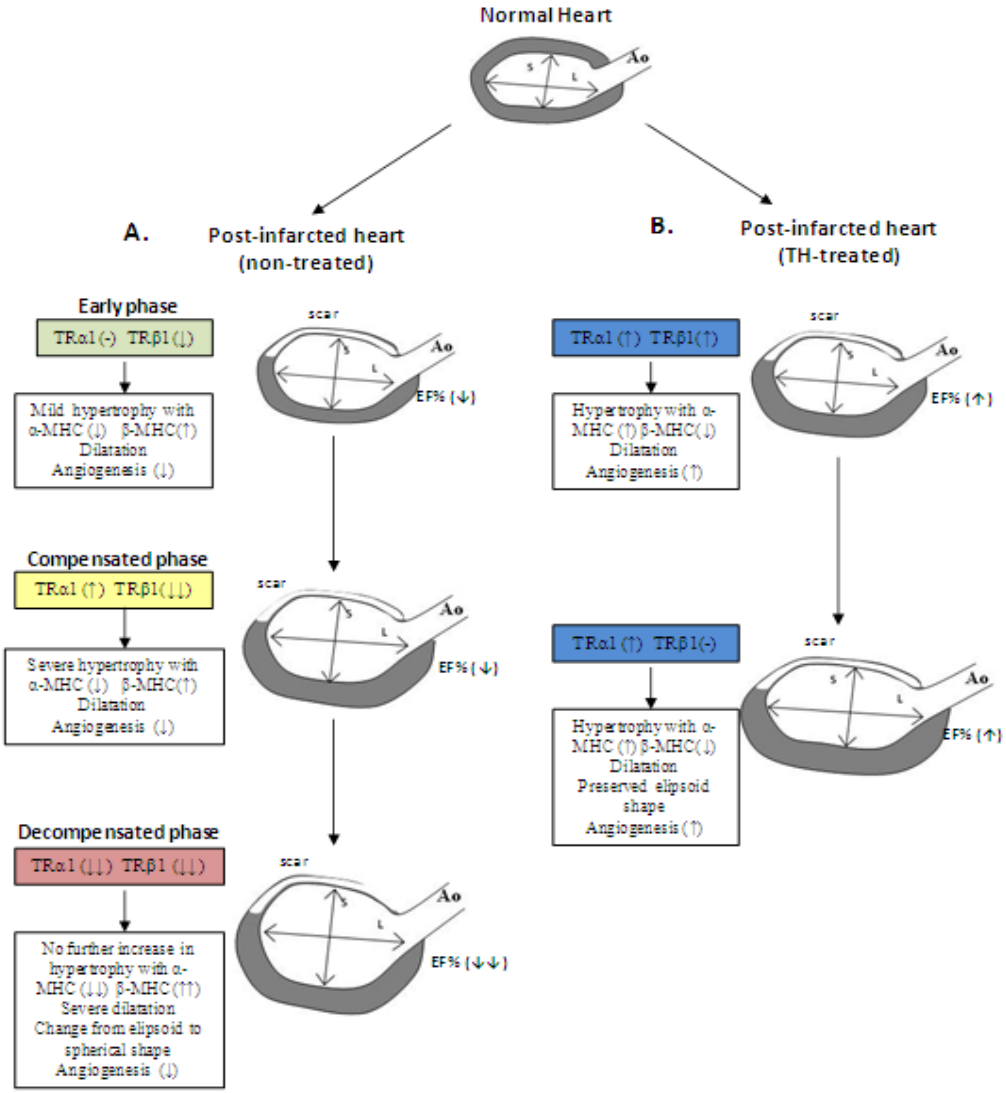


Overexpression of beta- myosin

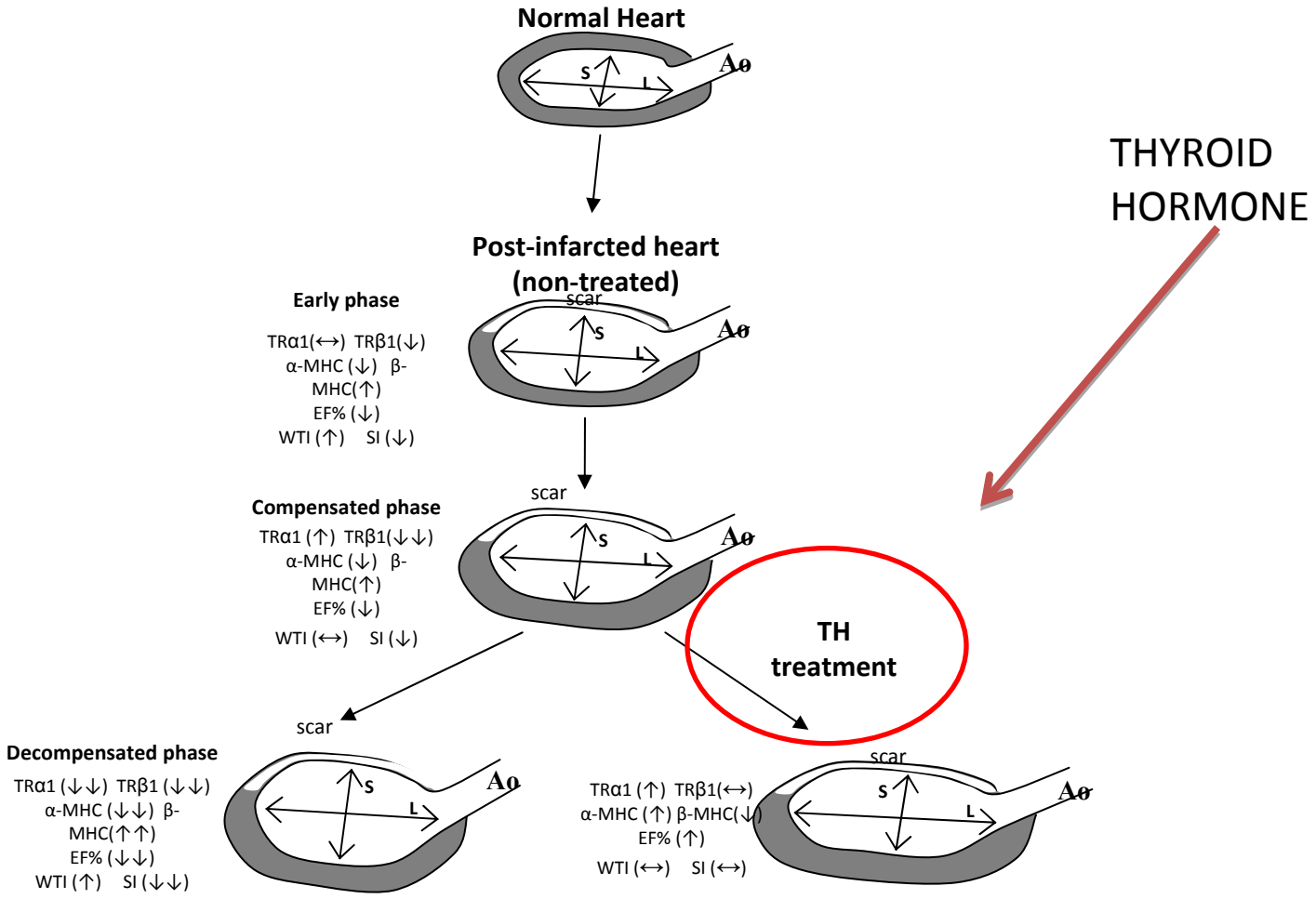


