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National Heart Centre Singapore
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Restricting Mitochondrial Fission as a Novel Cardioprotective Strategy

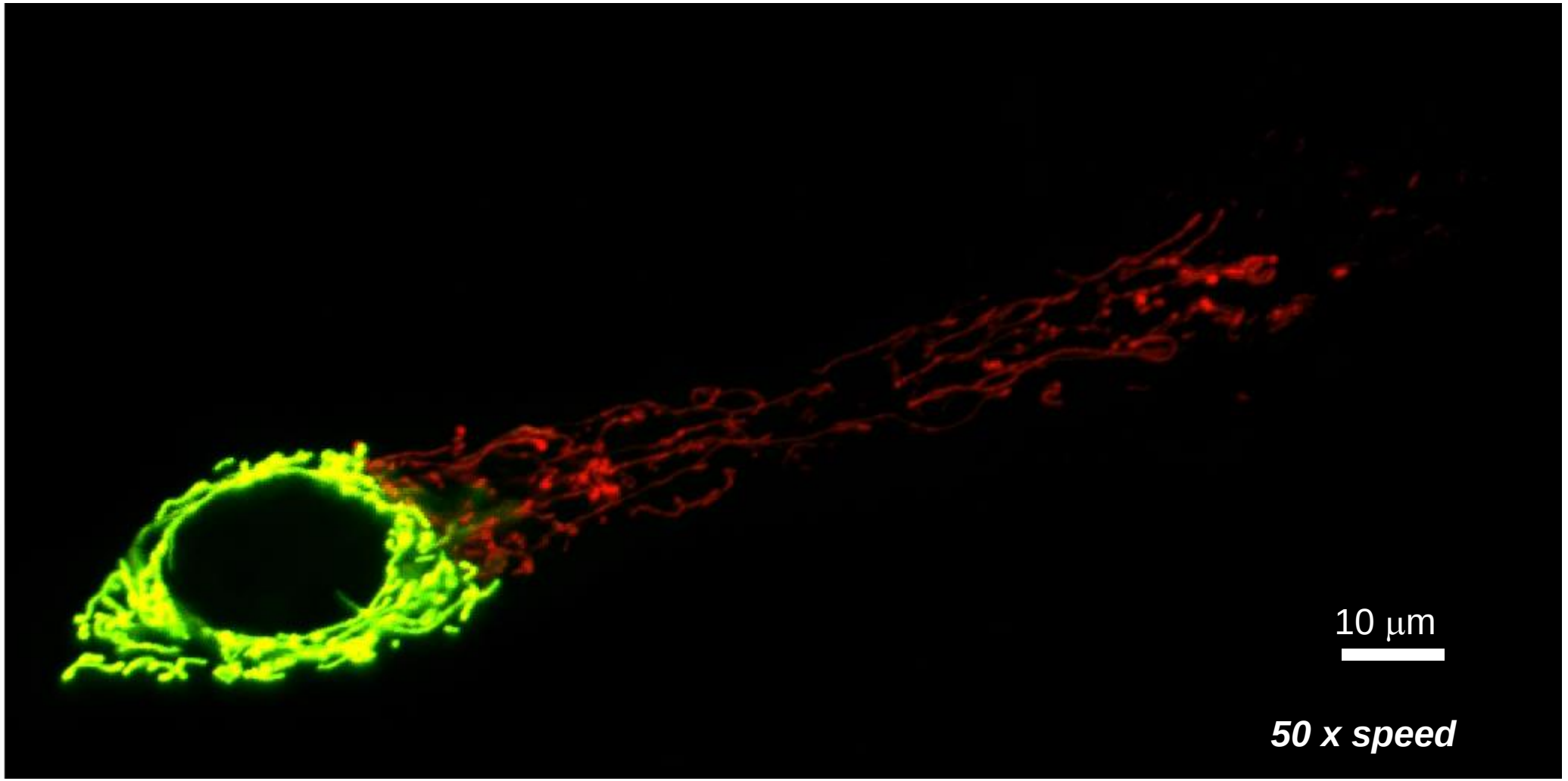
15th Joint Meeting of Coronary Revascularization (JCR 2015)

