also be used for other types of cell and gene therapy applications, such as, for example, genetically modified CD34+ cell therapies.

[0010] In some example implementations, a bead is composed of a perfluorocarbon droplet with a lipid coating. The bead is manufactured by preparing a lipid compound, combining a perfluorocarbon with the lipid compound and agitating the combination. In some examples, agitation is performed using centrifugation of the combination to obtain the beads. The beads may be used in a cell selection process by functionalizing the beads to have an affinity or linkage that can bind the beads to desired cells in a fluid that also entrains other cells or cellular material. The bead-cell complex is exposed to an acoustic field to manipulate the complex, such as by retaining the complex in a certain region.

[0011] The particles may be constructed to include a liquid core; and a lipid shell encapsulating the liquid core. The liquid in the liquid core may be composed of a perfluorocarbon. The perfluorocarbon may be perfluoropentane, perfluorohexane, perfluorooctane, perfluorooctyl bromide, perfluorodichlorooctane, or perfluorodecalin.

[0012] The lipid shell can be formed from dipalmitoylphosphatidylcholine (DPPC), 1,2-palmitoyl-phosphatidic acid (DPPA), a lipid-polyethylene glycol conjugate, or a complex of a lipid with albumin. The lipid shell can be functionalized with, for example, streptavidin, biotin, avidin, desthiobotin, an aptamer, an oligonucleotide and/or an antibody, collectively referred to herein as a linker, either in part or in whole. The lipid shell may completely or partially encapsulate the liquid core.

[0012a] In one aspect, the present disclosure refers to a particle for use in cell selection, comprising: a perfluorocarbon core; and a lipid shell that covers at least a portion of the core; wherein the lipid shell is functionalized with a linker.

[0013] A process known as acoustic droplet vaporization (ADV) can be used to generate a phase shift of the liquid core of such particles from liquid to gas using an acoustic wave. The vapor pressure of the liquid is a function of temperature, and is not necessarily based upon the liquid chemistry. Any liquid that has a normal boiling point near or below the body temperature can be used for these processes. Perfluorocarbons may be utilized in these processes because of their low toxicity and high contrast factor.

[0014] A spacer may be placed in between the particle and the linker. The spacer can be implemented as a polyethylene glycol (PEG) molecule. The PEG molecule may permit less charge interference from the particle when

[0017] The droplet/particle/bead may be incubated with one or more different types of ligands or linkers, such as NeutrAvidin/StreptAvidin/CaptAvidin depending on the application. The final droplet/particle/bead is used for further applications, such as cell selection or sorting in an acoustic device. The final droplet/bead/particle solution may have BSA/HSA or some stabilizer/surfactant in the aqueous part of the solution.

[0018] The droplet/particle/bead may be used for positive or negative selection of cells. In some examples, The droplet/particle/bead functionalized with desthiobiotin in the encapsulation is used for positive selection of cells. The droplet/particle/bead could be eluted from a complex by the addition of biotin buffer. The functionalization of the droplet/particle/bead can be formed as a reversible link for binding with a cell. For example, a biotin-Neutravidin bond can be separated to detach the droplet/particle/bead from the cell.

[0019] According to an example implementation, a method for manufacturing particles is provided that includes preparing a lipid compound, combining a perfluorocarbon with the liquid compound, and agitating the combination. In one aspect, the present disclosure refers to a method for manufacturing particles, comprising: preparing a lipid compound; combining a perfluorocarbon with the liquid compound; and agitating the combination. The agitation may be achieved by a combination of one or more of centrifugation, sonication, homogenization or mechanical agitation. The agitation may be implemented to achieve a predetermined particle size distribution. The particle size distribution may be in a range of from about 400 nm to about 300 microns. The particle may be manufactured by combining different lipids in a sequence based on a characteristic of each lipid, such as by preparing a solution with a lipid solvent, heating the solution and adding the different lipids to the solution in order of solubility.

[0020] The lipid compound may include one or more of DPPA, DPPC, DSPC, PEG40 Stearate, DSPE-mPEG(2000), DSPE-PEG(2000)-Biotin, DSPE-PEG-5000-Biotin, DSPE-PEG(2000)-Desthiobiotin, PBS buffer, glycerol, propyleneglycol, or DSPE-PEG(2000)-Maleimide. The perfluorocarbon may be one or more of perfluoropentane, perfluorohexane, perfluorooctane, perfluorooctyl bromide, perfluorodichlorooctane, or perfluorodecalin. The particle may be functionalized with a linker, such as a reversible linker, including one or more of Avidin, Neutravidin, Streptavidin, Captavidin, biotin, desthiobiotin, an antibody, an aptamer or an oligomer. The

particle may include a stabilizer or surfactant, which may be in the liquid core portion.

[0020a] In one aspect, the present disclosure refers to a particle manufactured according to the disclosed method.

[0021] The particle may be used in a method for separating target particles from a fluid, where the method includes receiving functionalized particles in the fluid in a chamber, receiving target particles in the chamber, permitting the target particles to bind with the functionalized particles, and applying an acoustic wave to the chamber to influence the functionalized particles to be collected or blocked by the acoustic wave. In one aspect, the present disclosure refers to a method for separating target particles from a fluid, comprising: receiving functionalized particles disclosed herein in the fluid in a chamber; receiving target particles in the chamber; permitting the target particles to bind with the functionalized particles; applying an acoustic wave to the chamber to influence the functionalized particles to be collected or blocked by the acoustic wave.

[0022] The developed particles yield very high purity and recovery of cells. The acoustic affinity particle in the presence of acoustic field performed well at all the scales in a reasonable amount of time, without compromising the output and health of cell.

[0023] In this work an acoustic affinity particle was developed for the purpose of isolating cells. As the cell separation is based on acoustic force, so a biocompatible liquid with high compressibility such as perfluorohexane (PFH) was selected as core of the particle/droplet. Phospholipids were used as an emulsifier. For cell targeting, one of the phospholipids is biotinylated and biotin-neutravidin interaction is used for targeting. In applications where elution of cell is desired from the perfluorohexane droplet, the regular biotin molecule in the encapsulation is replaced with desthiobotin. The droplet manufacturing process was designed to achieve a size distribution which was responsive to the acoustic wave and at the same time should have sufficient surface area for binding with the cells. The binding and separation of cells using PFH droplets were investigated for both negative and positive selection applications. In the test cases the PFH droplets in the presence of acoustic wave yielded high purity and recovery of the target cells. Desthiobiotin may be conjugated to the droplets. In positive selection of cells, the droplets are modified to elute from the cell-antibody-droplet complex and the elution technique resulted in high elution efficiency without any detrimental effect on the cells.

[0024] An acoustic affinity particle is developed for the purpose of isolating cells. An acoustically responsive liquid such as perfluorohexane (PFH) is used as core and Phospholipids as an emulsifier. The droplet manufacturing process was designed to achieve a size distribution suitable for binding and good acoustic response. Biotin-neutravidin interaction was used for targeting. For