Left ventricle (LV) becomes spherical

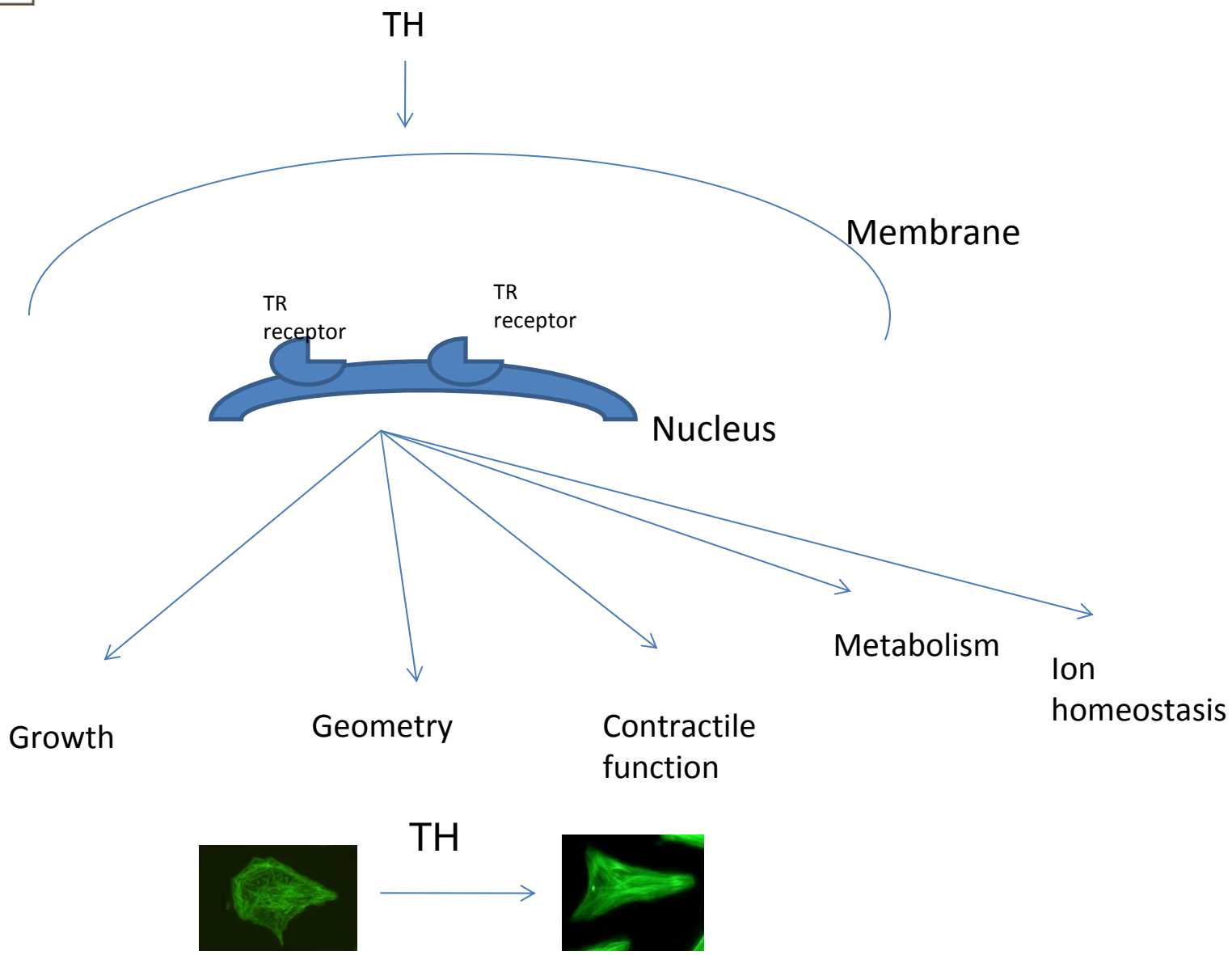
TRs and remodeling

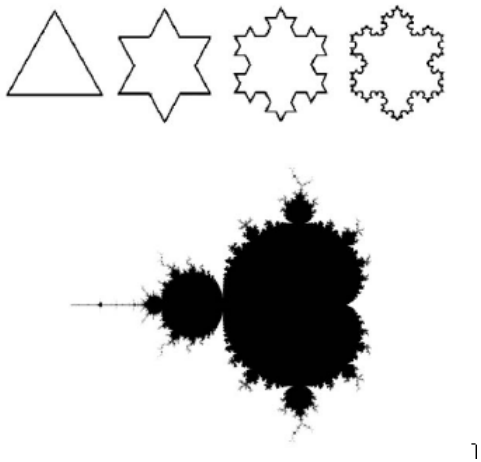


