- washing said magnetized cell fraction using a washing solution to reduce non-specific binding;
- separating said magnetized cell fractionation of target cells from said sample;

wherein said sample solution is subjected to an adjustable external magnetic field gradient throughout said adding, incubating, washing and separating steps, and

wherein said sample solution is rotated at least during said adding, incubating and washing steps.

In another aspect, there is provided a device for labelling magnetic or magnetizable particles onto biological material that comprises

- at least one rotatable mount for sample containers having an essentially cylindrical geometry and a longitudinal cylinder axis which allows concentric rotation at various speeds using a mount-coupled driving motor,
- a magnetic device that provides adjustable magnetic field strengths as well as magnetic field gradients at the location of the sample container, said magnetic device consisting of a permanent magnet that generates a magnetic field having a magnetic field strength of equal distribution along the magnet's longitudinal axis and a magnetic field gradient in a direction perpendicular to the magnet's longitudinal axis, and
- a controller to control driving motor and the magnetic device.

An "external magnetic field gradient" in the sense of the present invention is an artificially created magnetic field gradient, i.e. a field gradient in addition to the natural field gradient of the earth's magnetic field, created by one or more magnets arranged outside external to the sample.

The method of the invention is conducted in the perpetually presence of a magnetic field gradient that has direct influence on a sample solution containing magnetic or magnetizable particles and is adjustable in strength and adapted to each of said steps

Claims

1. A method for the isolation of non-magnetic cells from a heterogeneous sample solution containing biological material including desired and undesired cells, comprising the steps of:
   - adding magnetic or magnetizable particles to the sample solution, wherein said particles have sizes in a range from 100 nm to 4 µm and exhibit surface components which support specific association with target cells, wherein said target cells comprise are either said desired or said undesired cells;
   - incubating said sample solution with said magnetic particles to obtain a magnetized cell fraction;
   - washing said magnetized cell fraction using a washing solution to reduce non-specific binding;
   - separating said magnetized cell fractionation of target cells from said sample;

   wherein said sample solution is subjected to an adjustable external magnetic field gradient throughout said adding, incubating, washing and separating steps, and wherein said sample solution is rotated at least during said adding, incubating and washing steps.

2. The method of claim 1, further comprising the steps of:
   - establishing an external magnetic field gradient before said adding step;
   - decreasing said external magnetic field gradient after said adding step and before said incubating step;
   - increasing said external magnetic field gradient before said separating step.

3. The method of one of claims 1 or 2, wherein said sample solution is provided in a sample container which is rotated concentrically at different speeds during said adding, incubating and washing steps.

4. The method of one of claims 1 to 3, wherein the incubation step consists of several incubation cycles, wherein each incubation cycle comprises;
   - a magnetic labelling step at a slow rotational speed of the incubation container that is slower than a fast rotational speed during addition of the particles for the purpose of generating a magnetic particle bound cell fraction; and

- a mixing step to establish an equal distributions in the heterogeneous sample suspension as present after said magnetic labelling step.

5. The method of claim 4, wherein said magnetic field gradient is further decreased between said magnetic labelling step and said mixing step and, if an incubation cycle is repeated, increased again before the subsequent labelling step.

6. The method of one of claims 1 to 5, wherein the washing step comprises one or more washing cycles, wherein each washing cycle comprises the following steps:
   - removal of the supernatant from the magnetically separated cell fraction;
   - resuspension of the magnetically separated cell fraction in iso-osmolaric washing solution that is low or void of protein and in the presence of a weak magnetic field gradient that is lower than magnetic field gradient applied during the incubation step, wherein the container is rotated at a high speed that is higher than the rotation speed applied during the magnetic labelling step;
   - magnetic separation of the magnetically labelled cell fraction within the cell suspension as a consequence of a high magnetic field gradient that is higher than the magnetic field gradient applied during the incubation step and at a medium rotation speed that is lower than the fast rotation speed during the preceding resuspension step.

7. The method of one of claims 1 to 6, wherein in the magnetic separation step the target cells are fixed magnetically and the remaining suspension is removed from the fixed target cells.

8. The method of claim 7, wherein the target cells include the desired cells.

9. The method of claim 7, wherein the removed suspension includes the desired cells.

10. The method of one of claims 1 to 9, wherein said magnetic or magnetizable particles comprise superparamagnetic materials.

11. The method of one of claims 1 to 10, wherein the sample is incubated in a buffered solution prior to addition of magnetic or magnetizable particles that contains macromolecules for saturation of non-specific binding sites.

12. Device for labelling magnetic or magnetizable particles onto biological material that comprises
    - at least one rotatable mount for sample containers having an essentially cylindrical geometry and a longitudinal cylinder axis which allows concentric rotation at various speeds using a mount-coupled driving motor,
    - a magnetic device that provides adjustable magnetic field strengths as well as magnetic field gradients at the location of the sample container, said magnetic device consisting of a permanent magnet that generates a magnetic field having a magnetic field strength of equal distribution along the magnet's longitudinal axis and a magnetic field gradient in a direction perpendicular to the magnet's longitudinal axis, and
    - a controller to control driving motor and the magnetic device.

13. Device according to claim 12, wherein an inclination of the longitudinal axis of the magnetic device with reference to the cylindrical axis or shape of the mounted sample container is adjustable.

14. Device according to one of claims 12 or 13, further comprising means for isolating desired cells from a sample of various biological materials, wherein the means for isolating include a mounted syringe that is functional and operated by programmable logic controllers and can interact with the sample container and the magnet device.

15. Device according to claim 14, wherein said mounted syringe is tiltably mounted.

16. Device according to one of claims 12 to 15, wherein said sample container is designed for handling fluid volumes in range of 1 µl to 100 ml.