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, preferably wherein the transcriptional regulator protein is a reverse tetracycline transactivator (rtTA); ~~and~~
   b) targeted insertion of the coding sequence of the transcription factor PU.1 ~~(SEQ ID NO: 1)~~ into a second genomic safe harbour site, wherein the coding sequence~~gene~~ of PU.1 is operably linked to an inducible promoter, which is regulated by the transcriptional regulator protein; insertion of the coding sequence of at least one further transcription factor; expression of PU.1 ~~(SEQ ID NO: 2)~~and of the at least one further transcription factor; and
   c) culturing the stem cells received from steps a) and b) 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 m~~M~~ethod according to claim 1, wherein the at least one growth factor or small molecule is selected from the group consisting of Activin A ~~(SEQ ID NO: 7)~~, BMP4 ~~(SEQ ID NO: 8)~~, FGF ~~(SEQ ID NO: 9)~~, VEGF-A ~~(SEQ ID NO: 10)~~, LY294002, CHIR99021, SCF ~~(SEQ ID NO: 11)~~, IL-3 ~~(SEQ ID NO: 12)~~, IL-6 ~~(SEQ ID NO: 13)~~, CSF1 ~~(SEQ ID NO: 14)~~, IL-34 ~~(SEQ ID NO: 15)~~, CSF2 ~~(SEQ ID NO: 16)~~, CD200 ~~(SEQ ID NO: 17)~~, CX3CL1 ~~(SEQ ID NO: 18)~~, TGFβ1~~(SEQ ID NO: 19)~~, and IDE1.

3. The m~~M~~ethod according to claim 1 or 2, wherein the at least one growth factor is CSF1 ~~(SEQ ID NO: 14)~~ or IL-34 ~~(SEQ ID NO: 15)~~.

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

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

6. The m~~M~~ethod of any one of the previous claims, further comprising insertion of the coding sequence ~~of the gene~~ of the transcription factor CEBPB ~~(SEQ ID NO: 3)~~ and expression thereof.

7. The mMethod of any one of the previous claims, further comprising insertion of the coding sequence ~~of the gene~~ of the transcription factor RUNX1 ~~(SEQ ID NO: 4)~~ and expression thereof.

8. The mMethod of any one of the previous claims, further comprising insertion of the coding sequence ~~of the gene~~ of the transcription factor IRF8 ~~(SEQ ID NO: 5)~~ and expression thereof.

9. The mMethod of any one of the previous claims, further comprising insertion of the coding sequence ~~of the gene~~ of the transcription factor SALL1 ~~(SEQ ID NO: 6)~~ and expression thereof.

10. The mMethod of any one of the previous claims, wherein the transcriptional regulator protein is the reverse tetracycline transactivator (rtTA) ~~(SEQ ID NO: 20)~~ and the activity thereof is controlled by doxycycline or tetracycline.

11. The mMethod of any one of the previous claims, wherein the inducible promoter includes a Tet Responsive Element (TRE) ~~(SEQ ID NO: 21)~~.

12. The mMethod 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 ~~(SEQ ID NO: 22)~~, the AAVS1 locus ~~(SEQ ID NO: 23)~~, the CLYBL gene ~~(SEQ ID NO: 24)~~, the CCR5 gene ~~(SEQ ID NO. 25)~~, the HPRT gene ~~(SEQ ID NO. 26)~~ or genes with the site ID 325 on chromosome 8 ~~(SEQ ID NO: 27)~~, site ID 227 on chromosome 1 ~~(SEQ ID NO: 28)~~, site ID 229 on chromosome 2 ~~(SEQ ID NO: 29)~~, site ID 255 on chromosome 5 ~~(SEQ ID NO: 30)~~, site ID 259 on chromosome 14 ~~(SEQ ID NO: 31)~~, site ID 263 on chromosome X ~~(SEQ ID NO: 32)~~, site ID 303 on chromosome 2 ~~(SEQ ID NO: 33)~~, site ID 231 on chromosome 4 ~~(SEQ ID NO: 34)~~, site ID 315 on chromosome 5 ~~(SEQ ID NO: 35)~~, site ID 307 on chromosome 16 ~~(SEQ ID NO: 36)~~, site ID 285 on chromosome 6 ~~(SEQ ID NO: 37)~~, site ID 233 on chromosome 6 ~~(SEQ ID NO: 38)~~, site ID 311 on chromosome 6~~134 (SEQ ID NO: 39)~~, site ID 301 on chromosome 7 ~~(SEQ ID NO: 40)~~, site ID 293 on chromosome 8 ~~(SEQ ID NO: 41)~~, site ID 319 on chromosome 11 ~~(SEQ ID NO: 42)~~, site ID 329 on chromosome 12 ~~(SEQ ID NO: 43)~~ and site ID 313 on chromosome X ~~(SEQ ID NO: 44)~~.

13. The mMethod 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 mMethod 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) (SEQ ID NO: 45), ITGAX (CD11C) (SEQ ID NO: 46), CD14 (SEQ ID NO: 47), CD16 (SEQ ID NO: 48), ENTPD1 (CD39) (SEQ ID NO: 49), PTPRC (CD45) (SEQ ID NO: 50), CD68 (SEQ ID NO: 51), CSF1R (CD115) (SEQ ID NO: 52), CD163 (SEQ ID NO: 53), CX3CR1 (SEQ ID NO: 54), TREM2 (SEQ ID NO: 55), P2RY12 (SEQ ID NO: 56), TMEM119 (SEQ ID NO: 57), and HLA-DR (SEQ ID NO: 58).

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

17. Use of microglia according to claim 15 or 16 for *in vitro* diagnostics of a disease.

18. Use of microglia according to claim 17, wherein the disease is selected from the group consisting of diseases of the central nervous system, preferably neurodegenerative diseases; more preferably Alzheimer's disease, Parkinson's disease, frontotemporal dementia or Amyotrophic Lateral Sclerosis; neuroinflammatory or autoimmune diseases, preferably Multiple Sclerosis, auto-antibody-mediated encephalitis or infectious diseases, neurovascular diseases; preferably stroke, vasculitis; traumatic brain injury, and cancer.

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