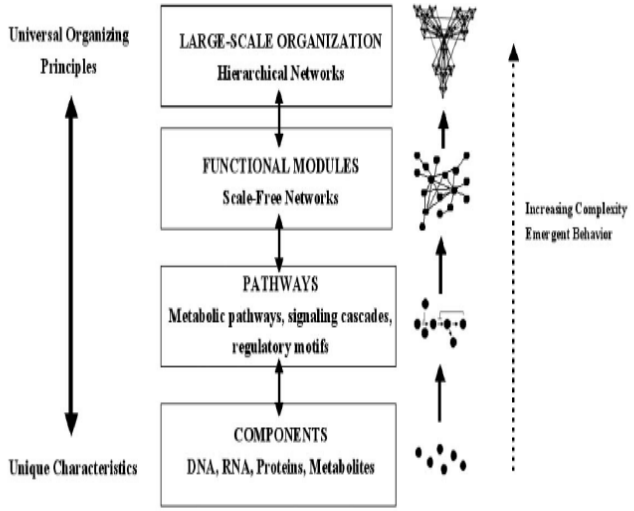
TH SWITCHES PATHOLOGICAL HYPERTROPHY TO PHYSIOLOGICAL HYPERTROPHY



TH AND CARDIAC GEOMETRY







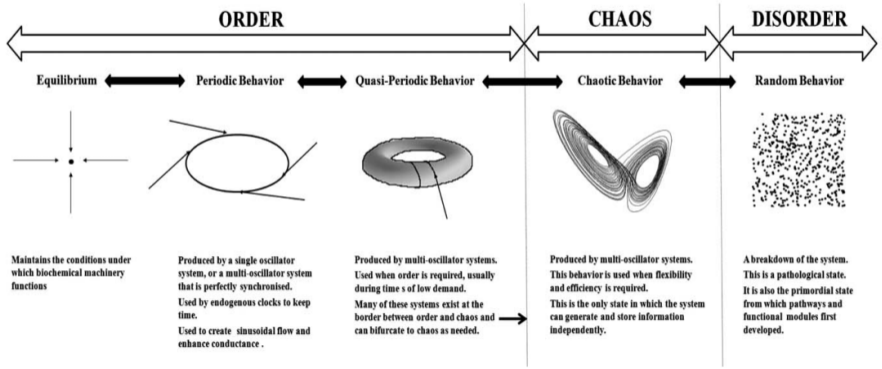
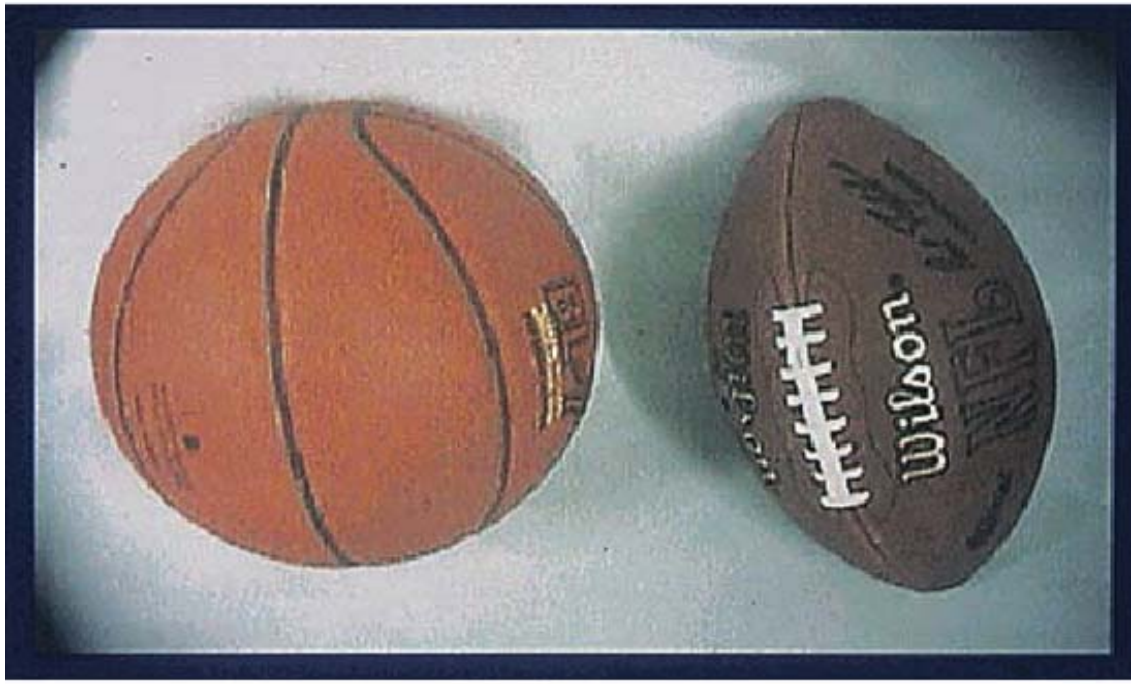
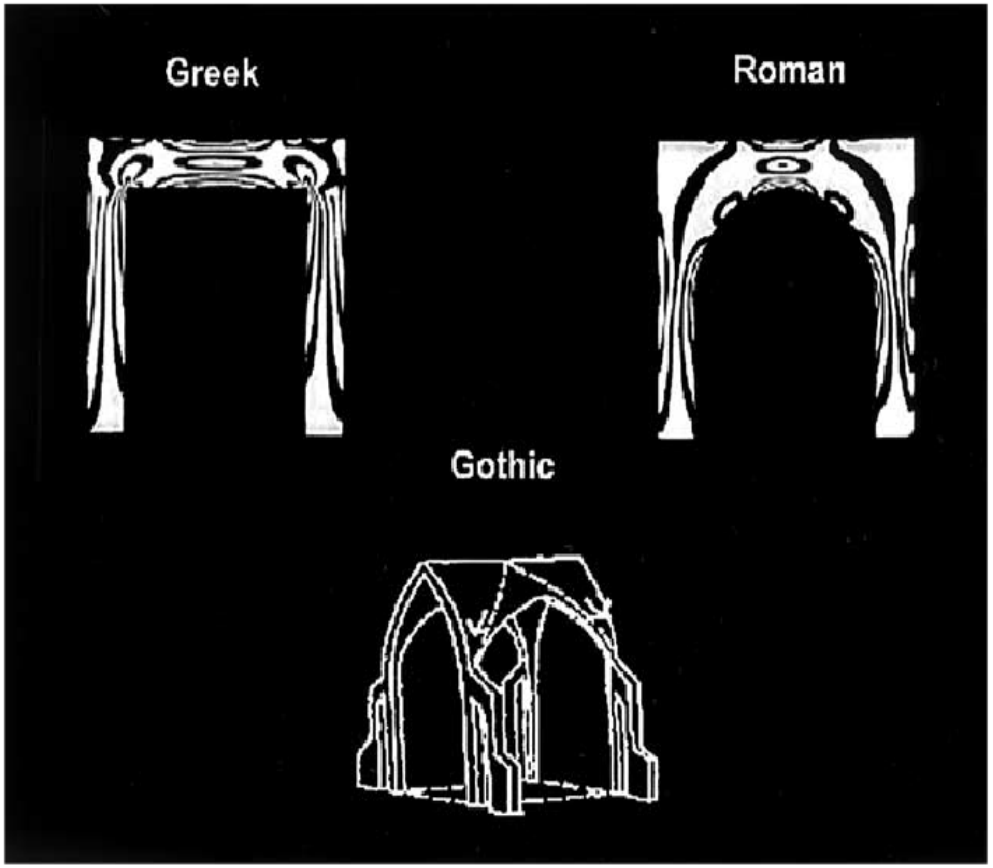


