Claims

1. An apparatus for continuously harvesting a biological substance produced by a cultured cell, wherein the apparatus comprises:
   (a) filter 1 which is at least one filter(s) having pore size(s) which do(es) not allow the cell to pass through the filter, but allow the biological substance to pass through the filter, and
   (b) filter 2 which is at least one filter(s) having pore size(s) which do(es) not allow both the cell and the biological substance to pass through the filter, but keep fluid-flow-through of the filter,
   wherein the filter 1 and the filter 2 are fluidly connected to an apparatus for culturing the cell in a parallel manner.

2. The apparatus of claim 1, wherein the filter 1 and the filter 2 are fluidly connected to the apparatus for culturing the cell
   (a) directly and separately,
   (b) via a branched pipe, or
   (c) a combination of (a) and (b).

3. The apparatus of claim 1 or 2, wherein the filter 1 has a pore size of about 0.08 μm to 0.5 μm~~.~~,

~~4. The apparatus of claim 1 or 2, wherein the filter 1 has a pore size of~~preferably about 0.1 μm to 0.4 μm~~.~~,

~~5. The apparatus of claim 1 or 2, wherein the filter 1 has a pore size of~~more preferably about 0.2 μm.

~~6.~~4. The apparatus of claim 1 or 2, wherein the filter 2 has a

molecular weight cut-off (MWCO) of 50 kD or less.

~~7.~~5. The apparatus of claim 1 or 2 further comprising a device for regulating filtering rate of the filter 1 and/or a device for regulating filtering rate of the filter 2.

~~8.~~6. The apparatus of claim 1 or 2, wherein either or both of the filter 1 and the filter 2 is/are alternating tangential flow (ATF) filter(s) or tangential flow filtration (TFF) filter(s).

~~9.~~7. The apparatus of claim ~~8~~6, wherein either or both of the filter 1 and the filter 2 is/are hollow fiber filter(s).

~~10.~~8. The apparatus of claim 1 or 2, wherein

- the number of the filter 1 is 1, 2, 3 or more, and/or
- the number of the filter 2 is 1, 2, 3 or more.

~~11.~~9. A system for producing a biological substance, wherein the system comprises:

(a) an apparatus for culturing a cell with a basal medium and a feed medium in a perfusion manner; and

(b) the apparatus of any one of claims 1 to ~~10~~8.

~~12.~~10. The system of claim ~~11~~9 further comprising an apparatus for continuously capturing the biological substance from the materials harvested by the apparatus of any one of claims 1 to ~~10~~8.

~~13.~~11. The system of claim ~~11~~9 or ~~12~~10 further comprising a microsparger.

~~14.~~12. A method for continuously harvesting a biological substance produced by a cultured cell, which is carried out by the apparatus of any one of claims 1 to ~~10~~8.

~~15.~~13. A method for producing a biological substance, which is carried out by the system of any one of claims ~~11~~9 to ~~13~~11.

~~16.~~14. The method of claim ~~14~~12 or ~~15~~13, wherein the cells comprise mammalian cells.

~~17.~~15. The method of claim ~~16~~14, wherein the mammalian cells comprise CHO (Chinese Hamster Ovary) cells, hybridomas, BHK (Baby Hamster Kidney) cells, or myeloma cells.

~~18.~~16. The method of claim ~~14~~12 or ~~15~~13, wherein the biological substance is chosen from receptors, enzymes, fusion proteins, blood proteins (such as blood proteins from the blood coagulation cascade), multifunctional proteins (such as erythropoietin), viral or bacterial proteins (such as viral or bacterial proteins used in vaccines), and immunoglobulins (such as antibodies (such as IgG or IgM) or multi-specific antibodies (such as bi-specific antibodies)).

~~19. The method of claim 18, wherein the blood proteins are from the blood coagulation cascade.~~

~~20. The method of claim 18, wherein the multifunctional proteins are erythropoietin.~~

~~21. The method of claim 18, wherein the viral or bacterial proteins are used in vaccines.~~

~~22. The method of claim 18, wherein the immunoglobulins are antibodies or multi-specific antibodies.~~

~~23. The method of claim 22, wherein the antibodies are IgG or IgM.~~

~~24. The method of claim 22, wherein the multi-specific antibodies are bi-specific antibodies.~~