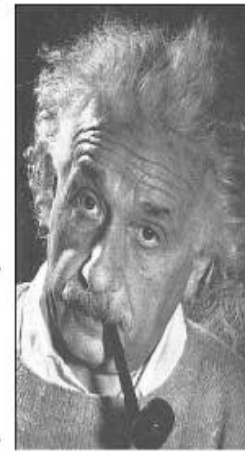
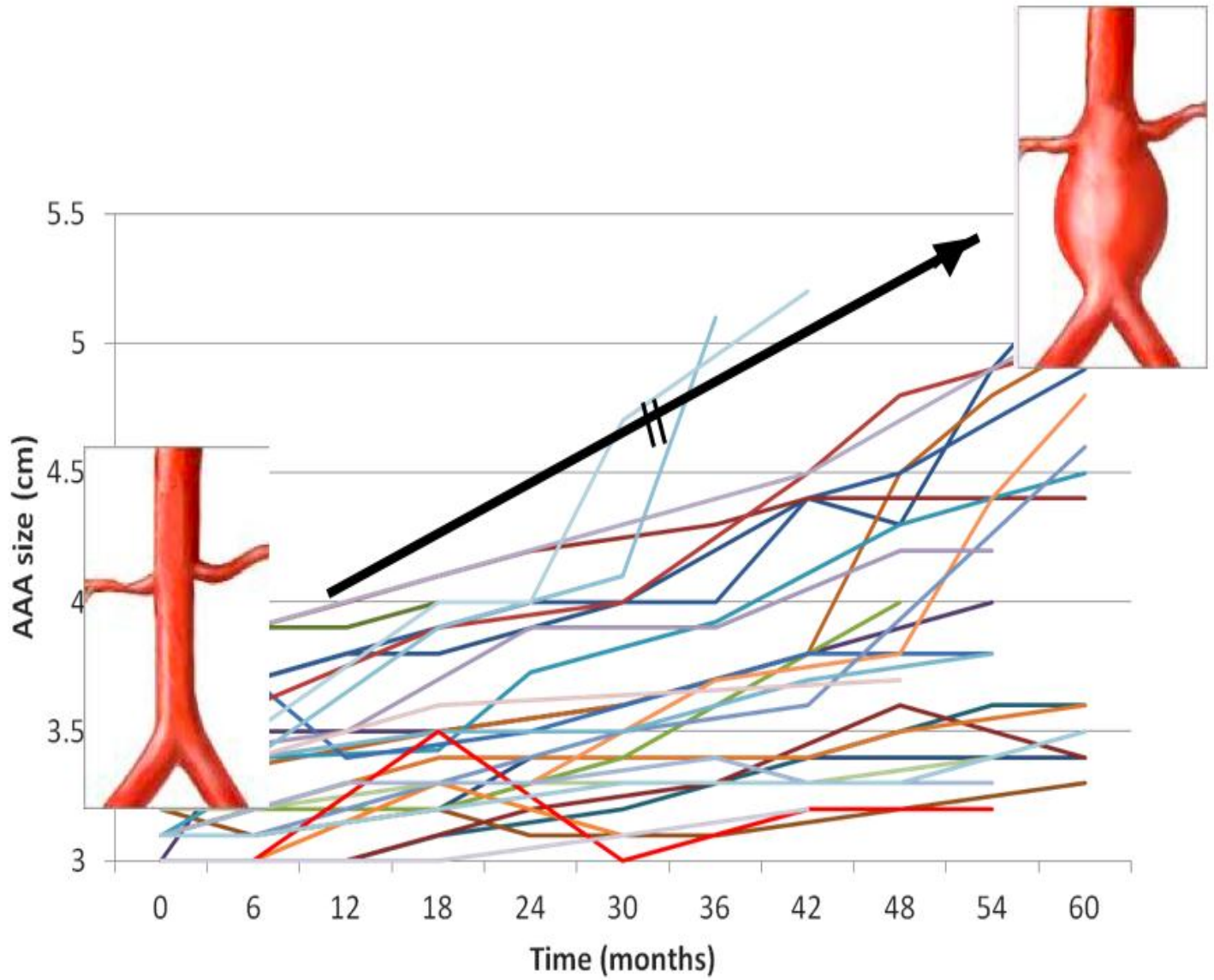
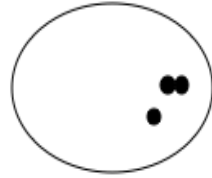


