the planar surface as well as magnetic reach and hold. The magnetic array 5 can be fixed in space preferably at a 45° angle with the magnets 7 facing downwards. Alternatively, it can be affixed to the magnetic array 5 placing the magnetic array 5 in direct contact with the processing chamber 2 such that both the magnetic array and the processing chamber can be rotated or translated as a unit. Clearly when the magnetic array 5 is brought into contact with the processing chamber 2 a strong magnetic gradient is imposed on the contents of the processing chamber.

Detailed protocols and methodology for using the system 1 to isolate CD3+ T cells from peripheral blood mononuclear cells (PBMC) as well as the advantages of the rotational and translation properties of the processing chamber 2 were disclosed in '3032. Briefly, the processing chamber 2, in a near vertical position, is filled with a volume PBMC and a second volume anti-CD3 FF and mixed by rotational and/or translational oscillation of the processing chamber 2 during which CD3 T cells will become magnetically labeled. Next, the processing chamber 2 is translated into contact with the magnetic array 5 which causes magnetically labeled cells onto the upper inside surface of the processing chamber 2 where they are held sufficiently strong such that fluid passed over them within the processing chamber 2 does not dislodge them. It was disclosed in '3032 that buffer fluids as well as menisci gently passed over target cells so held are capable by this moderate agitation in forcing bystander cells entrained during the magnetic separation step back into suspension, leading to very high levels of purity. After 2 or 3 cycles of such washes (or 'meniscus scrubs'), the processing chamber 2 can be brought to its vertical orientation, the magnetic array 5 can be removed and product cells can be suspended in some desired volume of buffer employing the rotational and lateral translational properties of the system 1.

Summary ~~of the Invention~~

In accordance with the present ~~invention~~disclosure Applicant has recognized, that because of the need to apply a maximum magnetic gradient to the contents of a processing chamber, the collecting wall of processing chambers needs to be very thin because gradients generated by planar magnetic arrays fall sharply as a function of distance from those planar surfaces. The thinness makes such fragile chambers not only costly because they are difficult to fabricate and sterilize, but the thin walls need a support system to keep the processing chamber from distorting during process steps that require the processing chamber to be rotated or rocked side to side as for

example to perform a mixing operation or a 'meniscus scrub' process (referring to the process of passing buffer menisci over magnetically held target cells to achieve high purity).

In accordance with the present ~~invention~~disclosure, Applicant has also recognized an imaginative solution to those chamber issues by creating a narrow rectangular-like rigid walled chamber from a flexible bag, e.g., an appropriately sized blood bag. This may be accomplished by confining such a bag between substantially parallel walls and placing the bag under moderate pressure, which forces the walls of the flexible bag into intimate contact with the confining walls and provides a rigid chamber with a wrinkle free collection surface. The need for that flat-wrinkle free surface cannot be over emphasized as magnetic gradients of the type used here fall off sharply as a function of distance from the planar magnets. Wrinkles in such collection surfaces would cause significant target cell losses because their height above a planar magnet array are at diminished magnetic gradients. It should be noted that in addition to employing synchronous pumps to keep collection processing chambers under pressure to create rigid chambers, a simple ballast type auxiliary chamber of appropriate volume filled with pressurized air and fitted with a pressure limit valve can be employed. Large (2L) blood bags fitted with an appropriate limit valves have been employed successfully.

As further disclosed below, Applicant has inventively devised coupling a magnetic assembly with the narrow rectangular-like rigid walled processing chamber in the form of a bag, such as a blood bag, placed between substantially parallel walls and with the bag optionally under moderate pressure. The coupling of the magnetic assembly with the processing chamber in the form of the bag may be permanent with the gradient of magnetic assembly and bag perfectly aligned.