Dr Sang-Bing Ong, *PhD CSci CBiol EurProBiol*

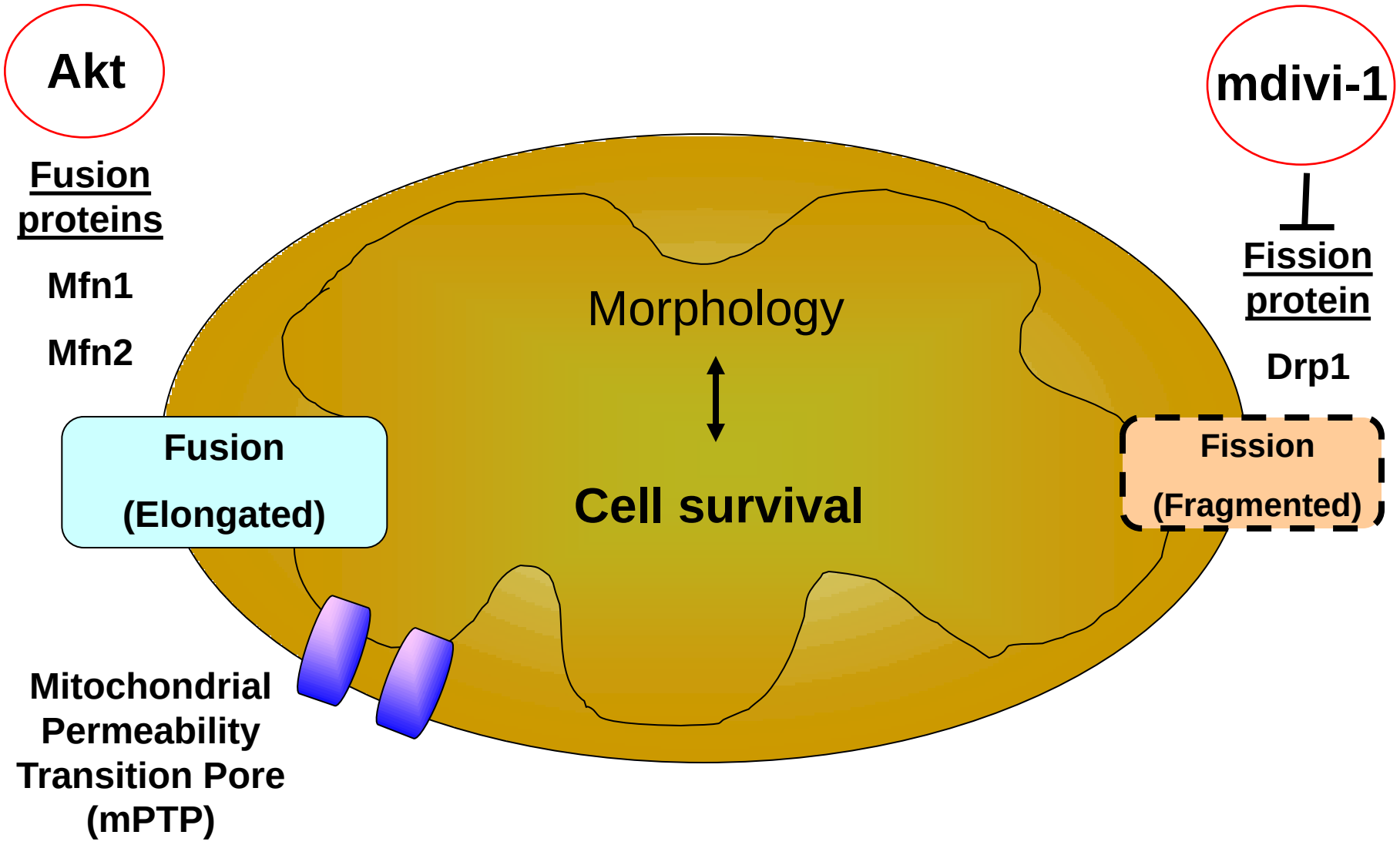
Background

- Novel cardioprotective strategies need to be developed.
- The mitochondrial permeability transition pore (mPTP) is a critical mediator of cell death.
- Changes in mitochondrial morphology have been shown to impact on mPTP opening and apoptosis in non-cardiac cells.
- Whether mitochondrial morphology impacts on cardioprotection is unknown.