THE INVOLVEMENT OF CELL DEATH IN ABDOMINAL AORTIC ANEURYSM

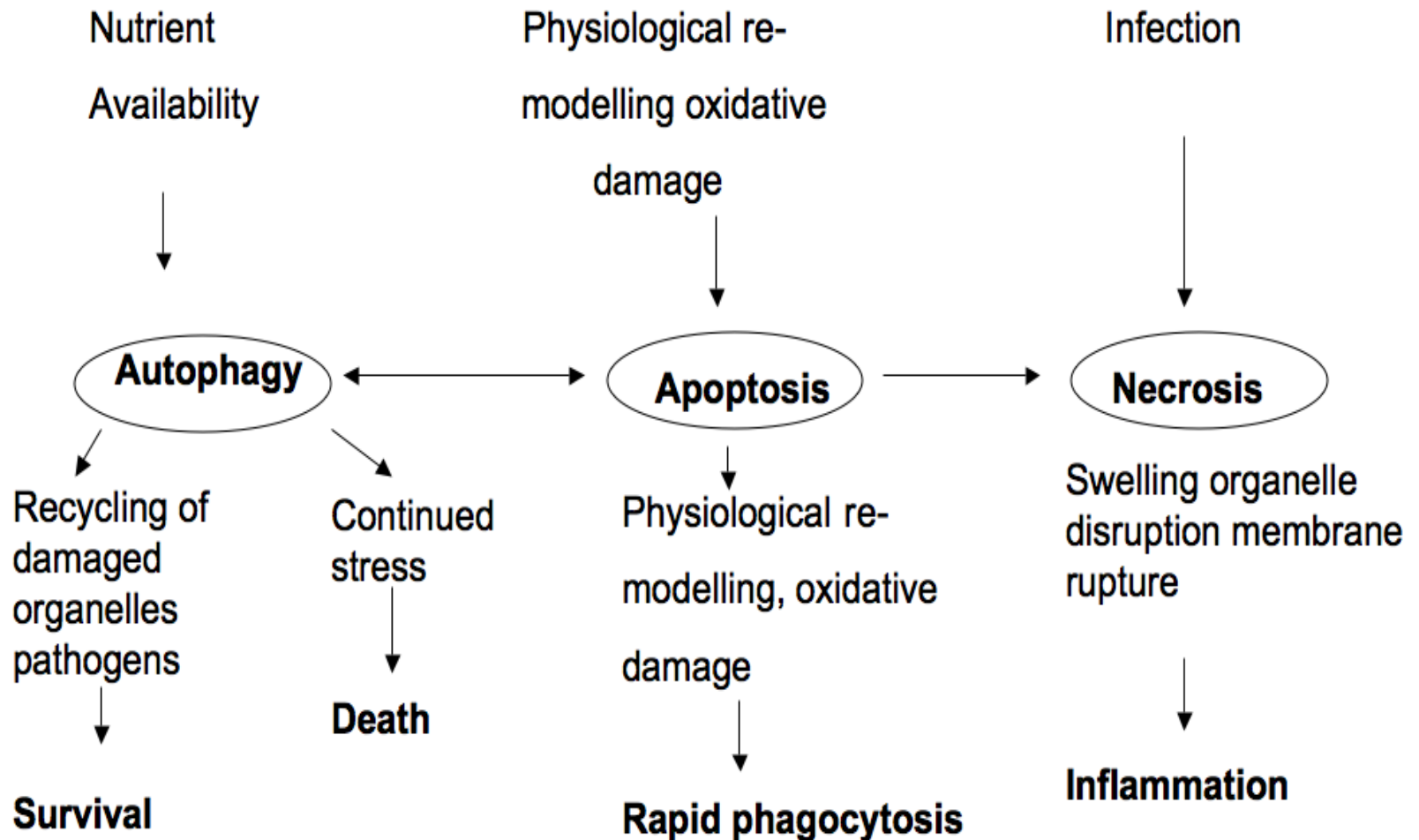
Gillian W Cockerill



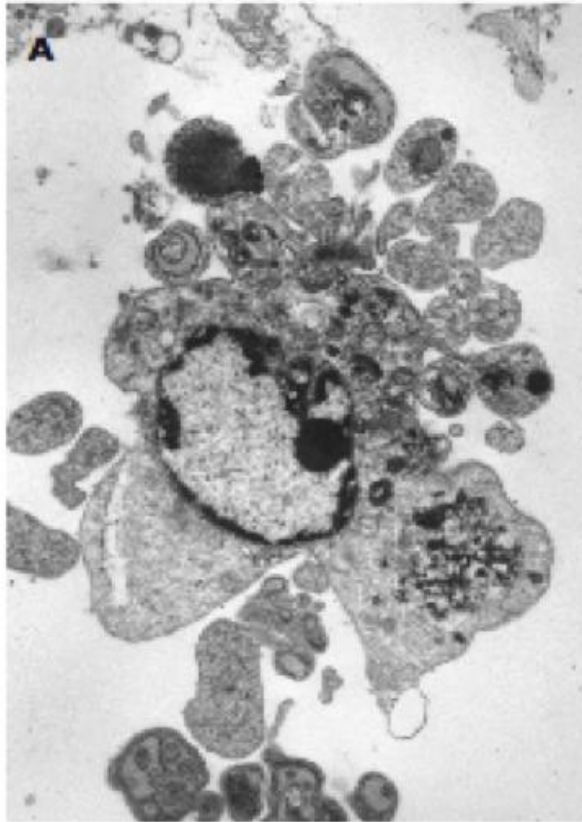




CELL DEATH

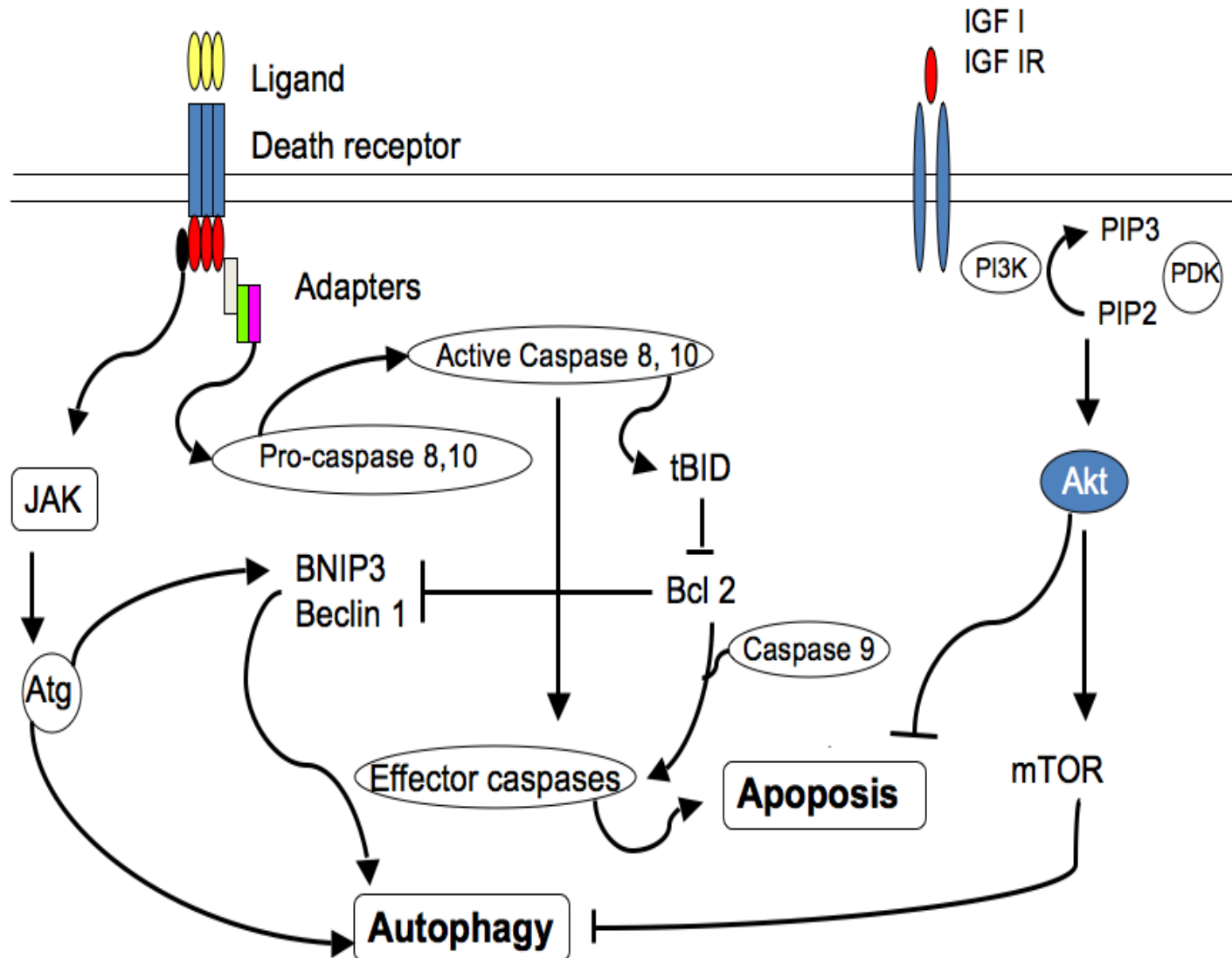


Apoptosis

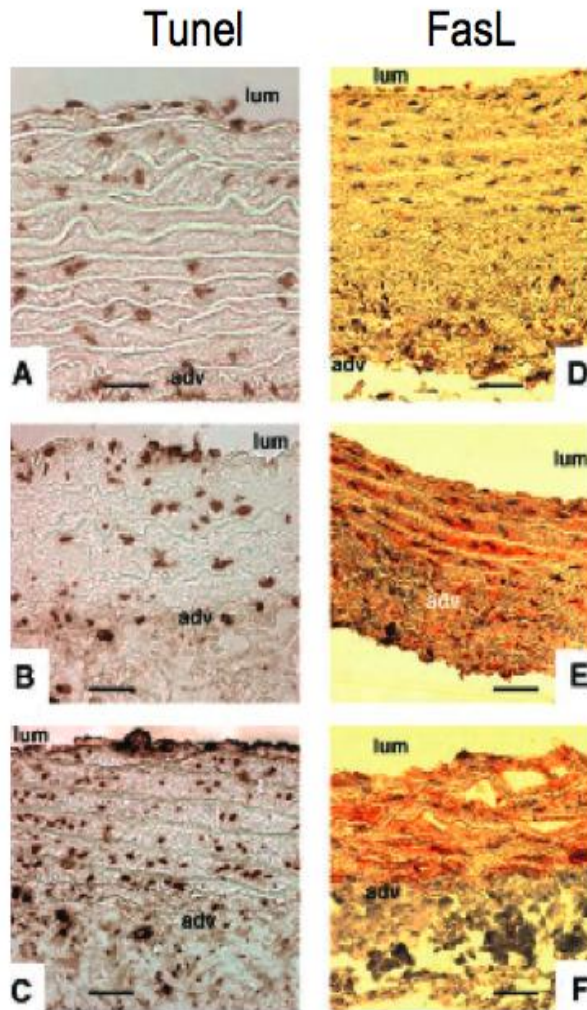


- Membrane blebbing
- Nuclear condensation
- Shrinkage