Fig. (4). An overview of the relationship between dynamics and physiological function.

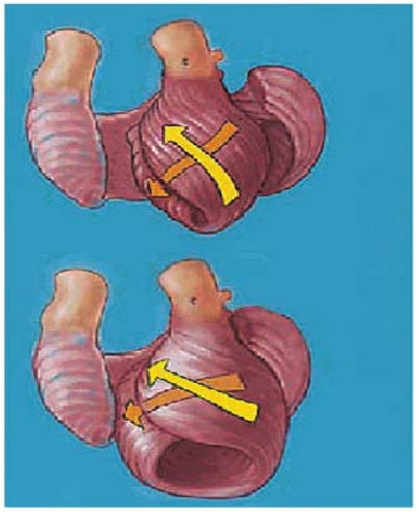
CARDIAC GEOMETRY

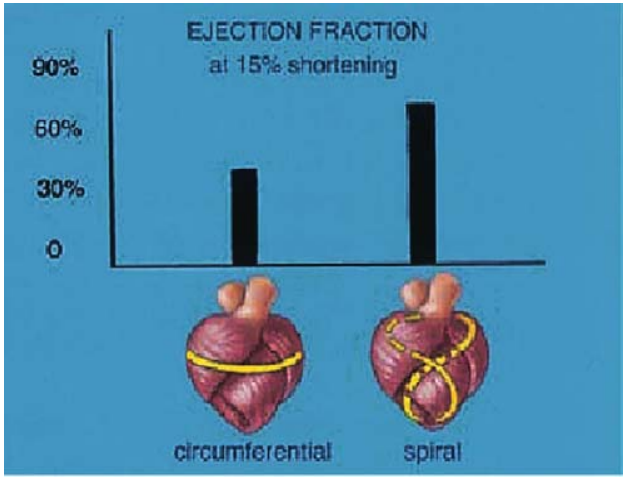


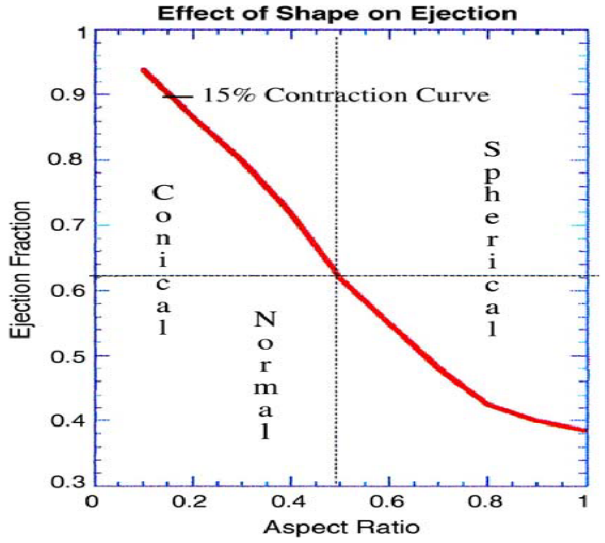
CARDIAC GEOMETRY



CARDIAC GEOMETRY

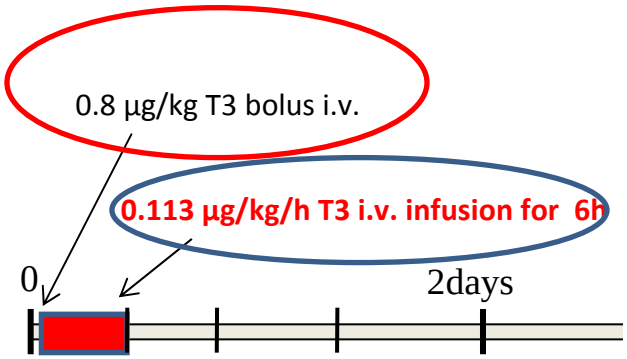






Translational implications of TH actions

T3 administration in pts with AMI



- Myocardial enzymes
- SBP, DBP, HR
- Echocardiography
- BNP
- T3, T4, TSH, FT3, FT4

- Myocardial enzymes
- SBP, DBP, HR
- Echocardiography
- BNP
- T3, T4, TSH, FT3, FT4

- Myocardial enzymes
- SBP, DBP, HR
- Echocardiography