In one aspect, the present disclosure provides a system for magnetic separation of a target bioentity from a fluid suspension of target bioentities and bystander bioentities in a processing chamber, comprising: a platform configured to receive the processing chamber at an upper surface of the platform, the chamber having an opening through which the processing chamber can be filled with a cell suspension having magnetized or magnetizable target bioentities, wherein the processing chamber is a fluid chamber having a collection surface; and a magnetic element mounted to the platform and movable relative to the platform such that in a first selected position of the platform the magnetic element is magnetically coupled to the processing chamber

to apply a magnetic field to the collection surface to attract the target bioentities to the collection surface.

In another aspect, the present disclosure provides a system for magnetic separation of a target bioentity from a fluid suspension of target bioentities and bystander bioentities in a processing chamber in the form of a bag, the chamber having an opening through which the chamber can be filled with a cell suspension having magnetized or magnetizable target bioentities, wherein the processing chamber is a fluid chamber having a collection surface, the system comprising: a platform having a cavity extending therethrough from an upper surface to an opposing lower surface; a plurality of longitudinal non-magnetic bars disposed parallel to one another in spaced apart relation in the cavity with a plurality of openings disposed between respective pairs of the longitudinal non-magnetic bars; and a plurality of magnets disposed in the plurality of openings in the cavity proximate the upper surface and movable relative to the platform, such that in a first selected position of the platform the plurality of magnets is magnetically coupled to the processing chamber to apply a magnetic field to the collection surface to attract the target bioentities to the collection surface.

In another of its ~~aspect~~examples the present ~~invention~~disclosure may provide a device where the i) narrow rectangular-like rigid walled processing chamber in the form of a bag, such as a blood bag, placed between substantially parallel walls and ii) the magnetic assembly can be coupled and uncoupled at will and with the precise alignment required for reproducible processing. Such a configuration presents significant challenges for the following reasons: (1) the processing chamber is a large thin-walled, narrow rectilinear-like chamber that is operated under pressure that must retain its shape throughout cycles of coupling and uncoupling and (2) magnetic gradients produced by magnetic array fall off rapidly from its planar surface making its proximity to all regions of the collection surface of processing chamber a critical issue. In one of

its ~~aspect~~examples, disclosed herein is a system that accomplishes the task of coupling and uncoupling these key components with the precision that is required for reproducible processing. The configurations of the disclosed exemplary systems may facilitate automation by employing commonly available actuators. Additionally, since this separation system can employ gravity in cell separation processes via its pivoting capability, gravity may also be employed or assist in the coupling and uncoupling of magnetic array and processing chamber.

Reversible coupling of magnetic assembly and the processing chamber may be accomplished by creating a novel and independent housing for the processing chamber that has a strong cover, preferably clear so that the processing chamber can be observed during processing, and a floor or bottom platform that is uniquely structured to allow intimate contact of the processing chamber and magnetic assembly, i.e. the processing chamber and the magnetic array. That bottom floor can be achieved by starting with a rigid rectangular plate, preferably aluminum, that is somewhat larger than the dimensions of the backing plate of the magnet array and cutting a substantial central rectangular area from the plate, such that the magnets of the magnetic array can in their entirety be inserted into that space to a degree that the tops of individual magnets are at the same level as the top surface of the plate or floor. To keep the bottom pressurized surface of the processing chamber in place, a support structure is required. That can be accomplished by (1) placing in the cutout space and in the direction that corresponds to the direction of individual magnets of the magnetic array, horizontal and parallel placed thin members that are affixed to two of the opposite surfaces created by the cut out - thus creating a grill like structure, (2) employing support members that can fit between individual magnets of the magnetic array with sufficient tolerance that than can easily move in and out of that space, (3) so spacing support members such that they can fit either between adjacent magnets or every other magnet when the slotted or grill like floor is placed over the magnetic array and (4) by placing a thin sheet, e.g., 1 mm rigid Plexiglas® brand acrylic sheet, over that grid-like support structure to create a smooth perfectly flat bottom confining wall for the processing chamber. By appropriate selection of the thickness of rigid bottom plate or floor and the height of block magnets employed for constructing the magnetic array, it is possible to bring the planar surface of those arrays within 0.5 to 1.0 mm of the bottom surface of the processing chamber which effectively allows maximum magnetic gradient to be imparted on the contents of that chamber.

