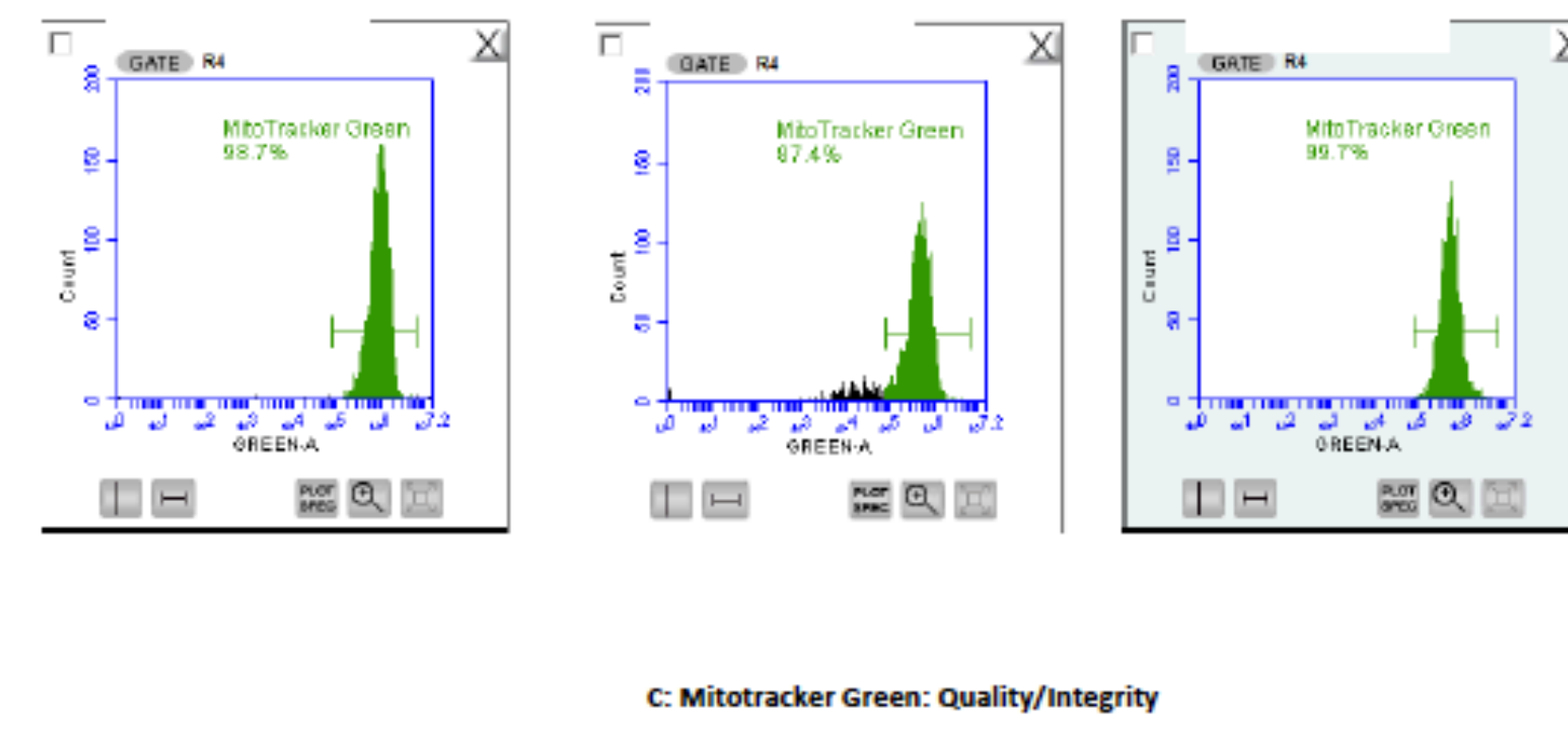
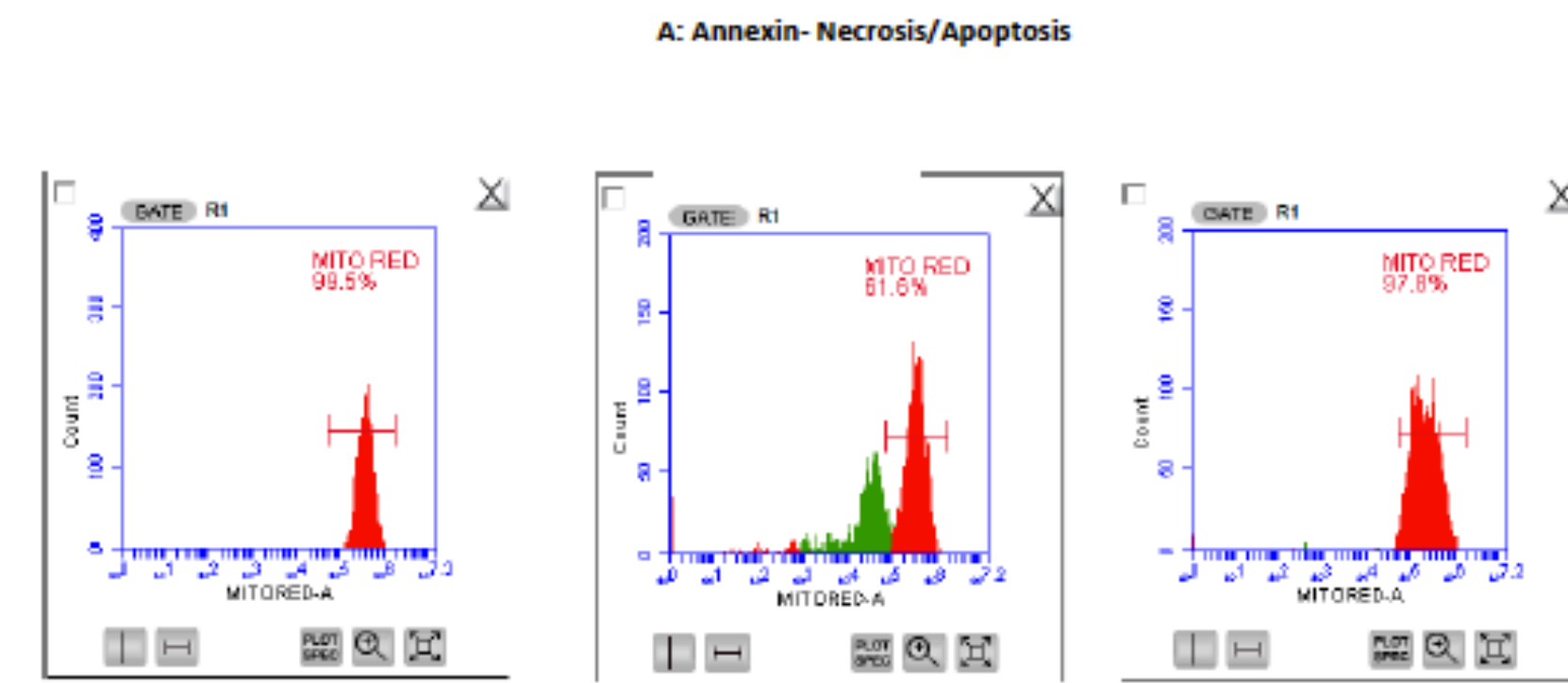