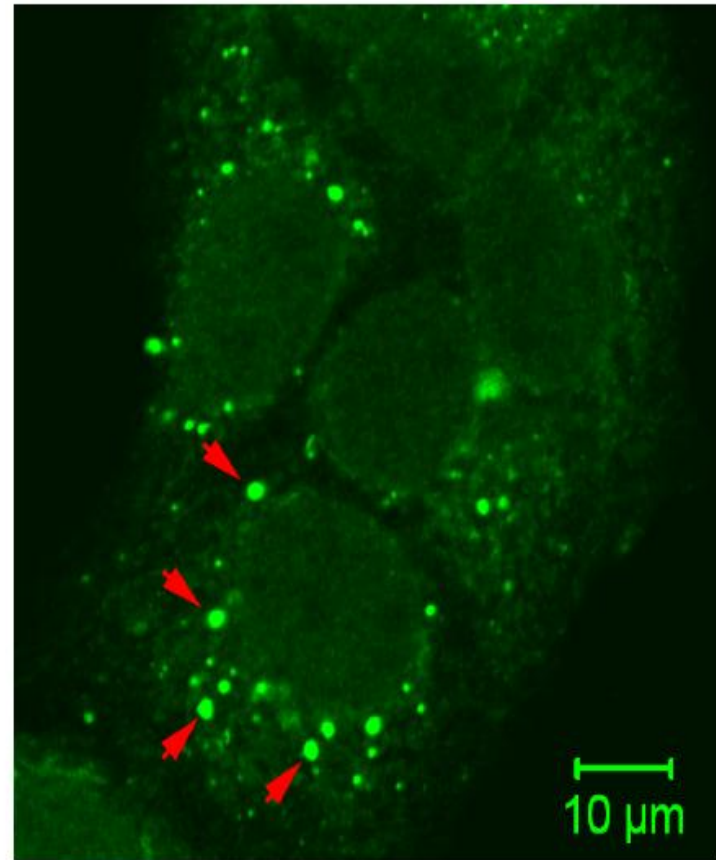
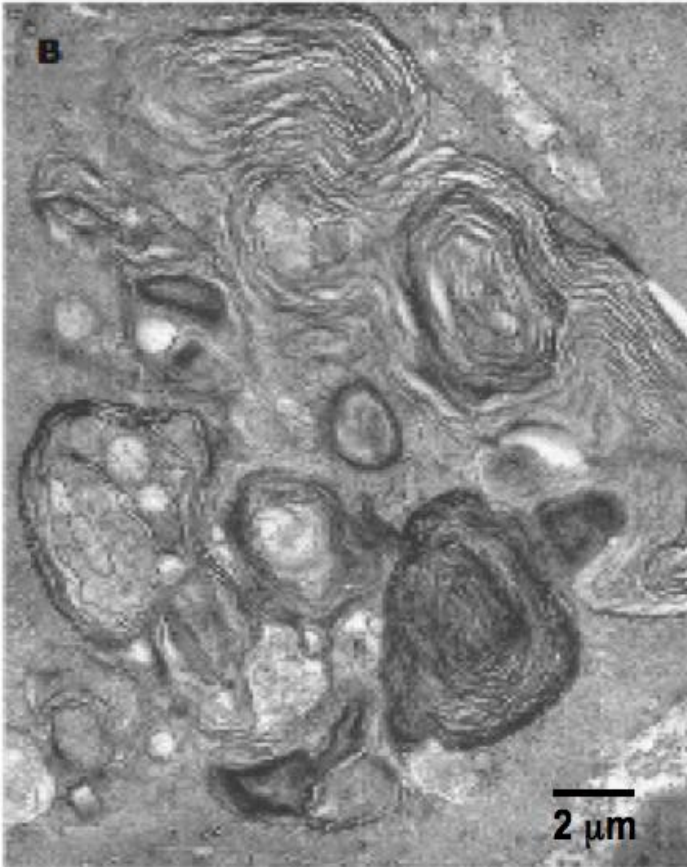
Pathways of apoptosis and autophagy:



Apoptosis in experimental aneurysm models:



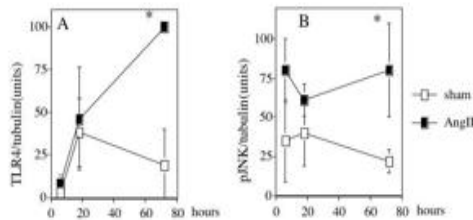
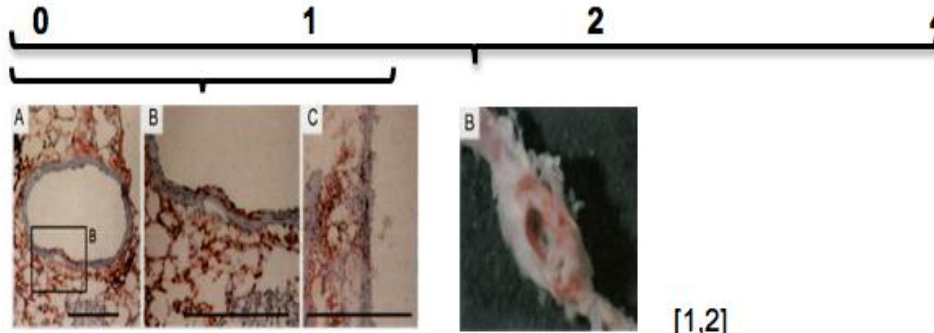
AUTOPHAGY:



Clark *et al.*, *Heart* 2007

Angiotensin II-induced ApoE deficient mouse model of AA:

Time (weeks)
from pump
implantation



[4] Chemokine
protein

Fold Increased

expression vs sham (day 3)

Rantes	(CCL5)	6.9
MIP-1	(CCL9)	3.4
MCP-1	(CCL2)	1.70

[1] Egelton *et al.*, *J Surg Res.*2006;135;345-51

[2] Saraff *et al.*, *ATVB.*2003;23;1621-26

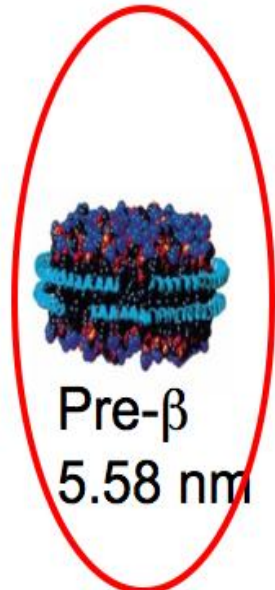
[3] Jones *et al.*, *Circulation.*2009.