From the foregoing, it would be clear in view of the teaching of the present disclosure that many advantages described in '3032, particularly regarding system automation and the elimination of operator tasks are created with the capability of decoupling these two primary components -the processing chamber and magnetic array. This approach also has another very significant advantage because it eliminates the need for a separate processing station for magnetically labeling target cells prior to their being introduced as is required for the coupled units. Decoupling the processing chamber and magnetic array also simplifies harvesting products by just draining them from the processing chamber.

In one of its ~~aspect~~example~~s~~ the present ~~invention~~disclosure may provide a system for magnetic separation of a target bioentity from a fluid suspension of target bioentities and bystander bioentities in a processing chamber. The processing chamber may be provided in the form of a blood bag. The system may include a platform configured to receive the processing chamber at an upper surface of the platform, the chamber having an opening through which the processing chamber can be filled with a cell suspension having magnetized or magnetizable target bioentities, wherein the processing chamber is a fluid chamber having a collection surface. In addition, the system may include a magnetic element mounted to the platform and movable relative to the platform such that in a first selected position of the platform the magnetic element is magnetically coupled to the processing chamber to apply a magnetic field to the collection surface to attract the target bioentities to the collection surface. A chamber control assembly may also be provided connected with the processing chamber and the magnetic element; the chamber control assembly may be operable to pivot the separation chamber and the magnetic element about an axis to move the magnetic element from the first selected position to a second selected position in response to rotation of the platform with the second selected position further away from the platform than the first selected position. The magnetic element may be movable in a direction perpendicular to the upper surface.

Further, the platform may include one or more posts on which the magnetic element is movably mounted to permit the magnetic element to move from the first selected position to a second selected position on the one or more posts, the second selected position maybe further away from the platform than the first selected position. The magnetic element may be configured to move on the one or more posts from the first selected position to the second selected position in response to rotation of the platform. The magnetic element may be

configured to move from the first selected position to a second selected position further away from the platform than the first selected position in response to rotation of the platform. The magnetic element may include an array of magnets, and the platform may include a cavity extending therethrough with the magnetic element dimensioned to fit within the cavity.

Still further, the system may include a plurality of longitudinal non-magnetic bars disposed parallel to one another in spaced apart relation in the cavity with a plurality of openings disposed between respective pairs of the longitudinal non-magnetic bars. The magnetic element may include an array of longitudinally extending magnets dimensioned to fit within respective ones of the plurality of openings when the magnetic element is in the first selected position. The platform may also include a non-magnetic sheet disposed over and in contact with the plurality of longitudinal non-magnetic bars to provide a flat surface for engagement with the processing chamber. A cover may be disposed over the upper surface to define a space between the cover and upper surface for receiving and retaining the processing chamber. In addition, a cam may be provided in contact with the upper surface and the cover, the cam rotatable to vary a distance between the upper surface and the cover, and the cover may be movable along a direction perpendicular to the upper surface to vary the distance therebetween.

In yet another of its ~~aspect~~examples, the present ~~invention~~disclosure may provide a system for magnetic separation of a target bioentity from a fluid suspension of target bioentities and bystander bioentities in a processing chamber in the form of a bag. The chamber may have an opening through which the chamber can be filled with a cell suspension having magnetized or magnetizable target bioentities, wherein the processing chamber is a fluid chamber having a collection surface. The system may include: a platform having a cavity extending therethrough from an upper surface to an opposing lower surface; a plurality of longitudinal non-magnetic bars disposed parallel to one another in spaced apart relation in the cavity with a plurality of openings disposed between respective pairs of the longitudinal non-magnetic bars; and a plurality of magnets disposed in the plurality of openings in the cavity proximate the upper surface, such that the plurality of magnets may be magnetically coupled to the processing chamber to apply a magnetic field to the collection surface to attract the target bioentities to the collection surface. The system may also include a non-magnetic sheet disposed on the upper surface and in contact with the plurality of longitudinal non-magnetic bars to provide a flat surface for receiving and supporting the processing chamber.

