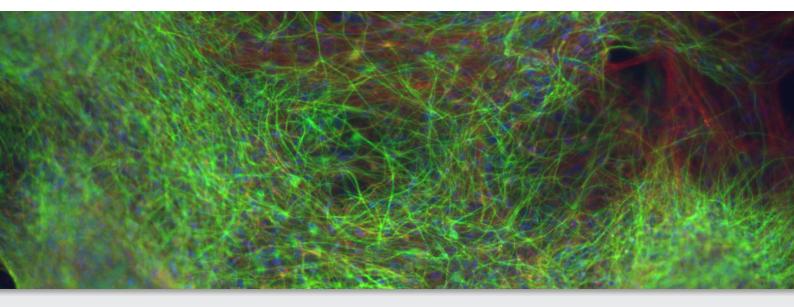


DOPAMINE DIFFERENTIATION

ON HUMAN RECOMBINANT BIOLAMININ111



LN111 SUPPORTS HIGH YIELD DOPAMINERGIC PROGENITOR DIFFERENTIATION FROM HUMAN PS CELLS

The cause of Parkinson's Disease is selective and focal degeneration of mesencephalic dopamine (DA) neurons in the basal ganglia in the brain. Applying knowledge from developmental biology the exact mechanism producing these cells can be recapitulated upon differentiation.

By using human recombinant Biolaminin 111 LN (LN111) as a substrate for the two-stage, 16-day differentiation, the process is defined and animal origin-free, adherent throughout, reliable and robust, and can be made GMP-compatible.

LN111 supports efficient differentiation of a homogenous population of human PS cell-derived DA progenitor cells compared to EB-based protocols. The yield of progenitors is >40x, thus using LN111 saves cell manufacturing costs and reduces time significantly.

Human ES cells expanded on human recombinant Biolaminin 521 LN (LN521) and differentiated on LN111, demonstrate efficient DA differentiation and maturation both in vitro and after grafting in vivo.

FEATURES AND SPECIFICATIONS:

- Defined and animal origin-free (primary level) substrates
- GMP-compatible differentiation protocol based on the use of LN111
- >40-fold DA progenitor yield increase
- Robust protocol replicated with >10 human PSC lines in different laboratories worldwide
- Using LN111 reduces experimental variation
- Biologically relevant
- Contaminating PSCs are effectively removed using LN111 for 16 days of differentiation
- LN111 differentiated progenitors have a homogeneous expression profile
- Significant reduction of costs due to differentiation efficiency and phenotype authenticity
- Scientifically proven
- For research use only



Direct link to more information online

SIGNIFICANT INCREASE OF DOPAMINERGIC LN111 ENHANCES SAFETY BY REMOVING PROGENITORS WHEN LN111 IS USED

Yield of VM progentitors d16 Starting from 1*10⁶ cells on day 0 43x 500 Starting from 1*10⁶ cells 400 Cell counts (10⁶) 300 200 100 0 GMP Research ΕB LN-111

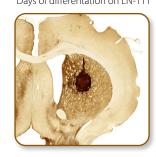
Human ES cells differentiated on LN111 with a GMP-adapted DA differentiation protocol shows a 43-fold increase in the yield of DA progenitors compared to research-grade EB-based protocol.

UNDIFFERENTIATED HUMAN PS CELLS 1.0 mRNA levels (rel. to undiff hESC) 0.8 ОСТ4 - NANOG 0.6 0.4

2 Days of differentation on LN-111

0.2

0.0



Culturing human ES cells in pluripotency medium on LN111, resulted in rapid detachment compared to cells on a pluripotency supportive matrix.

Removal of contaminating, residual PS cells is pivotal for safety after transplantation.

Transplanted LN111 DA progenitors become TH+ neurons at the site of transplantation in rats.

REPRODUCIBLE AND HOMOGENOUS RNA & MARKER EXPRESSION WITH LN111 BASED PROTOCOL



The differentiated DA progenitors express a very high overlap (purple) of the predictive markers FoxA2 (red) and Lmx1a (green). The expression profile of selected markers is more homogenous at day 16 of differentiation on LN111 and addition of FGF8 to the GMP-protocol (d9-d16) causes an efficient induction of markers predictive of TH-rich grafts. The LN111 based GMP-compatible protocol generates DA progenitors of homogenous character with the correct DA progenitor phenotype, bridging the translational gap.

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