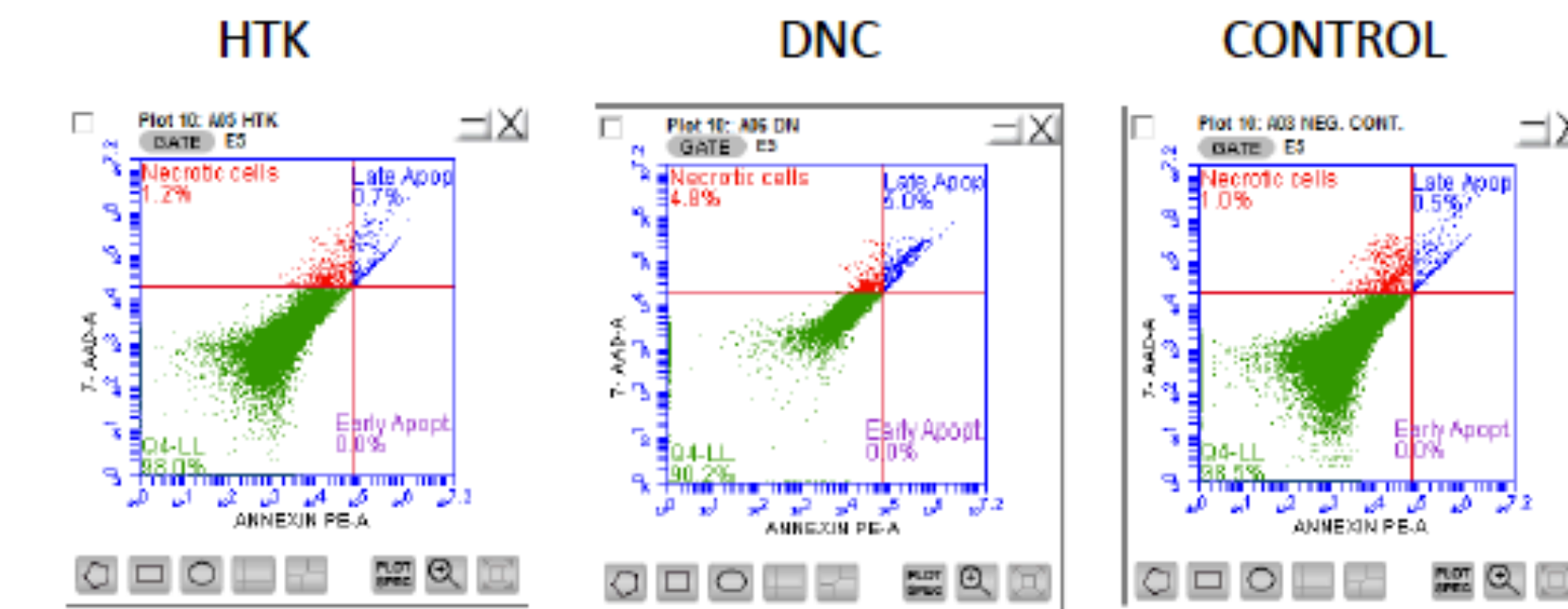


