production of microparticles by the contacted conditionally-immortalised cell increases or decreases compared to a control.

A further aspect of the invention provides a kit when used in a method for producing a microparticle, comprising: (a) a medium; (b) a conditionally-immortalised cell as defined herein; (c) optionally the one or more transforming growth factor-beta (TGF-β), interferon-gamma (IFN-γ) and/or tumour necrosis factor-alpha (TNF-α) as defined herein; (d) optionally the microparticle as defined herein suitable for use as a control; (e) optionally a detection agent suitable for specific detection of the produced microparticles; and (f) instructions for producing the microparticle as disclosed herein using the kit.

Further aspects and embodiments of the invention are defined below, and in the claims.
The invention also relates to the finding that neural stem cells contain microparticles that are therapeutically useful. The methods discussed herein with regard to the production of microparticles from neural stem cells may be applied to methods of producing microparticles from the other cell types described for the first aspect of the invention.

One aspect of the invention provides a neural stem cell microparticle. The microparticle may be an exosome, microvesicle, membrane particle, membrane vesicle, exosome-like vesicle, ectosome-like vesicle, ectosome or exovesicle. Typically, the microparticle is an exosome. The microparticle may be derived from a conditionally-immortalised neural stem cell that has been cultured in an environment that allows stem cell differentiation. The microparticle may be isolated from partially-differentiated neural stem cells. In one embodiment, an environment that allows stem cell differentiation is a multi-compartment bioreactor, typically where the cells are cultured for more than seven days. The microparticle may be derived from a neural stem cell line. In some embodiments, the neural stem cell line may be the "CTX0E03" cell line, the "STR0C05" cell line, the "HPC0A07" cell line or the neural stem cell line disclosed in Miljan et al Stem Cells Dev. 2009. In some embodiments, the microparticle is derived from a stem cell line that does not require serum to be maintained in culture. The microparticle may have a size of between 30 nm and 1000 nm, or between 30 and 200 nm, or between 30 and 100 nm, as determined by electron microscopy; and/or a density in sucrose of 1.1-1.2 g/ml. The microparticle may comprise RNA. The RNA may be mRNA, miRNA, and/or any other small RNA. The microparticle may comprise one, two, three or four of hsa-miR-1246, hsa-miR-4492, hsa-miR-4488 and hsa-miR-4532. The microparticle may comprise one or more lipids, typically selected from ceramide, cholesterol, sphingomyelin, phosphatidylserine, phosphatidylinositol, phosphatidylcholine. The microparticle may comprise one or more tetraspanins, typically CD63, CD81, CD9, CD53, CD82 and/or CD37. The microparticle may comprise one or more of TSG101, Alix, CD109, thy-1 and CD133. The microparticle may comprise at least 10 of the

10. A method of producing a microparticle according to claim 9, wherein:

(i) the cell-conditioned medium comprises one or more of transforming growth factor-beta (TGF-β), interferon-gamma (IFN-γ) and tumour necrosis factor-alpha (TNF-α), which induce the release of microparticles by the stem cells into the medium;

(ii) the cells were cultured under hypoxic conditions;

(iii) the cells were co-cultured with a different cell type;

(iv) the cells were cultured in a multi-compartment bioreactor; and/or

(v) the cells were stem cells that were partially-differentiated.

11. A kit when used in the method of claim 9 comprising: (a) a medium; (b) a conditionally-immortalised cell as defined in claim 1; (c) optionally one or more of transforming growth factor-beta (TGF-β), interferon-gamma (IFN-γ) and tumour necrosis factor-alpha (TNF-α); (d) optionally a microparticle obtainable by the method of claim 9 suitable for use as a control; (e) optionally a detection agent suitable for specific detection of the produced microparticles; and (f) instructions for producing the microparticle using the kit.

12. A method of screening for an agent that alters the rate of production of a microparticle by a conditionally-immortalised cell, comprising contacting a conditionally immortalised cell as defined in claim 1 with a candidate agent and observing whether the rate production of microparticles by the contacted conditionally-immortalised cell increases or decreases compared to a control.