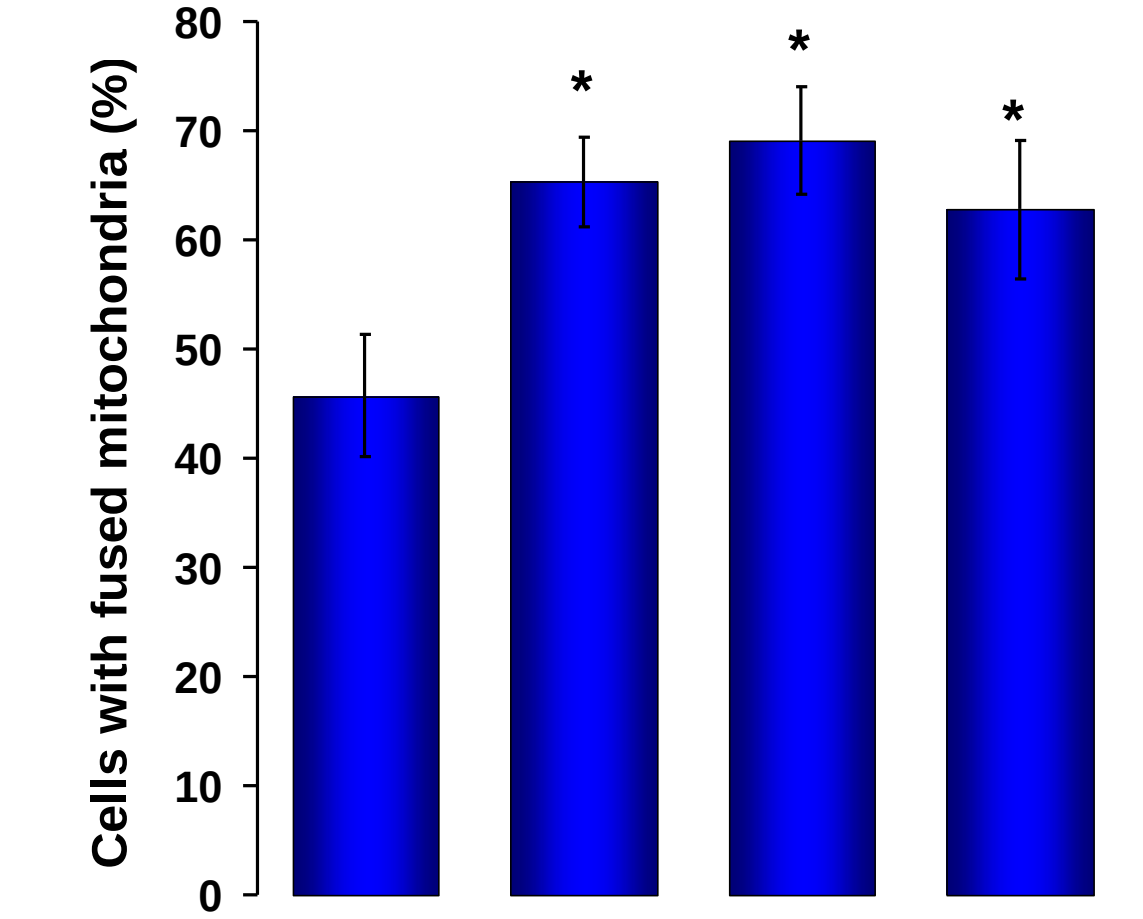
Real-time changes in mitochondrial morphology