The Impact of Long-acting Cardioplegic Solutions on Myocardial Mitochondrial Integrity and Viability

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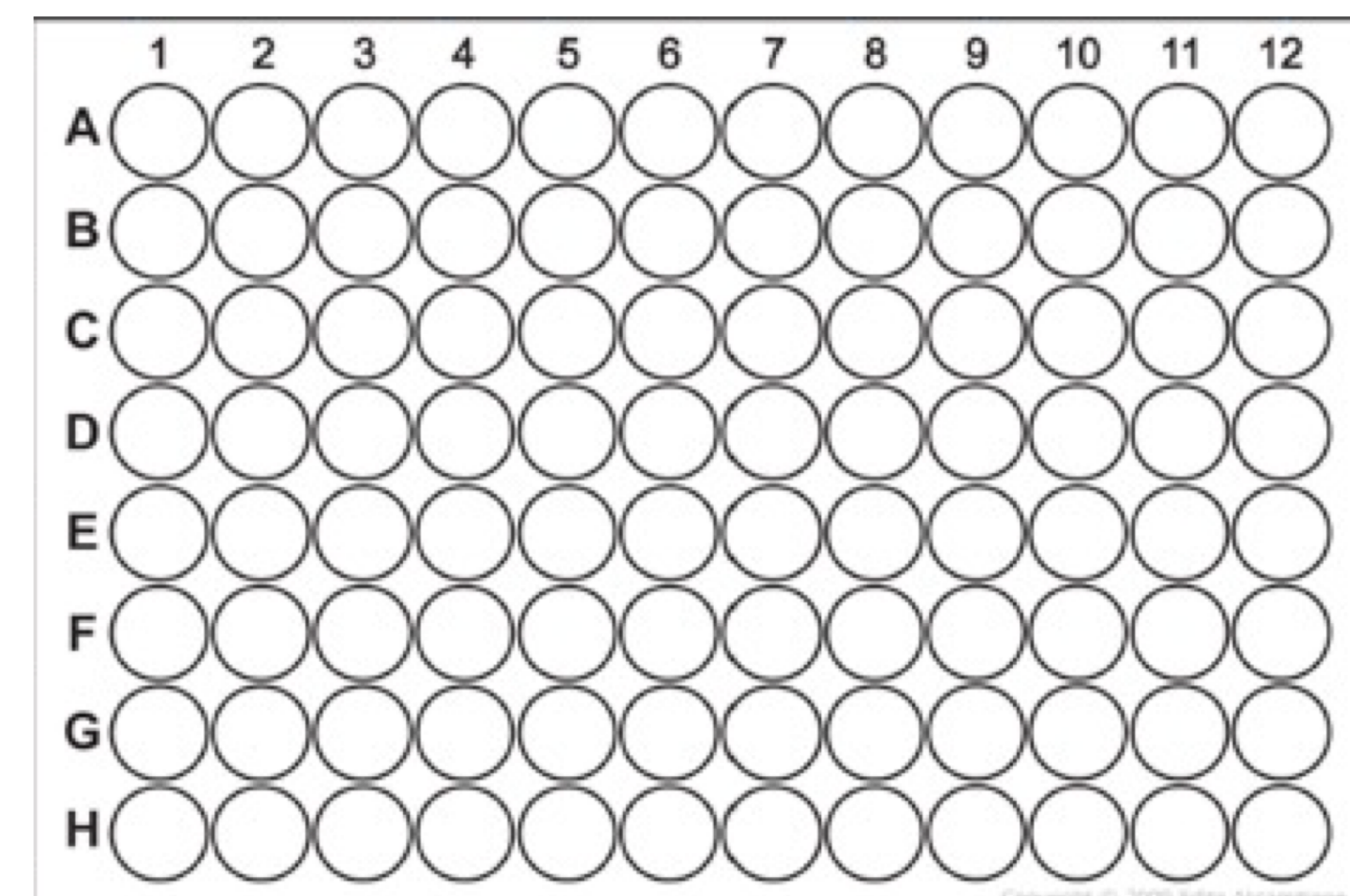
Figure: Mitochondrial parameters of long-acting cardioplegic solutions versus control