[4] Pirianov *et al.*, *Atherosclerosis (in press)*

High-density lipoproteins - nature's own nanoparticles:

rHDLs

CSL-111



α -4
7.43 nm



α -3
8.05 nm



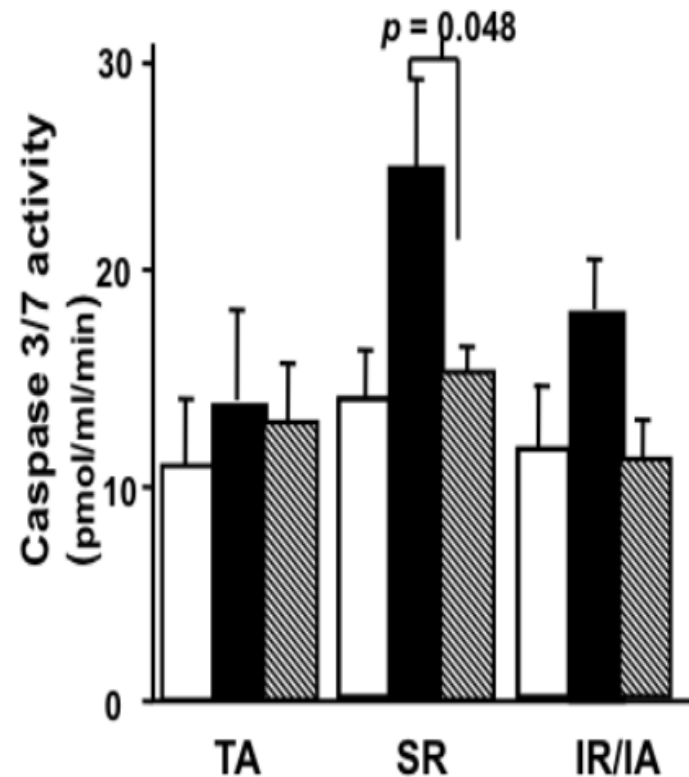
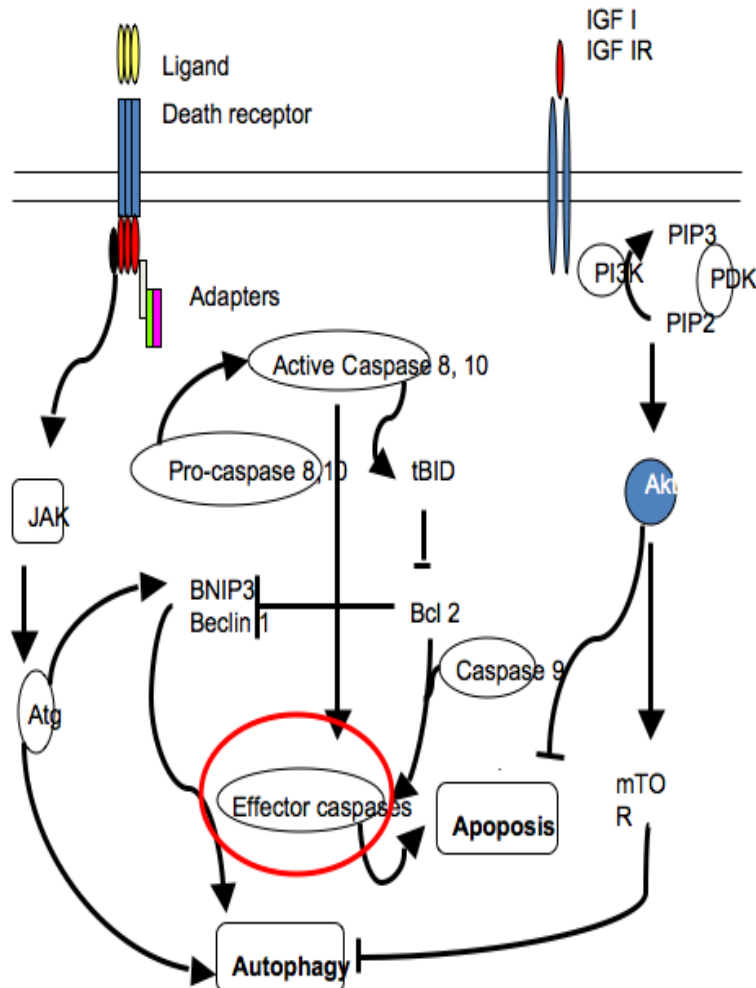
α -2
9.2 nm