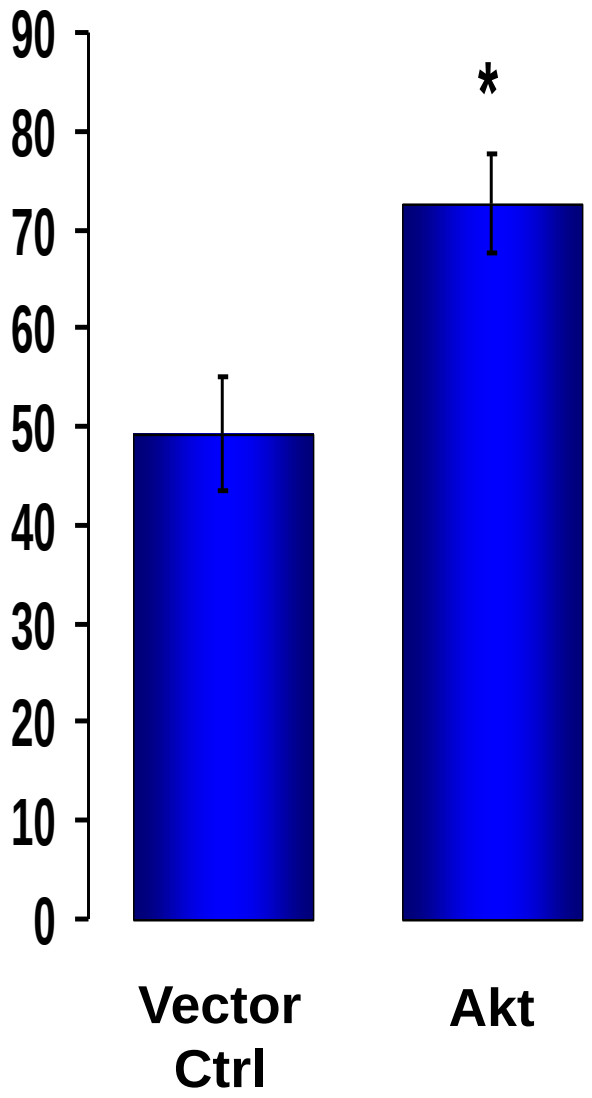
Changes in mitochondrial morphology



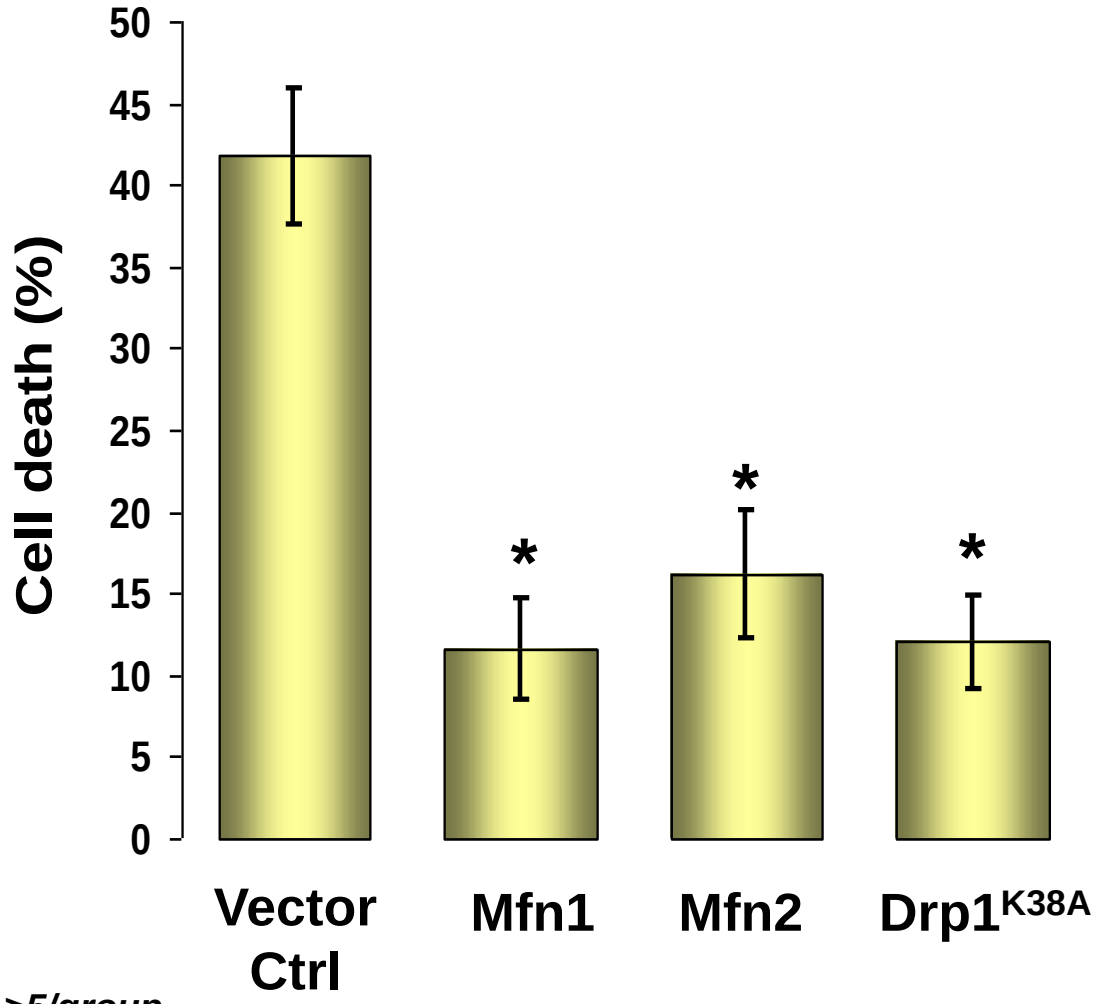
Modulation of mitochondrial morphology



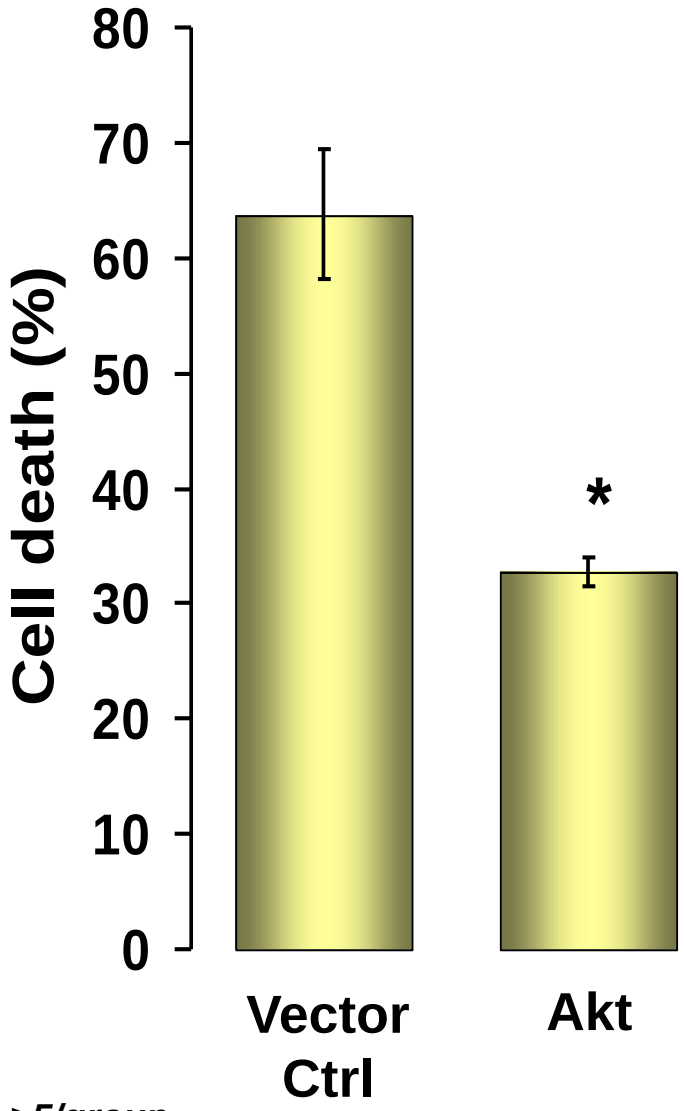