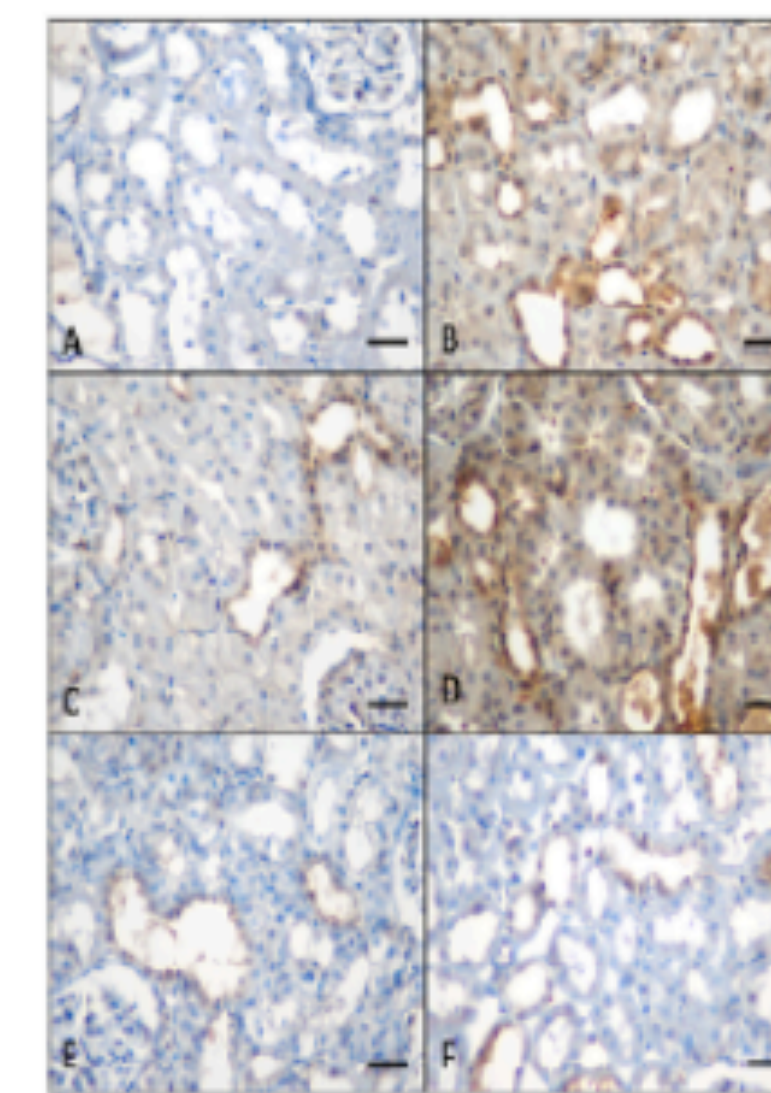
HTK: Histidine-tryptophan-ketoglutarate; DNC: del Nido Cardioplegia