- BNP
- T3, T4, TSH, FT3, FT4

- SBP, DBP, HR
- Echocardiography
- BNP
- T3, T4, TSH, FT3, FT4
- Ergospirometry

FP7-ICT-2009-4

Efficient Patient Recruitment for InnOvative CliNical Trials of Existing Drugs to other Indications

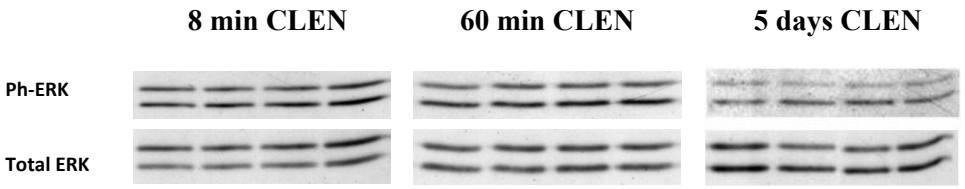
PONTE

DV Cokkinos

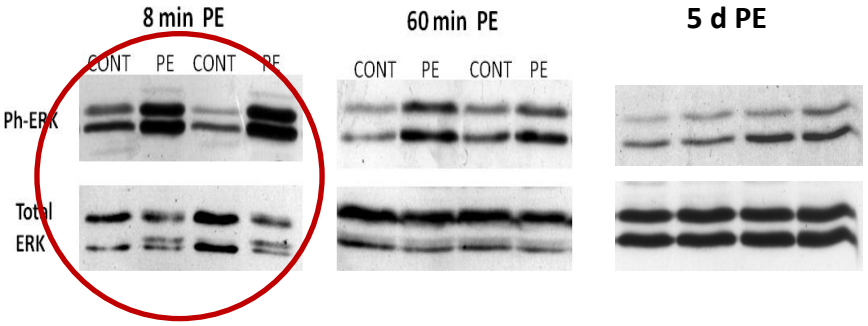
- C Pantos
- I Mourouzis
- V Malliopoulou
- C Xinaris
- E Karamanoli
- I Paizis
- S Tzeis
- P Moraitis
- D Kokkinos
- K Markakis
- A Dimopoulos
- T Saranteas
- K Mourouzis
- N Tsagoulis
- N Thempeyioti
- K Sfakianoudis
- A Kokkinos
- F Perimenis
- D Spanou
- G Galanopoulos