n >5/group
~ 100 cells
**p< 0.05*


90
80
70
60
50
40
30
20
10
0
*
Vector Ctrl
Akt

Cell death assay

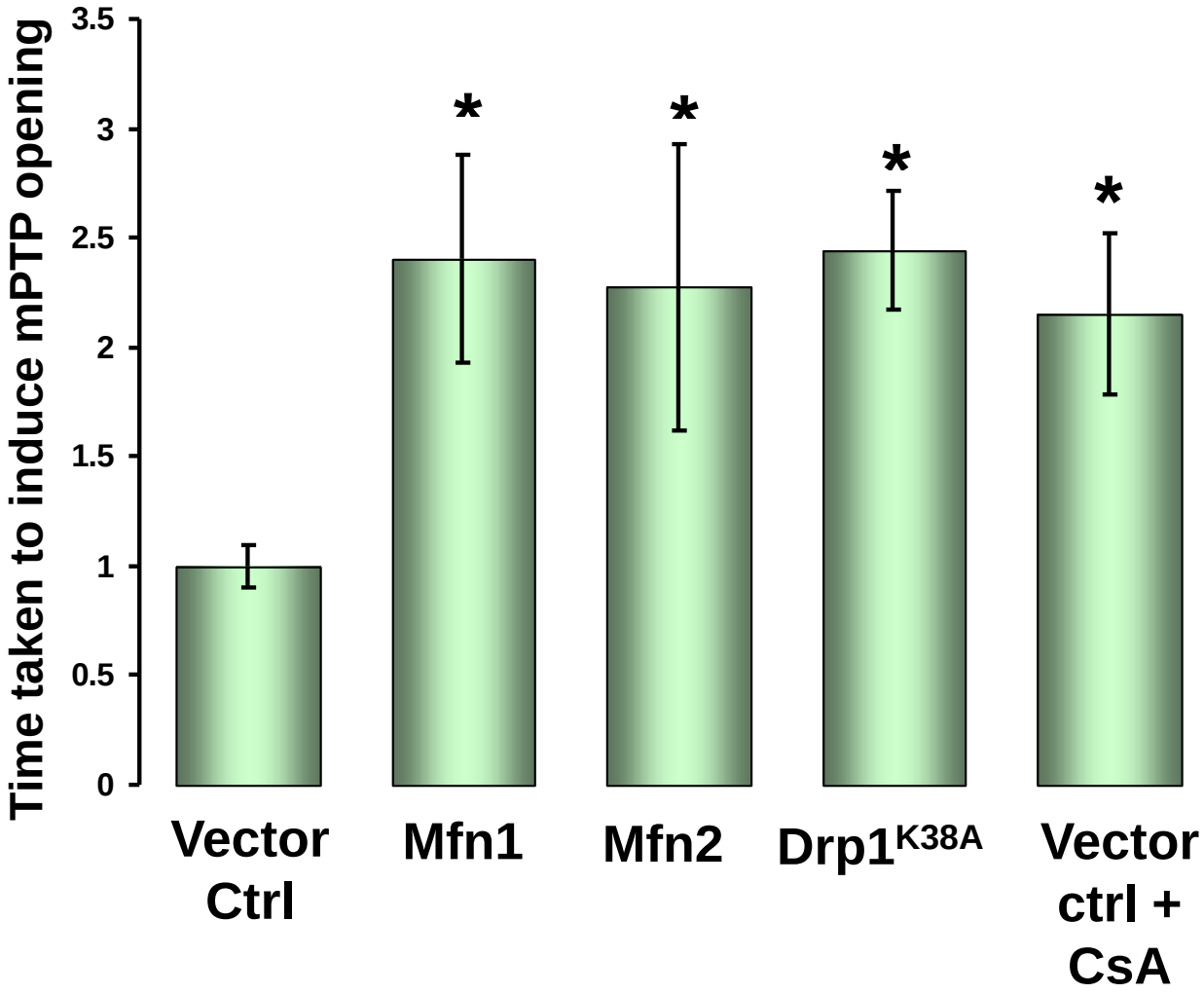


n >5/group
~ 400 cells