Results

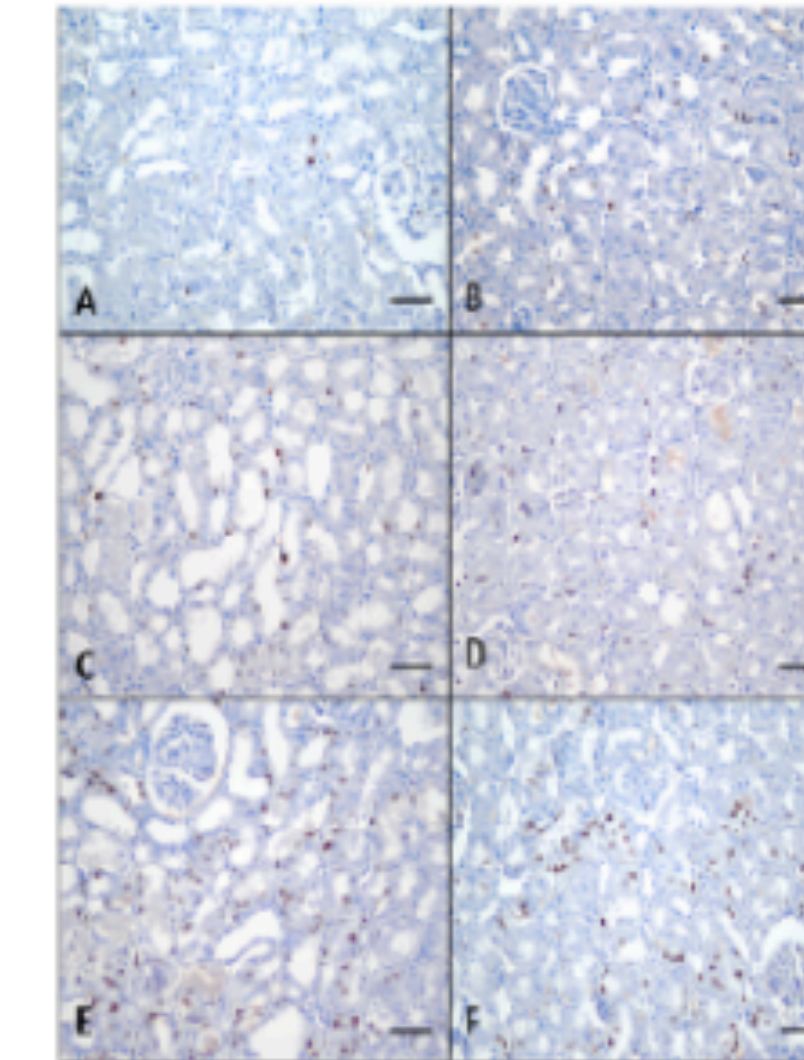
- Mean necrotic cell percentage of HTK was 1.2±0.1% (control: 1±0.1%) versus 4.8±0.3% in DNC (p=0.024)
- Late apoptosis was 0.7±0.08% in HTK (control: 0.5±0.05%) versus 5±0.2% in DNC (p=0.001)
- Mean mitotracker red positive cell percentage of HTK was 99.5±5% (control: 97.8±5%) versus 61.6±4% in DNC (p=0.01)
- Mean mitotracker green positive cell percentage of HTK was 98.7±5% (control: 99.7±5%) versus 87.4±5% in DNC (p=0.02)
- HTK was significantly better in the prevention of necrosis/ apoptosis via preservation of membrane integrity



