EXHIBIT FF
Cryopreservation of organs by vitrification: perspectives and recent advances.

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Abstract
The cryopreservation of organs became an active area of research in the 1950s as a result of the rediscovery of the cryoprotective properties of glycerol by Polge, Smith, and Parkes in 1949. Over the ensuing four decades of research in this area, the advantages of vitrification, or ice-free cryopreservation, have become apparent. To date, experimental attempts to apply vitrification methods to vascularized whole organs have been confined almost entirely to the rabbit kidney. Using techniques available as of 1997, it was possible to vitrify blood vessels and smaller systems with reasonable success, but not whole organs. Beginning in 1998, a series of novel advances involving the control of cryoprotectant toxicity, nucleation, crystal growth, and chilling injury began to provide the tools needed to achieve success. Based on these new findings, we were first able to show that an 8.4M solution (VMP) designed to prevent chilling injury at -22 degrees C was entirely non-toxic to rabbit kidneys when perfused at -3 degrees C and permitted perfusion-cooling to -22 degrees C with only mild additional damage. We next investigated the ability of the kidney to tolerate a 9.3M solution known as M22, which does not devitrify when warmed from below -150 degrees C at 1 degrees C/min. When M22 was added and removed at -22 degrees C, it was sometimes [corrected] fatal, but when it was perfused for 25min at -22 degrees C and washed out simultaneously with warming, postoperative renal function recovered fully. When kidneys loaded with M22 at -22 degrees C were further cooled to an average intrarenal temperature of about -45 degrees C (about halfway through the putative temperature zone of increasing vulnerability to chilling injury), all kidneys supported life after transplantation and returned creatinine values to baseline, though after a higher transient creatinine peak. However, medullary, papillary, and pelvic biopsies taken from kidneys perfused with M22 for 25min at -22 degrees C were found to devitrify when vitrified and rewarmed at 20 degrees C/min in a differential scanning calorimeter. It remains to be determined whether this devitrification is seriously damaging and whether it can be suppressed by improving cryoprotectant distribution to more weakly perfused regions of the kidney or by rewarming at higher rates. In conclusion, although the goal of organ vitrification remains elusive, the prospects for success have never been more promising.

PMID: 15094092 [PubMed - indexed for MEDLINE]

Historical Article
Research Support, Non-U.S. Gov't

MeSH Terms
Animals
Cryopreservation/history
Cryopreservation/methods*
Cryopreservation/trends
Cryoprotective Agents*
History, 20th Century
Kidney*
Kidney Transplantation
Organ Preservation/methods*
Organ Preservation/trends
Perfusion
Rabbits
Temperature
Time Factors
Tissue Survival*

Substances
Cryoprotective Agents

LinkOut - more resources

Full Text Sources
Elsevier Science

Other Literature Sources
Labome Researcher Resource - ExactAntigen/Labome