**p< 0.05*

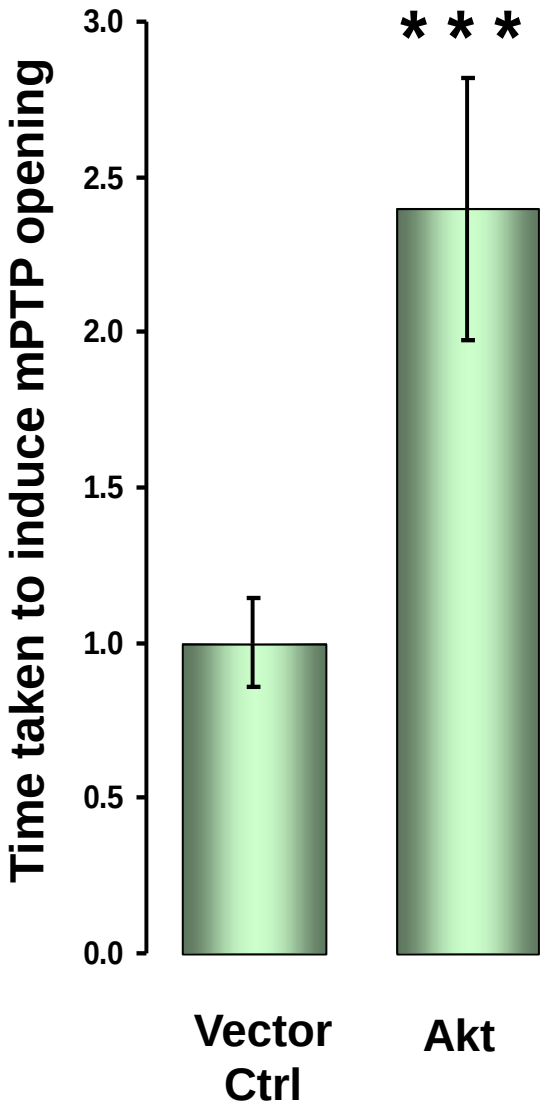


n >5/group
~ 400 cells
**p< 0.05*

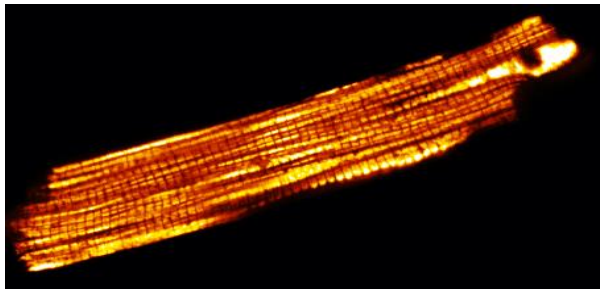
mPTP opening

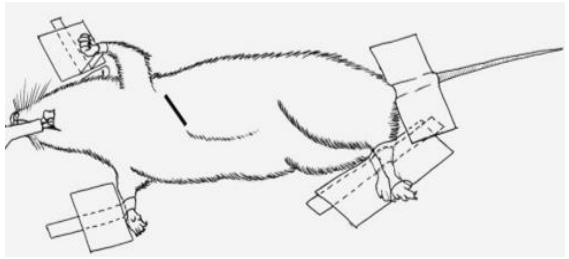