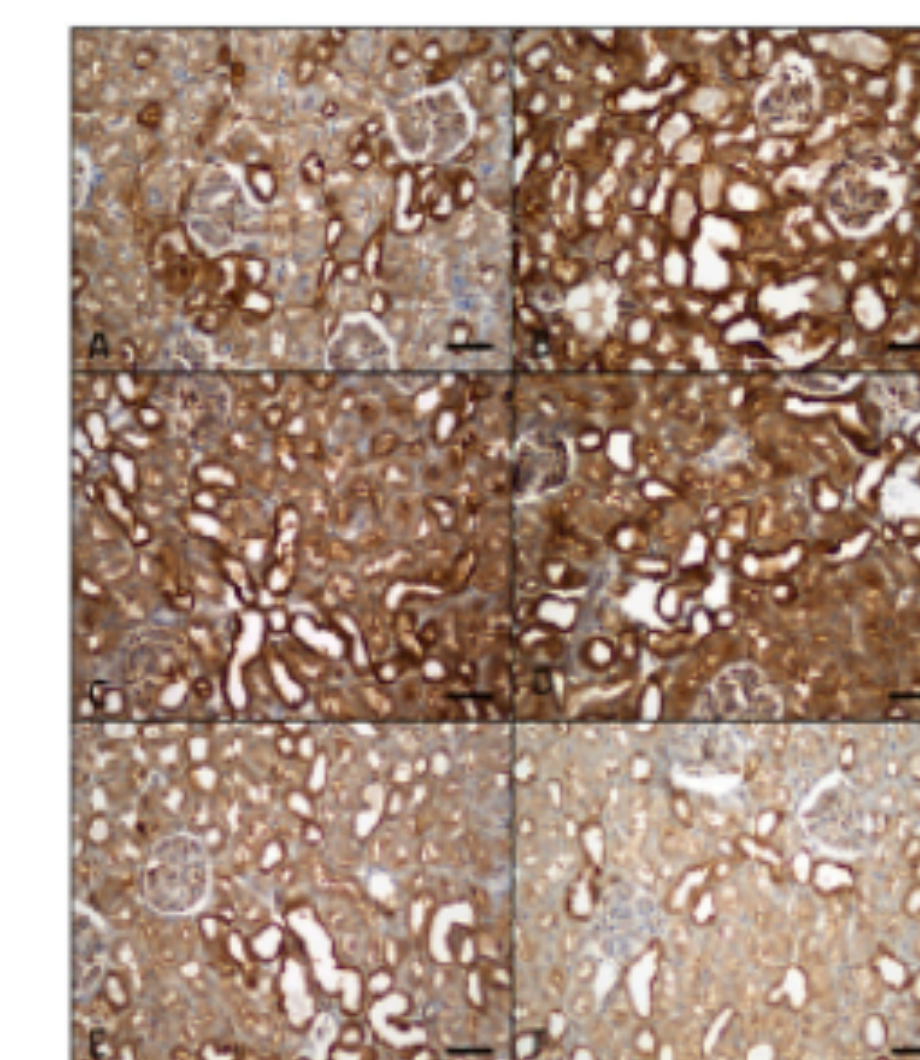
96-well plate for cell culture



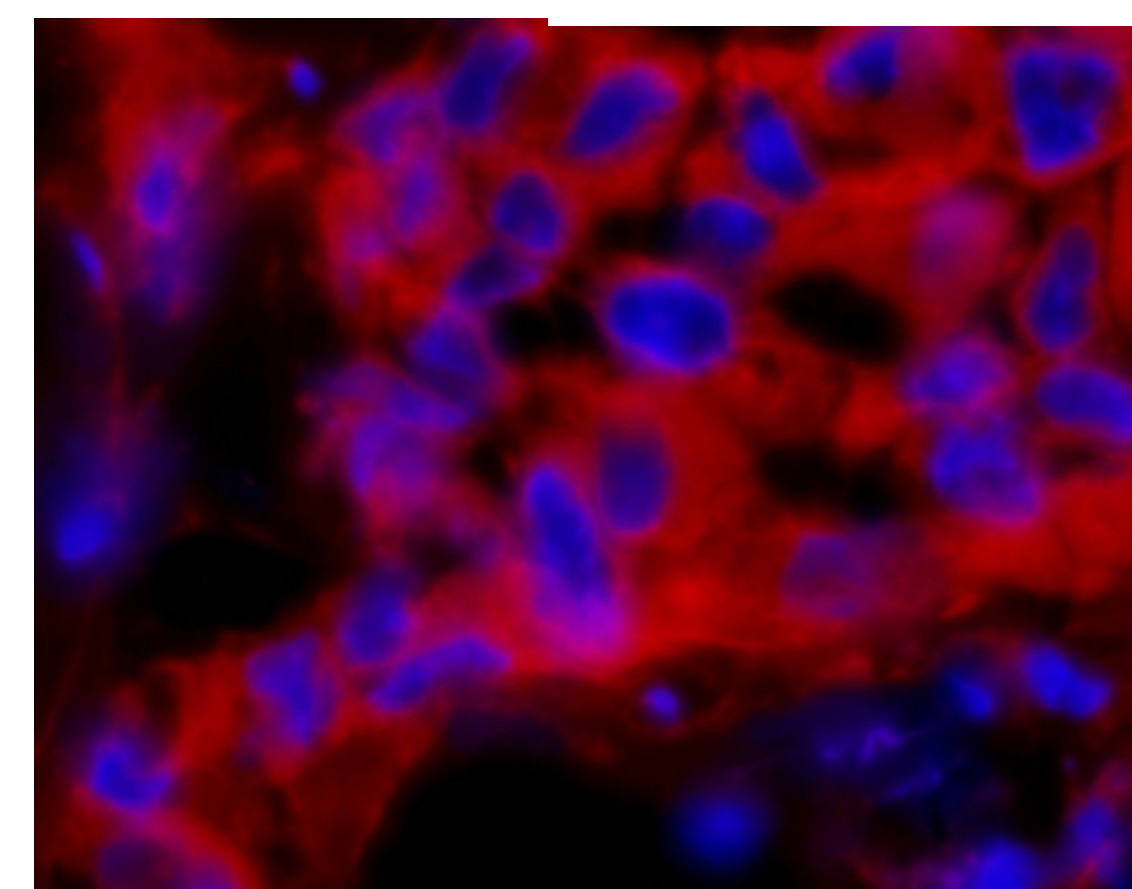
