CLAIMS

1. A method for the production of microglia from stem cells, comprising the steps of:

   a) targeted insertion of a nucleotide sequence encoding a transcriptional regulator protein into a first genomic safe harbour site in the stem cells, preferably wherein the transcriptional regulator protein is a reverse tetracycline transactivator (rtTA);

   b1) targeted insertion of the coding sequence of the transcription factor PU.1 into a second genomic safe harbour site in the stem cells from step a),

   wherein the coding sequence of PU.1 is operably linked to an inducible promoter, which is regulated by the transcriptional regulator protein; and

   b2) insertion of the coding sequence of at least one further transcription factor in the stem cells from step b1);

   for the expression of PU.1 and of the at least one further transcription factor; and

   c) culturing the stem cells received from step b2) with exposure to at least one growth factor or small molecule that recapitulates signaling during at least one stage of embryonic development of microglia or adult microglia proliferation, differentiation or polarization.

2. The method according to claim 1, wherein the at least one growth factor or small molecule is selected from the group consisting of Activin A, BMP4, FGF, VEGF-A, LY294002, CHIR99021, SCF, IL-3, IL-6, CSF1, IL-34, CSF2, CD200, CX3CL1, TGFβ1, and IDE1.

3. The method according to claim 1 or 2, wherein the at least one growth factor is CSF1 or IL-34.

4. The method according to any one of the previous claims, wherein the at least one small molecule is CHIR99021, LY294002 or IDE1.

5. The method according to any one of the previous claims, wherein the first and the second genomic safe harbour sites are different.

6. The method of any one of the previous claims, further comprising insertion of the coding sequence of the transcription factor CEBPB and expression thereof.

7. The method of any one of the previous claims, further comprising insertion of the coding sequence of the transcription factor RUNX1 and expression thereof.

8. The method of any one of the previous claims, further comprising insertion of the coding sequence of the transcription factor IRF8 and expression thereof.

9. The method of any one of the previous claims, further comprising insertion of the coding sequence of the transcription factor SALL1 and expression thereof.

10. The method of any one of the previous claims, wherein the transcriptional regulator protein is the reverse tetracycline transactivator (rtTA) and the activity thereof is controlled by doxycycline or tetracycline.

11. The method of any one of the previous claims, wherein the inducible promoter includes a Tet Responsive Element (TRE).

12. The method of any one of the previous claims, wherein said first and said second genomic safe harbour sites are selected from the group consisting of the hROSA26 locus, the AAVS1 locus, the CLYBL gene, the CCR5 gene, the HPRT gene or genes with the site ID 325 on chromosome 8, site ID 227 on chromosome 1, site ID 229 on chromosome 2, site ID 255 on chromosome 5, site ID 259 on chromosome 14, site ID 263 on chromosome X, site ID 303 on chromosome 2, site ID 231 on chromosome 4, site ID 315 on chromosome 5, site ID 307 on chromosome 16, site ID 285 on chromosome 6, site ID 233 on chromosome 6, site ID 311 on chromosome 6, site ID 301 on chromosome 7, site ID 293 on chromosome 8, site ID 319 on chromosome 11, site ID 329 on chromosome 12 and site ID 313 on chromosome X.

13. The method of any one of the previous claims, wherein said stem cell is a pluripotent stem cell, an induced pluripotent stem cell (iPSC), a neural progenitor cell, hematopoietic stem cell or an embryonic stem cell (ESC).

14. The method of any one of the previous claims, wherein said stem cell is a human or a mouse stem cell.

15. A microglia obtained by any one of the methods according to claims 1 to 14, preferably wherein the microglia expresses at least one microglia surface protein selected from the group consisting of ITGAM (CD11B), ITGAX (CD11C), CD14, CD16, ENTPD1 (CD39), PTPRC (CD45), CD68, CSF1R (CD115), CD163, CX3CR1, TREM2, P2RY12, TMEM119, and HLA-DR.

16. Microglia according to claim 15 for use in therapy.

17. Use of microglia according to claim 15 or 16 for *in vitro* culturing with brain organoids.