Researchers develop mixture of compounds to help preserve organs before transplantation

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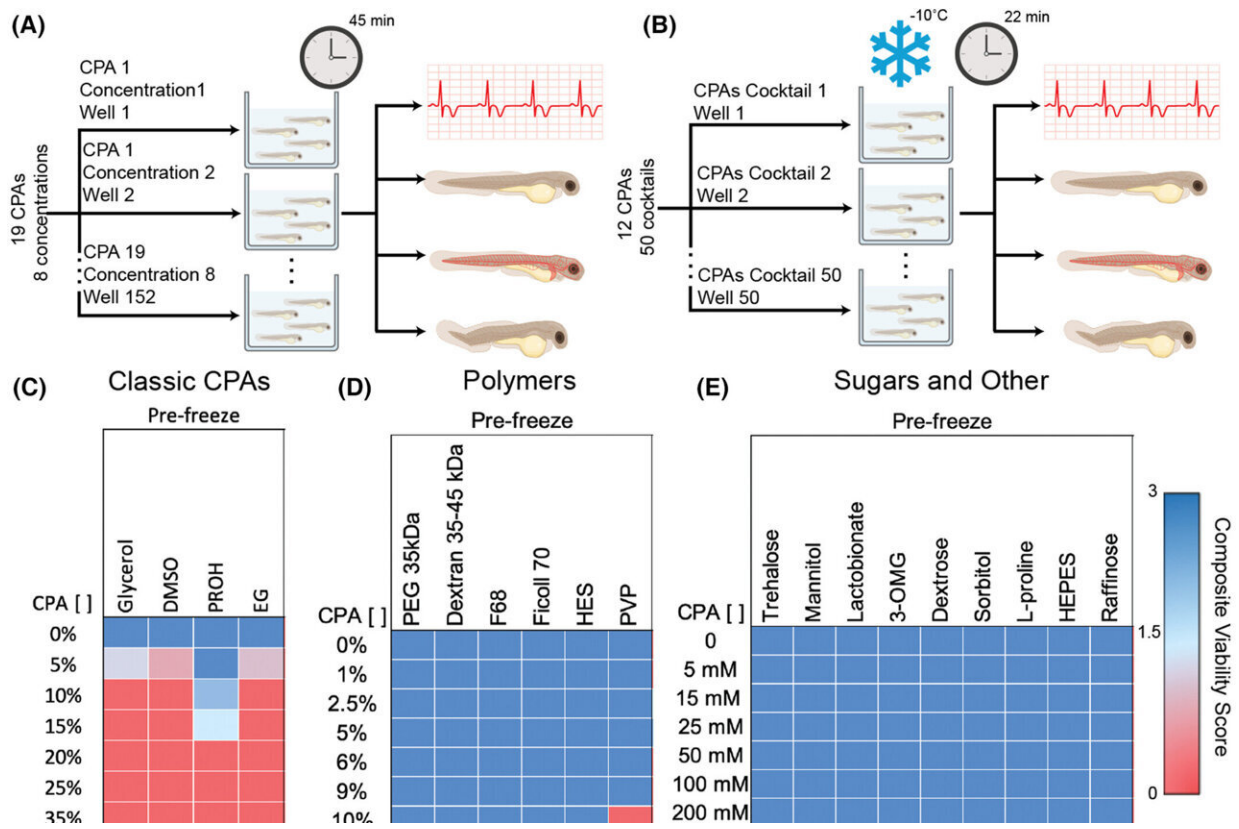

Individual CPA toxicity assay (A) and identification of best performing external CPAs cocktail capable of retaining larvae viability after 22 min of storage at −10°C when immersed in CPAs (B). Larvae viability was determined by quantifying heart rate, dehydration, blood circulation, and fish morphology and reported as the *External Composite Viability Score* (CVS_{Ext}). (C–E) Four classic CPAs, six polymers, seven sugars, and two other components (total of 19) were

tested to determine their individual toxicity prefreeze at eight different concentrations by incubating larvae for 45 min (n = 4 animals per CPAs concentration). (F) Twelve CPAs, from the previously tested nineteen, were arranged in a L50 Taguchi experimental design and tested at different concentrations (7) yielding 50 CPAs cocktails (n = 4 animals per CPAs cocktail). Prefreeze toxicity was determined after 30 min of incubation, with CPAs cocktails 33^{+} and 38^{+} resulting in the best larvae outcomes as determined by above threshold (>1.5) post-thaw CVS_{Ext} (1.75 and 1.625 respectively). Storage with above-threshold CPAs cocktails resulted in post-thaw retention of larva morphology (G) compared to untreated or unfrozen larvae (H), whereas storage without CPAs (I) or below the-threshold CPAs (J) resulted in significant loss of morphology and overall embryo integrity. Scale bar 1000 um. . Credit: *The FASEB Journal* (2023). DOI: 10.1096/fj.202300076R

Using zebrafish as a model, investigators have determined a suitable combination of chemical compounds in which to store hearts, and potentially other organs, when frozen for extended periods of time before transplantation.

The work, which is published in *The FASEB Journal*, involved a variety of methods, including assays at multiple developmental stages, techniques for loading and unloading agents, and the use of viability scores to quantify organ function.

These methods allowed scientists to perform the largest and most comprehensive screen of cryoprotectant agents to determine their toxicity and efficiency at preserving complex organ systems during storage at -10°C. As a result, adult zebrafish hearts' cardiac function was successfully preserved after 5 days of storage.

"Zebrafish are a powerful model system that have never been used in the context of solid organ preservation for transplantation, despite several

advantages," said corresponding author Shannon N. Tessier, Ph.D., of the Center for Engineering in Medicine and Surgery, Harvard Medical School. "We hope this research will encourage other in transplantation sciences to leverage this important model organism."

More information: Luciana Da Silveira Cavalcante et al, Zebrafish as a high throughput model for organ preservation and transplantation research, *The FASEB Journal* (2023). DOI: 10.1096/fj.202300076R

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