SUMMARY

[0007] Disclosed herein is a composition for cryo storage and preservation of eukaryotic cells in a therapeutic, pharmaceutical composition. The composition includes a freezing media, a freezing agent (e.g. dimethyl sulfoxide), and one or more organic polymers (e.g. hyaluronic acid). The present compositions also allow~~s~~ for freezing the therapeutic cells with and without an animal serum. The disclosed compositions and devices are able to maintain the cells' viability and sterility through freezing, storage at between -130 °C and -196 °C for extended periods of time, thawing, and administration of the cells to a patient.

[0008] Also disclosed are containers useful in freezing and thawing eukaryotic cells. In many embodiments, the containers are suitable for administration of the cells after thawing, and require little or no manipulation of the cell mixture prior to administration. In many embodiments, the container may define at least a part of a medical device, such as a syringe, wherein the container may maintain the sterility of the cell mixture during freezing and thawing and may be used to administer the mixture to a patient in need thereof. The container may comprise a lumen, and a first and second open end that may be configured to accept a cap, tip, plug, plunger, or other suitable structure for containing the mixture within the lumen. The container is made of a biocompatible material that maintains its integrity through the freezing and thawing process.

[0009] Disclosed herein are devices, compositions, and methods for use in maintaining the viability of therapeutic mammalian cells at low temperatures, the disclosed devices are also useful in reducing manipulation of cells prior to administration to a patient in need thereof. The disclosed compositions, devices, and methods maintain the cells' viability to help reduce loss of therapeutic effect.

[0010] Additional objects and advantages of the invention will be set forth, in part, in the description which follows and, in part, will be obvious from the description, or may be learned by practice of the invention. The objects and advantages of the invention will be realized and attained by means of the elements and combinations, particularly pointed out in the appended claims.

BRIEF DESCRIPTION OF THE DRAWINGS

[0011] FIG<u>S</u>. 1<u>A and 1B</u> show~~s~~ one embodiment of a device for freezing, storing, and applying the disclosed cell compositions. ~~The upper diagram~~<u>FIG. 1A</u> shows the various parts of the device, unassembled. ~~The lower portion of the figure~~ <u>FIG. 1B</u> shows the device in cross-sectional view.

[0012] FIG. 2. is a picture of an embodiment of the disclosed device assembled and configured to reduce contamination of the disclosed composition stored within the barrel lumen during freezing, storage, transportation, and thawing.

Table 1. Sample vial summary. Note that the vial diameters were measured by Lighthouse using calipers.

		Sample Format 1	Sample Format 2	Sample Format 3
Product Information	Formulation Fill Lot	Phosphate Buffer 500 µL N/A	Phosphate Buffer 500 µL N/A	Phosphate Buffer 500 µL N/A
Container Information	Manufacturer Type Material Color Outer Diameter Inner Diameter Nominal Volume Flange Closure	A Syringe Plastic Clear 9.48 mm 6.15 mm 1mL SOF Plunger	A Syringe Plastic Clear 9.48 mm 6.15 mm 1 mL SOF Plunger + 081 Stopper	A Syringe Plastic Clear 9.48 mm 6.15 mm 1 mL STF1 Plunger
Packaging Information	Nominal pressure Headspace gas	760 Torr Air	760 Torr Air	760 Torr Air
		Sample Format 4	Sample Format 5	Sample Format 6
Product Information	Formulation Fill Lot	Phosphate Buffer 500 µL N/A	Phosphate Buffer 500 µL N/A	Phosphate Buffer 500 µL N/A
Container Information	Manufacturer Type Material Color Outer Diameter Inner Diameter Nominal Volume Flange Closure	B Syringe Glass Clear 10.85 mm 8.45 mm 2.25 mL Plunger	C Syringe Plastic Clear 11.10 mm 6.20 mm 1 mL Plunger	D Syringe Plastic Clear 9.35 mm 6.30 mm 1 mL Plunger
Packaging Information	Nominal pressure Headspace gas	760 Torr Air	760 Torr Air	760 Torr Air
		Sample Format 7	Sample Format 8	Sample Format 9
Product Information	Formulation Fill Lot	Phosphate Buffer 500 µL N/A	Not Given Not Given N/A	Phosphate Buffer 500 µL N/A
Container Information	Type Material Color Outer Diameter Inner Diameter Nominal Volume Flange Closure	D Syringe Plastic Clear 9.35 mm 6.30 mm 1 mL Plunger + 420 Stopper	E Syringe Plastic Clear 10.60 mm 6.75 mm 1 mL Two Plungers	D Syringe Plastic Clear 9.35 mm 6.30 mm 1 mL Plunger + Barrel Seal
Packaging Information	Nominal pressure Headspace gas	760 Torr Air	760 Torr Air	760 Torr Air

Method and Materials

Sample Preparation and Handling

Table 1. Sample vial summary. Note that the vial diameters were measured by Lighthouse using calipers.

		Sample Format 1	Sample Format 2	Sample Format 3
Product Information	Formulation	Phosphate Buffer	Phosphate Buffer	Phosphate Buffer
	Fill	500 µL	500 µL	500 µL
	Lot	N/A	N/A	N/A
Container Information	Manufacturer	A	A	A
	Type	Syringe	Syringe	Syringe
	Material	Plastic	Plastic	Plastic
	Color	Clear	Clear	Clear
	Outer Diameter	9.48 mm	9.48 mm	9.48 mm
	Inner Diameter	6.15 mm	6.15 mm	6.15 mm
	Nominal Volume	1 mL	1 mL	1 mL
	Flange Closure	SOF Plunger	SOF Plunger + 081 Stopper	FTF1 Plunger
Packaging Information	Nominal pressure	760 Torr	760 Torr	760 Torr
	Headspace gas	Air	Air	Air

		Sample Format 4	Sample Format 5	Sample Format 6
Product Information	Formulation	Phosphate Buffer	Phosphate Buffer	Phosphate Buffer
	Fill	500 µL	500 µL	500 µL
	Lot	N/A	N/A	N/A
Container Information	Manufacturer	B	C	D
	Type	Syringe	Syringe	Syringe
	Material	Glass	Plastic	Plastic
	Color	Clear	Clear	Clear
	Outer Diameter	10.85 mm	11.10 mm	9.35 mm
	Inner Diameter	8.45 mm	6.20 mm	6.30 mm
	Nominal Volume	3.25 mL	1 mL	1 mL
	Flange Closure	Plunger	Plunger	Plunger
Packaging Information	Nominal pressure	760 Torr	760 Torr	760 Torr
	Headspace gas	Air	Air	Air

		Sample Format 7	Sample Format 8	Sample Format 9
Product Information	Formulation	Phosphate Buffer	Not Given	Phosphate Buffer
	Fill	500 µL	Not Given	500 µL
	Lot	N/A	N/A	N/A
Container Information	Manufacturer	D	E	D
	Type	Syringe	Syringe	Syringe
	Material	Plastic	Plastic	Plastic
	Color	Clear	Clear	Clear
	Outer Diameter	9.35 mm	10.60 mm	9.35 mm
	Inner Diameter	6.30 mm	6.75 mm	6.30 mm
	Nominal Volume	1 mL	1 mL	1 mL
	Flange Closure	Plunger + 420 Stopper	Two Plungers	Plunger + Barrel Seal
Packaging Information	Nominal pressure	760 Torr	760 Torr	760 Torr
	Headspace gas	Air	Air	Air

Method and Materials

Sample Preparation and Handling