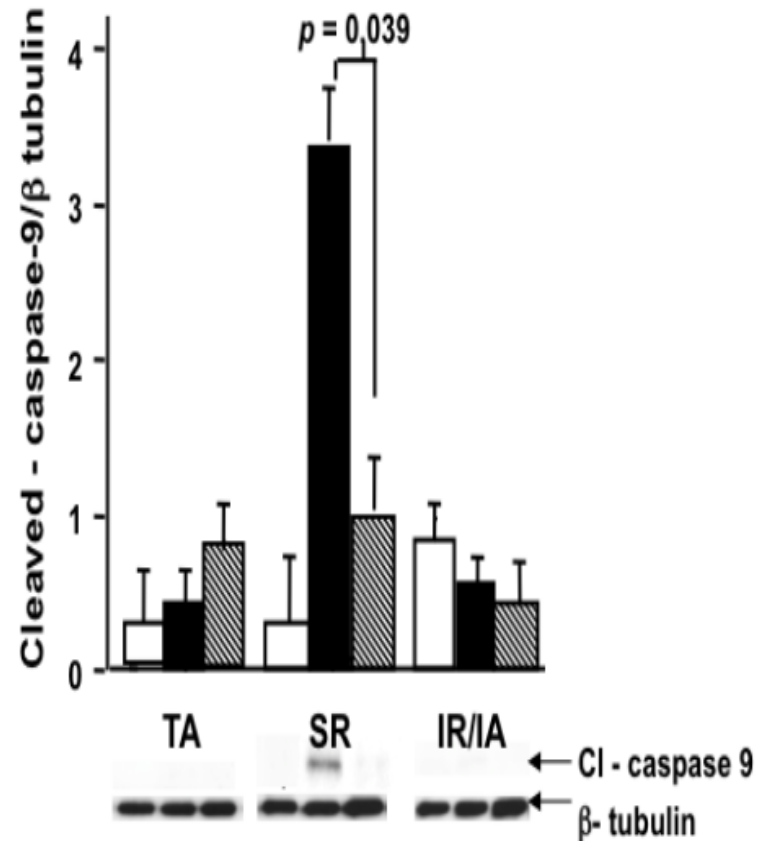
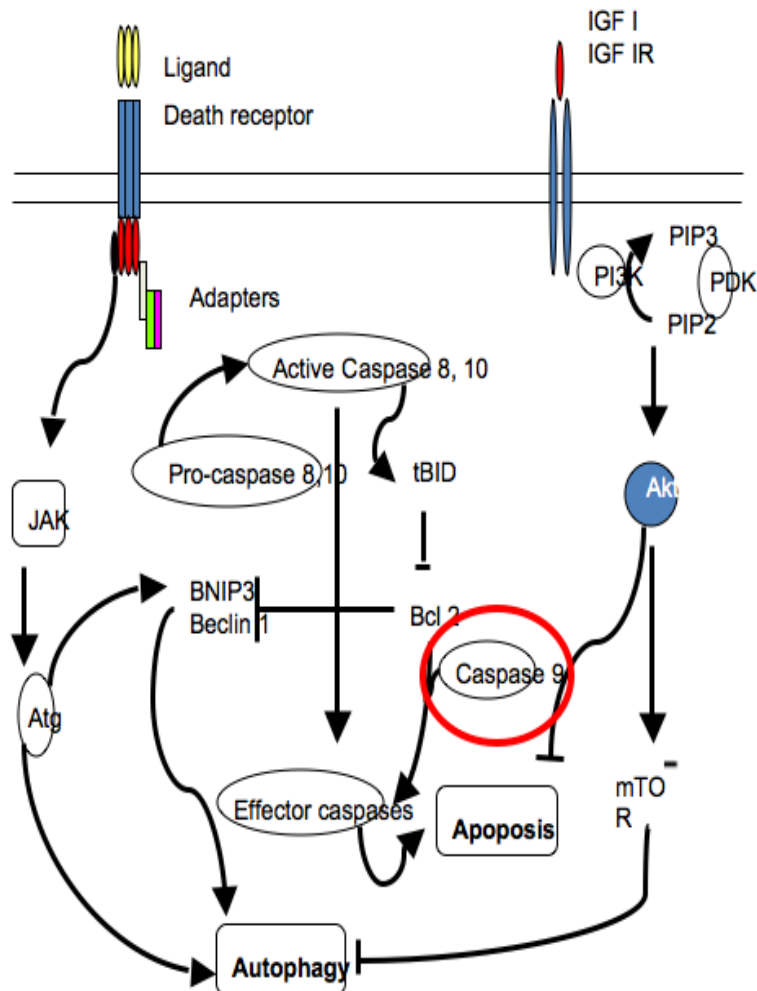
apo A-I amphipathic
alpha-helix
FC
PL

