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Mitochondrial superoxide anions induced by exogenous oxidative stress determine tumor cell fate: an individual cell-based study

Key words: Individual cell, Superoxide anion, Reactive oxygen species (ROS) dynamics, Intrinsic apoptotic pathway, Ca2+ signaling

Research Summary

- Modified microfluidics and imaging techniques
- Mitochondria-interrelated cytosolic Ca²⁺ levels
- Mitochondrial Ca²⁺ uptake
- Auto-amplification of intracellular ROS
- The intrinsic apoptotic pathway

Research Results

- 1 mM H₂O₂ induced a rapid increase in cellular O₂-levels (>27 vs >406 αmol in 20 min)
- Increased oxidative stress modulates the dynamics of Ca²⁺ release, allowing for an explosive efflux of cytosolic Ca²⁺ from internal stores (ER), and concomitant mitochondrial Ca²⁺ uptake.

• The mechanism involves endogenous ROS auto-amplification, regulation of pro-apoptotic and anti-apoptotic proteins, cytochrome c release, and increases in caspase activity

Innovation points

- We describe a pro-oxidative model in a single human lung carcinoma SPC-A-1 cell that was created by application of extracellular H₂O₂ stimuli
- ROS quantification and assessment of reaction networks have been build

 Mitochondria have pivotal roles in determining how exogenous oxidative stress affects cell fate