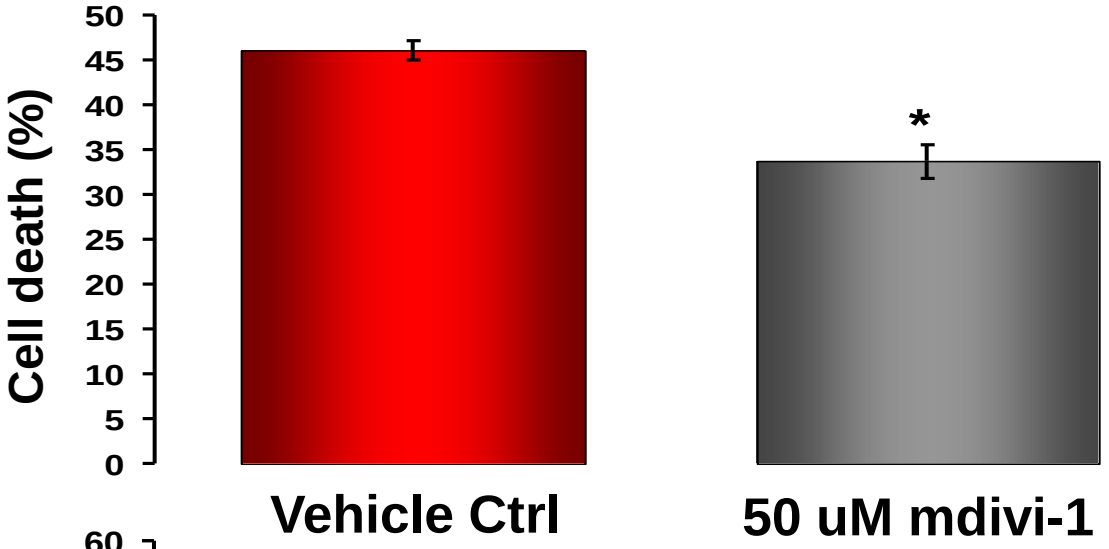
n >5/group
~ 60 cells
**p< 0.05*

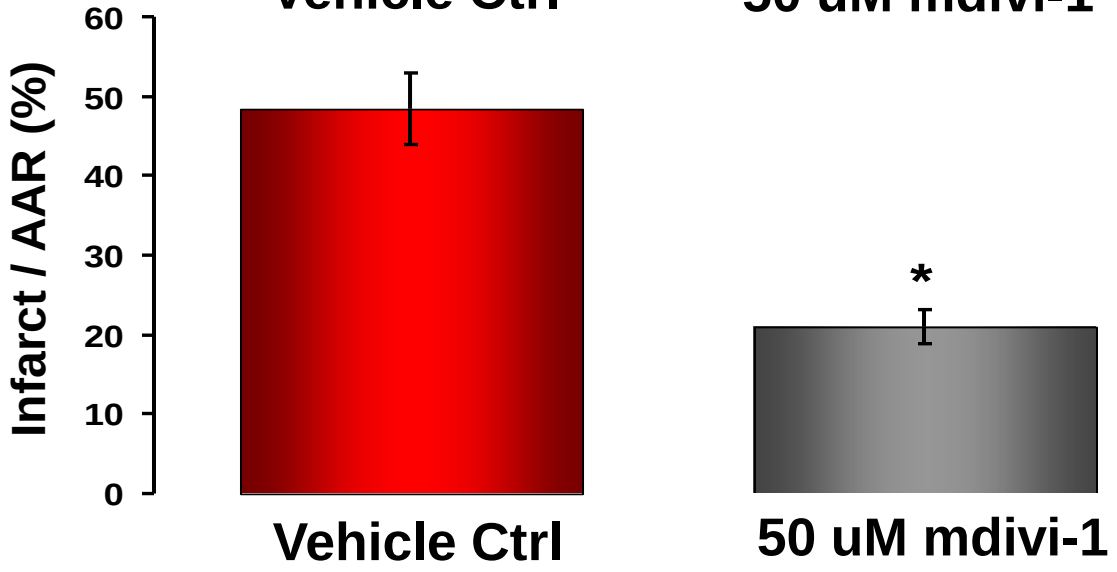

Time taken to induce mPTP opening
3.0
2.5
2.0
1.5
1.0
0.5
0.0
* * *
Vector Ctrl
Akt