α -1
11.0 nm

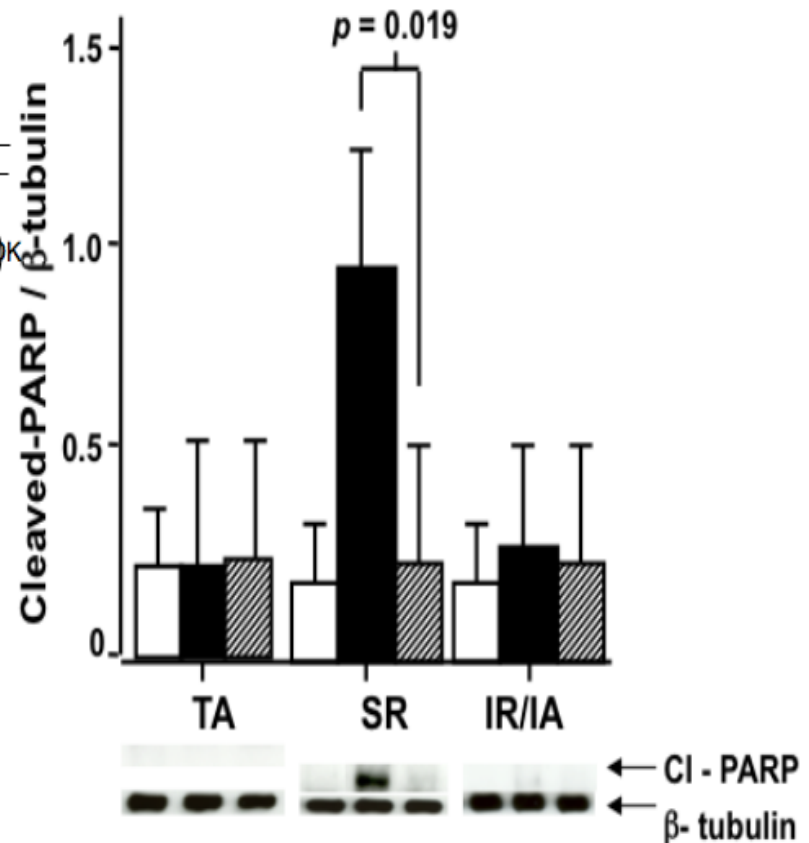
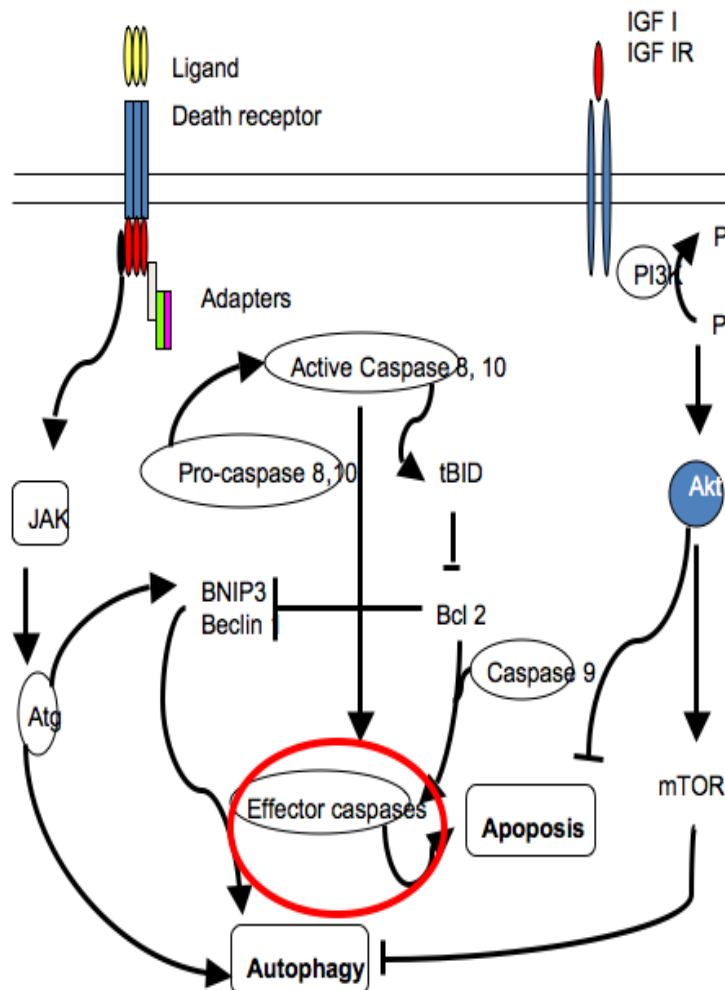
HDL inhibits AngII-induced caspase 3/7 activity in a site specific manner