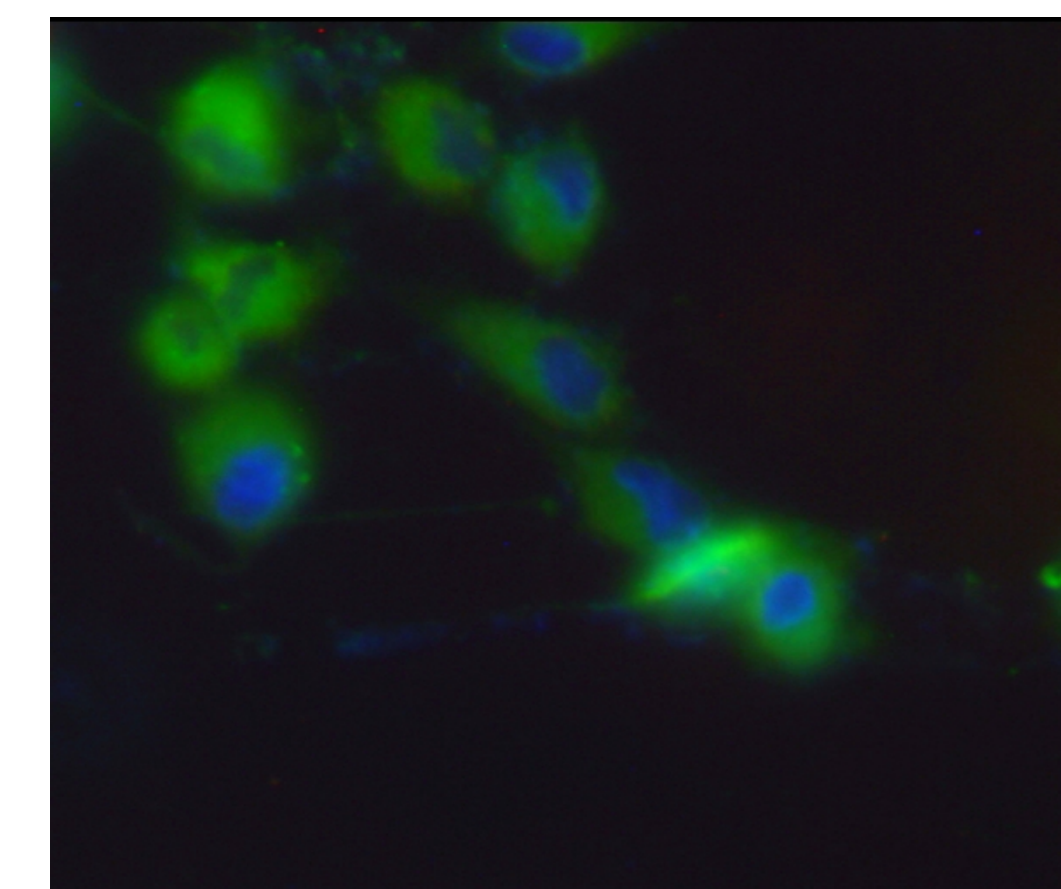
Decrease in the number of apoptotic cells