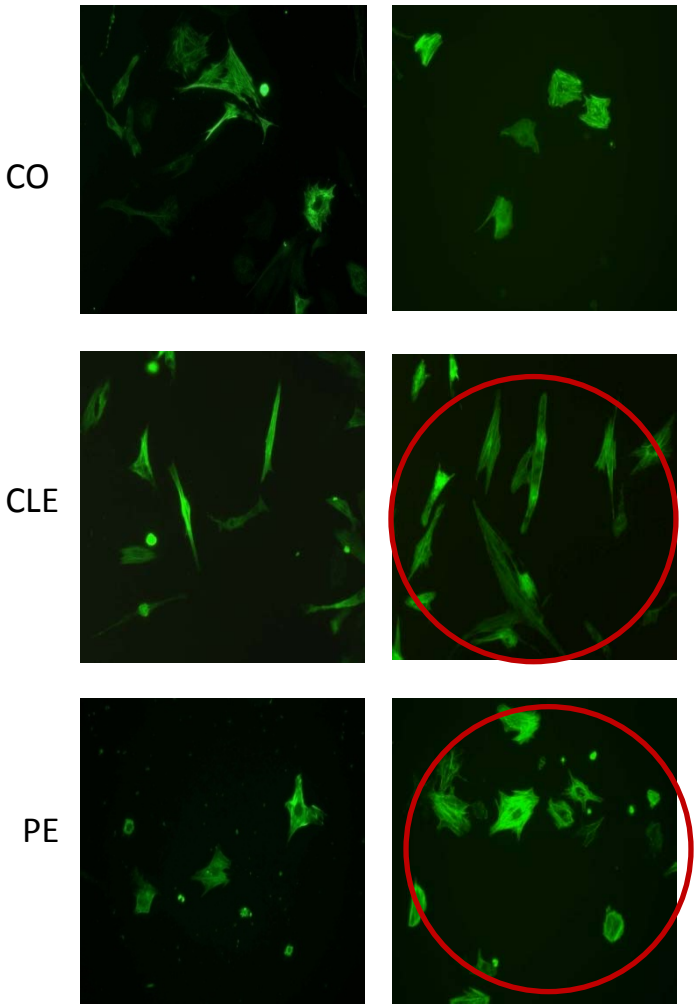
Cell models of pathological (PE) and physiological (Clenbuterol) growth

CLEN NO INCREASE IN ERK

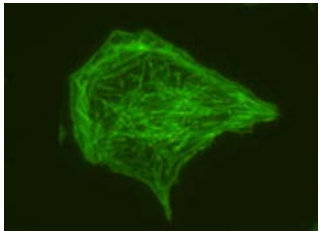
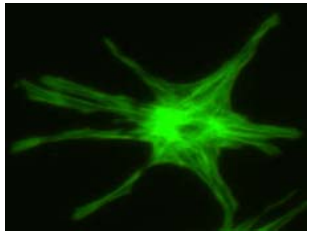
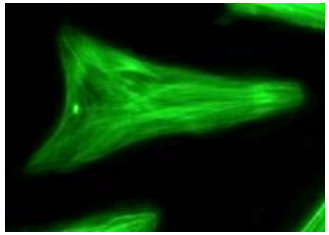
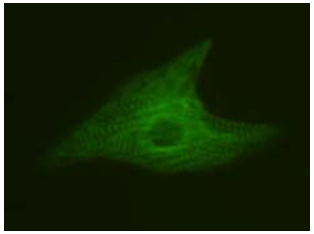
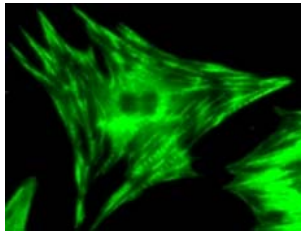
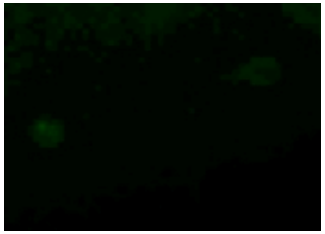