CLAIMS

What is claimed is:

1. A system for magnetic separation of a target bioentity from a fluid suspension of target bioentities and bystander bioentities in a processing chamber, comprising:

a platform configured to receive the processing chamber at an upper surface of the platform, the chamber having an opening through which the processing chamber can be filled with a cell suspension having magnetized or magnetizable target bioentities, wherein the processing chamber is a fluid chamber having a collection surface; and

a magnetic element mounted to the platform and movable relative to the platform such that in a first selected position of the platform the magnetic element is magnetically coupled to the processing chamber to apply a magnetic field to the collection surface to attract the target bioentities to the collection surface.

2. The system of claim 1, comprising a chamber control assembly connected with the processing chamber and the magnetic element operable to pivot the separation chamber and the magnetic element about an axis to move the magnetic element from the first selected position to a second selected position in response to rotation of the platform, the second selected position further away from the platform than the first selected position.

3. The system of any one the preceding claims, wherein the magnetic element is movable in a direction perpendicular to the upper surface.

4. The system of any one the preceding claims, wherein the platform includes one or more posts on which the magnetic element is movably mounted to permit the magnetic element to move from the first selected position to a second selected position on the one or more posts, the second selected position further away from the platform than the first selected position.

5. The system of claim 4, wherein magnetic element is configured to move on the one or more posts from the first selected position to the second selected position in response to rotation of the platform.

6. The system of any one the preceding claims, wherein magnetic element is configured to move from the first selected position to a second selected position further away from the platform than the first selected position in response to rotation of the platform.

7. The system of any one of the preceding claims, wherein the magnetic element comprises an array of magnets.

8. The system of any one of the preceding claims, wherein the platform includes a cavity extending therethrough.

9. The system of claim 8, wherein magnetic element is dimensioned to fit within the cavity.

10. The system of any one of claims 8-9, comprising a plurality of longitudinal non-magnetic bars disposed parallel to one another in spaced apart relation in the cavity with a plurality of openings disposed between respective pairs of the longitudinal non-magnetic bars.

11. The system of claim 10, wherein magnetic element includes an array of longitudinally extending magnets dimensioned to fit within respective ones of the plurality of openings when the magnetic element is in the first selected position.

12. The system of any one of claims 10-11, wherein platform includes a non-magnetic sheet disposed over and in contact with the plurality of longitudinal non-magnetic bars to provide a flat surface for engagement with the processing chamber.

13. The system of any one the preceding claims, comprising a cover disposed over the upper surface to define a space between the cover and upper surface for receiving and retaining the processing chamber.

14. The system of claim 13, comprising a cam in contact with the upper surface and the cover, the cam rotatable to vary a distance between the upper surface and the cover.

15. The system of any one of claims 13-14, wherein the cover is movable along a direction perpendicular to the upper surface to vary the distance therebetween.

16. The system of any one the preceding claims, wherein the processing chamber is a blood bag.

17. A system for magnetic separation of a target bioentity from a fluid suspension of target bioentities and bystander bioentities in a processing chamber in the form of a bag, the chamber having an opening through which the chamber can be filled with a cell suspension having magnetized or magnetizable target bioentities, wherein the processing chamber is a fluid chamber having a collection surface, the system comprising:

a platform having a cavity extending therethrough from an upper surface to an opposing lower surface;

a plurality of longitudinal non-magnetic bars disposed parallel to one another in spaced apart relation in the cavity with a plurality of openings disposed between respective pairs of the longitudinal non-magnetic bars; and

a plurality of magnets disposed in the plurality of openings in the cavity proximate the upper surface and movable relative to the platform, such that in a first selected position of the platform the plurality of magnets ~~may be~~is magnetically coupled to the processing chamber to apply a magnetic field to the collection surface to attract the target bioentities to the collection surface.

18. The system of claim 17, comprising a non-magnetic sheet disposed on the upper surface and in contact with the plurality of longitudinal non-magnetic bars to provide a flat surface for receiving and supporting the processing chamber.