Increase in cell proliferation



Decreased mitochondria fission



Display of mitochondriae inside the cells documented by Mitotracker Green & Red

References

- Gunaydin S, Akbay E, Gunertem OE, McCusker K, Onur MA, Ozisik K. Long-term protective effects of single-dose cardioplegic solutions in cell culture models. J Extra-corp Tech 2020; 52(4):279-288
- Gokhan Burcin Kubat, Oner Ulger, Serdar Gunaydin. Mitochondrial Transplantation and Transfer Biology, Methods, Applications, and Disease. Elsevier, Paperback ISBN: 9780443188589, USA

Conclusion

- All results concerning the cardioprotective effect of mitochondriae have been obtained so far in limited number of laboratories
- With regard to cardioprotection, possible mechanisms of their action remain the subject of heated debate
- The mitochondrial role during a relatively short period of IRI is important to find strategies in order to prevent the dysfunction during cardioprotection
- We documented the impact of different cardioplegic solutions on mitochondrial content to document long-term effects that we believe are the most underestimated fact in the literature
- HTK was significantly better in preservation of mitochondrial function

Introduction

- Mitochondria are unique in their own way containing their **own circular** DNA and their own ribosomes
- Mitochondrial function is a critical determinant of myocardial preservation generating ATP required to maintain normal heart contractile capacity therefore playing a key role in signaling pathways of ischemia-reperfusion injury (IRI) becoming an important marker for cardioprotection
- The aim of this study was to develop a method to evaluate mitochondrial content and viability in the context of myocardial protection capacity of different long-acting cardioplegic solutions

Materials & Methods

- Cardioplegic application methods and dosing were simulated from an 80-kg patient (approximate cell count in the heart) undergoing minimally invasive cardiac surgery at moderate hypothermia (32°C) as follows:
 - ✓ Group 1: Histidine-tryptophan-ketoglutarate (HTK)
 - ✓ Group 2: del Nido cardioplegia (1:4) (DNC)
 - ✓ Group 3: Control- 37°C with standard cultured medium
- Cultured human umbilical vein endothelial cells (2.3x10⁴ cells/mL) were seeded in 96-well plates
- Cell culture plates were set up to 32°C in a water bath
- HTK and DNC (4°C) (200 mL/well) were added and kept for 90 minutes
- After 90 minutes, study groups were washed with PBS and incubated with prewarmed control culture medium for additional follow-up of 6 hours in standard conditions (37°C, 5% CO₂)
- The comparative evaluation of cardioplegic solutions on mitochondrial parameters were all measured by flow cytometry at 6th hour:
 - ✓ Annexin V (viability-necrosis/apoptosis)
 - ✓ mitotracker red and mitotracker green (membrane integrity-quality)