PE INCREASE IN ERK

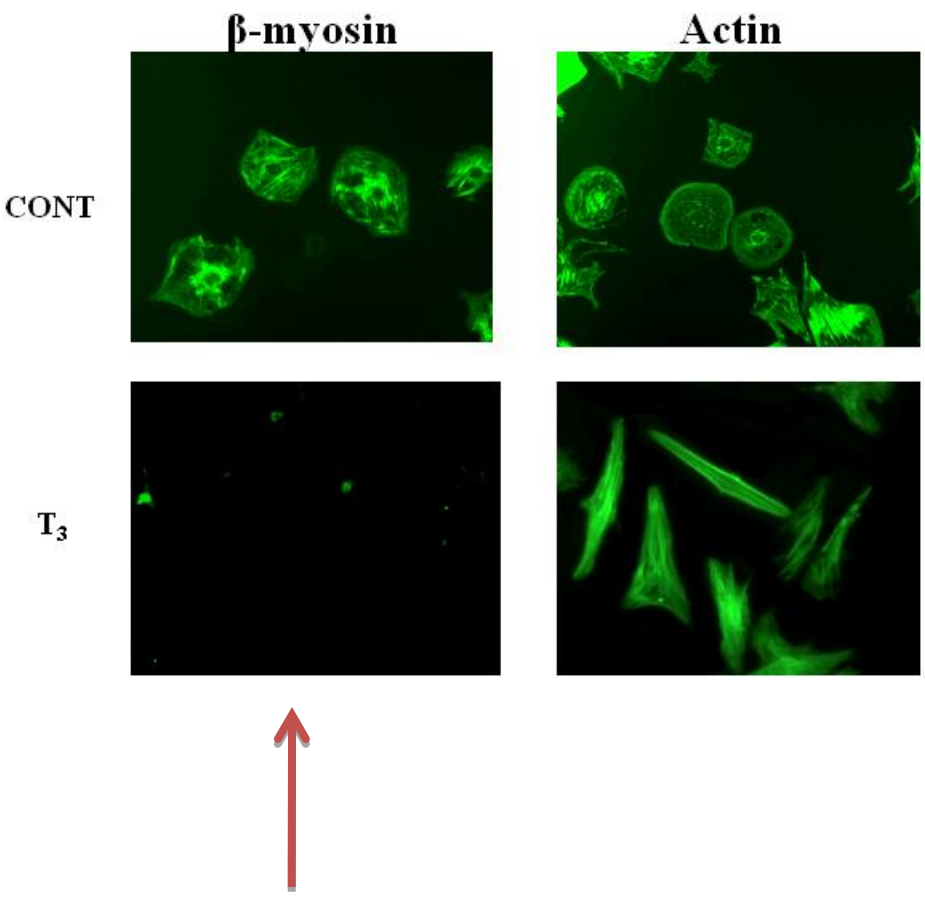


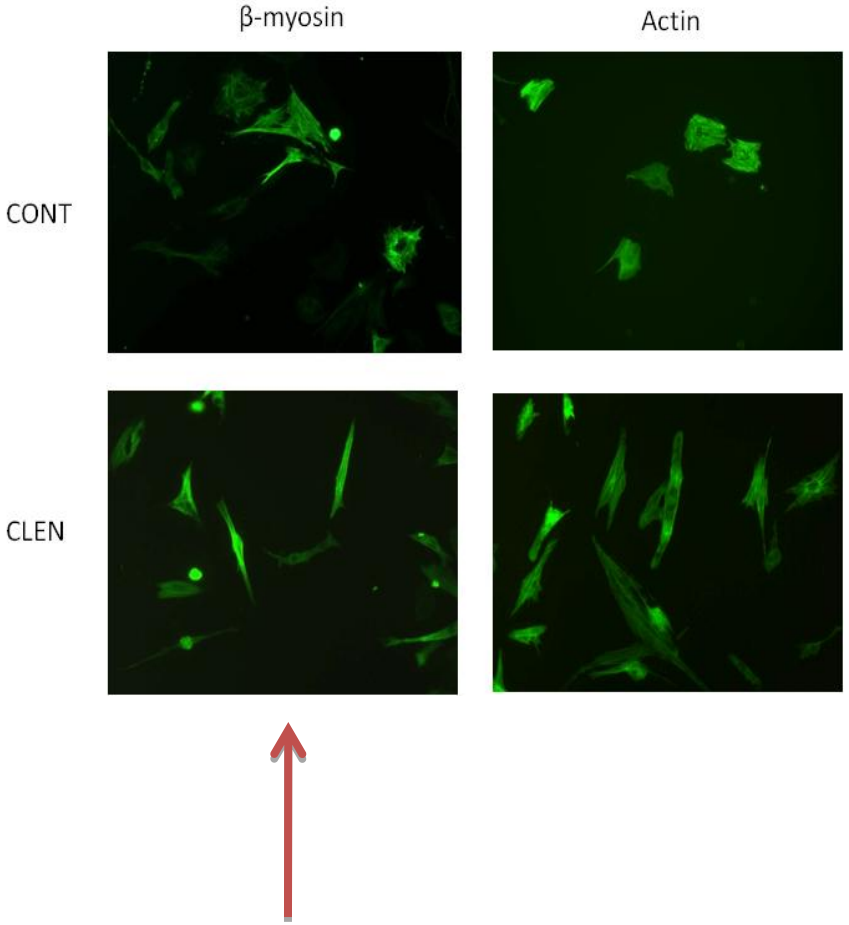


Cell models of pathological (PE) and physiological (T3) growth

	Phenylephrine (PE)	Thyroid hormone (T3)
	Pathological hypertrophy	Physiological hypertrophy
Actin		 
β-MHC		 

T3 is superior to CLEN





Marked decrease in β myosin

less decrease in β myosin