Restricting mitochondrial fission protects adult cardiomyocytes and limits infarct size

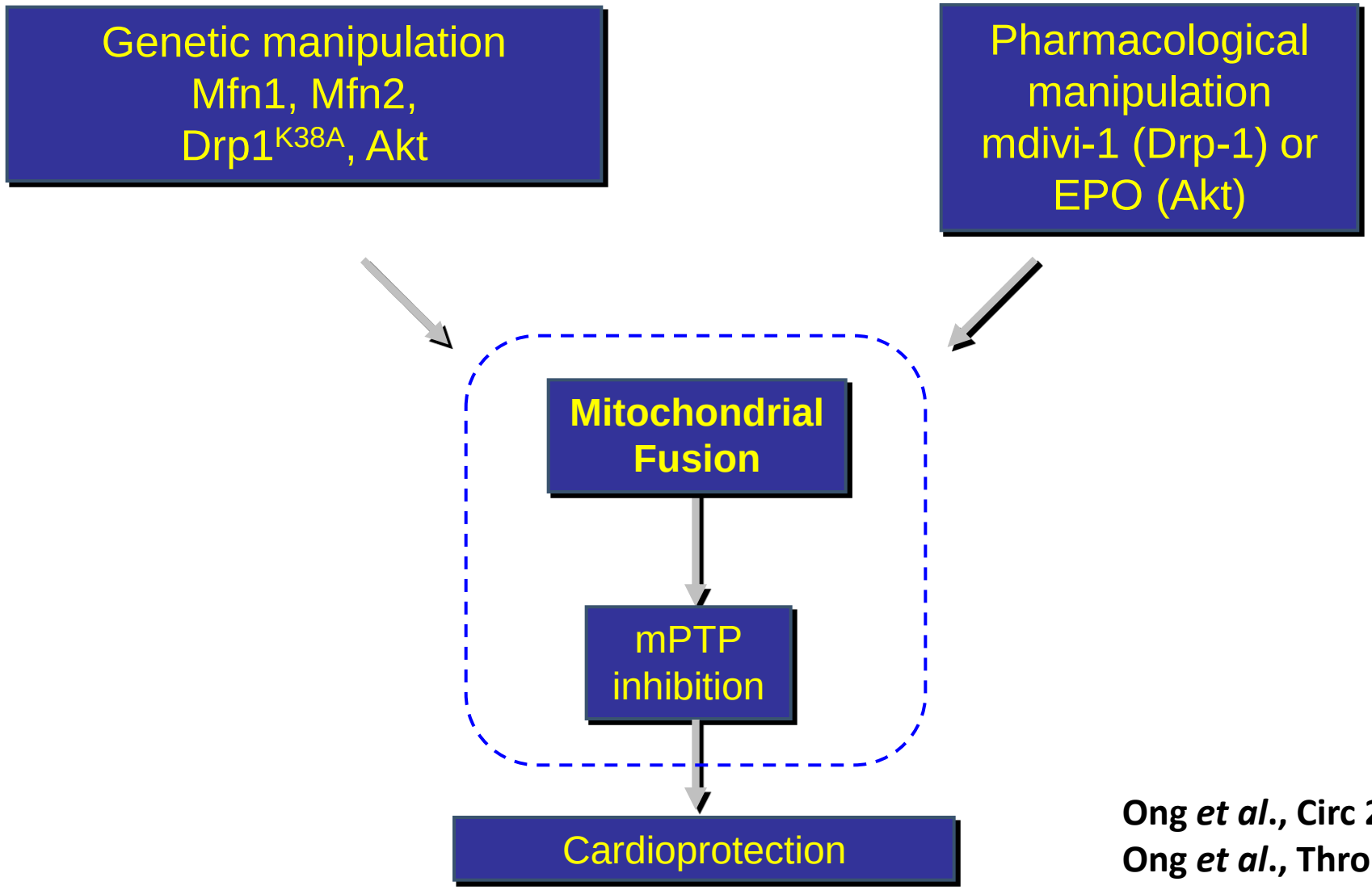








Conclusion



Ong *et al*., Circ 2010
Ong *et al*., Thromb Haemost 2015

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British Heart Foundation

British Heart Foundation