HDL inhibits AngII-induced caspase 9 cleavage in a site specific manner

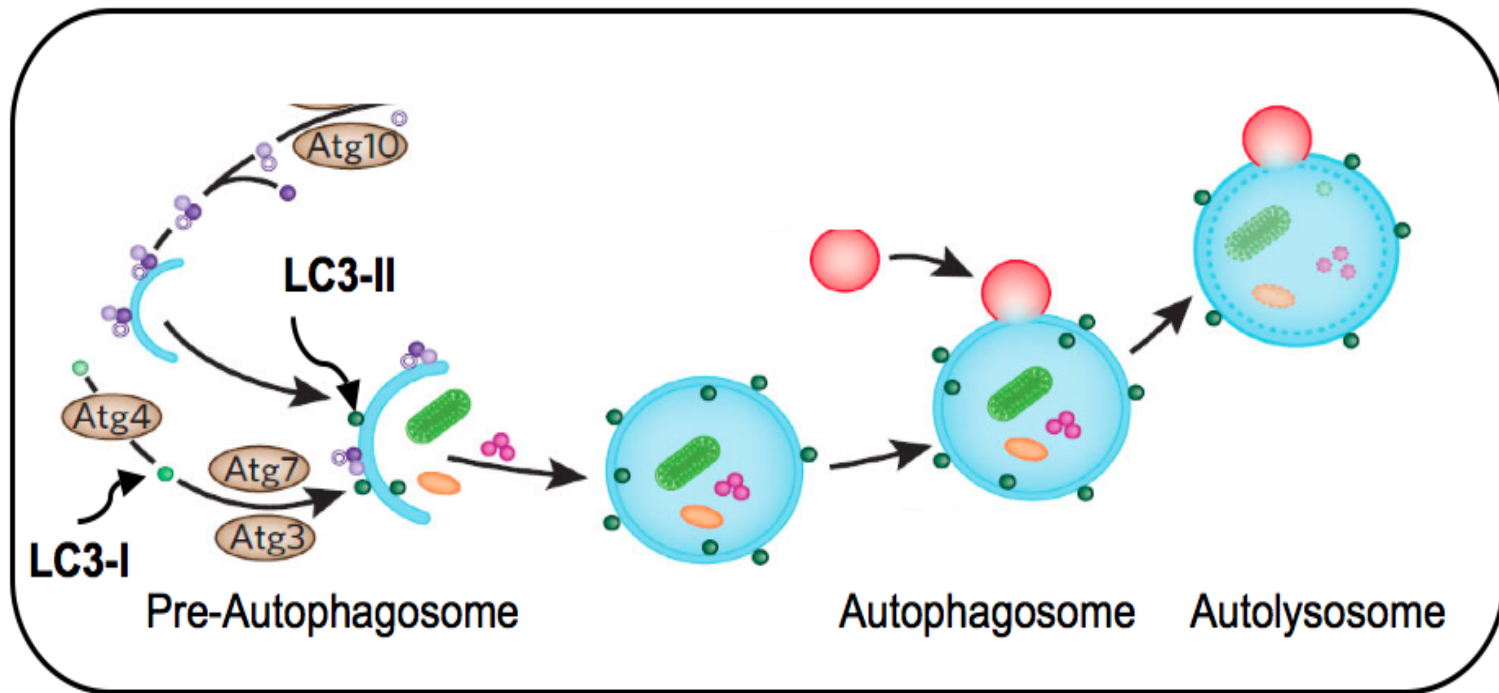


HDL inhibits AngII-induced caspase 9 cleavage in a site specific manner

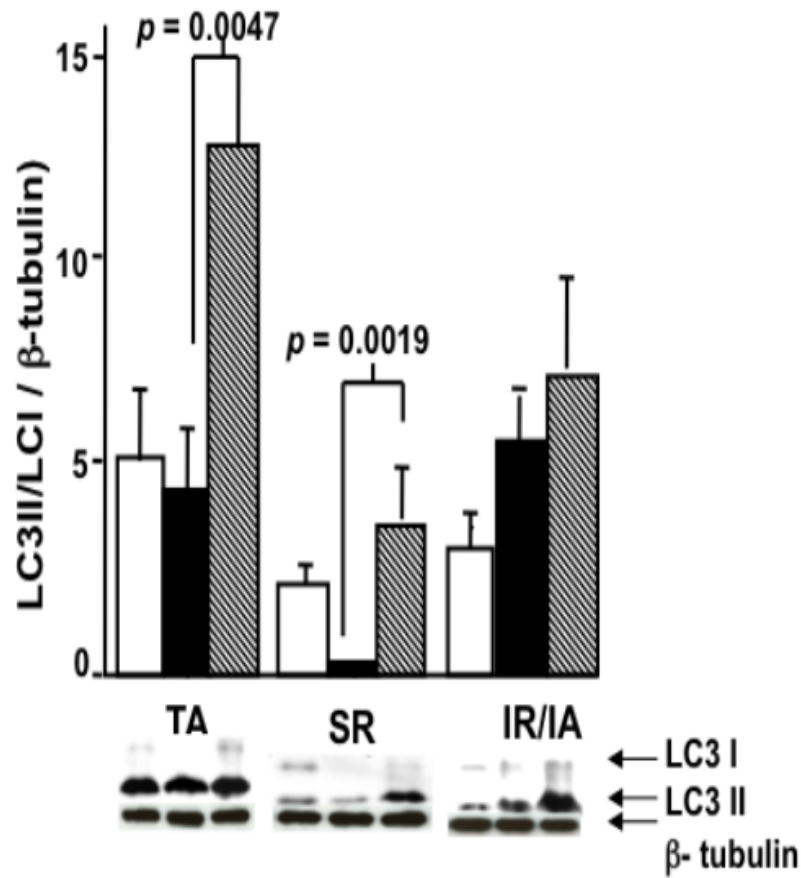


Torsney *et al.*, *ATVB* 2012

Conversion of microtubule associated light chain (LC3) during autophagy:



HDL differentially regulates autophagy throughout the aortic tree

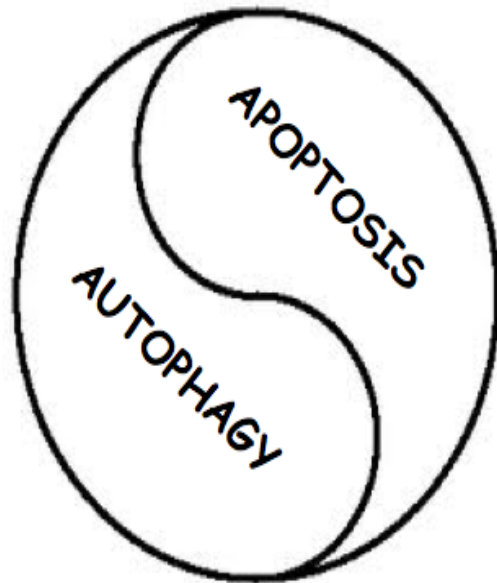


CONCLUSIONS:

Apoptosis can be measured in aneurysms, and is modifiable in response to agents which inhibit aneurysm development

Autophagy can be measured in aneurysms, and is modifiable in response to agents which inhibit aneurysm development.

- Cell death (apoptosis, autophagy, necrosis, anoikis etc.,) are part of the **mechanism of the developing aneurysm**
- Cell death (apoptosis, autophagy, necrosis, anoikis etc.,) are part of the **mechanism of vascular repair in aneurysm formation**



Understanding a little more about the relationship between cell death and AAA development will reveal new strategies/targets for treatment.

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wellcome trust



Garfield Weston
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