In vivo- terminal node

Cecilia Lundberg

1. **Short description of the infrastructure.**

   The terminal room contains two set ups for perfusion of rodents and instruments for fresh dissection of brains. Furthermore, there are facilities to prepare solutions and weigh drugs as well as store narcotic-classed drugs. Taken together, this ensures the proper handling and use of chemicals and drugs in accordance with rules and regulations such as working with hazardous chemicals etc. Attached to the node is a part time animal technician who's tasks it is to oversee the day-to-day running of the node, introduce new users and to offer user support.

2. **Is this infrastructure receiving support also from other Strategic Research Areas (SRAs) or organizations at Lund University (e.g. Medical faculty, LBIC). If yes, please specify the type of support and its amount.**
   No

3. **Number and names of MultiPark senior researchers using the infrastructure in the period 2018-2020[1].**
   13
   Cecilia Lundberg, Tomas Björklund, Malin Parmar, AngelaC Nilsson, Jia-Yi L, Johan Jakobsson, Gesine Paul, , Christian Hansen, Andreas Heuer, Maria Björkqvist, Iben Lundgaard, Åsa Petersén, Maria Swanberg

4. **Number and names of senior researchers outside of Multipark and/or non-academic partners using the infrastructure 2018-2020.**
   7
   Marco Ledri Merab Kokaia Zaal Kokaia, Henrik Ahlenius, Johan Bengzon, Anders Tingström, My Andersson

5. **Does the infrastructure have a steering document accessible to the users? If yes, when was it last updated?[2]**

   Yes, updated 2018-10-15

6. **Is the infrastructure charging user fees? If yes, state the amount and what is covered by the user fees.**

   Yes there is a charge. For 2019 it was 5379,50 SEK per user.
   Included in the technical platform:

[1] If the infrastructure was first established in 2020, please include this information.

[2] Note that the Multipark leadership may ask to see this document with a very short notice.

Equipment:
3 Balances
1 stirring with heat
1 stirring with no heat*
2 perfusion pumps
giliotine
2 brain slicers for mouse/rat
CO2 chamber
pH meter
Vortex
Disposables:
Syringes
Needles
Gloves
Plastic vials for perfused brains
Weighing boats
Filters
Razor blades
Re-usables
Erlenmeyer flasks, different sizes
Measuring cylinders
Stirring magnets
Funnel with glass fliter
Chemicals:
Paraformaldehyde
NaCl
NaOH
Sucrose
Na2HPO4
NaH2PO4
Service, repair and maintenance of common equipment
Attached to the node is a part time animal technician who's tasks it is to oversee the day-to-day running of the node, introduce new users and to offer user support.

7. **List publications generated with the help of this infrastructure during the past 3 years (2018-2020). Do not include manuscripts in preparation and please give the full reference (i.e., complete author list, complete title, journal name with year, volume, pages)[3].**

Jönsson ME, Garza R, Sharma Y, et al. Activation of endogenous retroviruses during brain development causes an inflammatory response [published online ahead of print, 2021 Mar 1]. EMBO J. 2021;e106423. doi:10.15252/embj.2020106423

Brattås PL, Hersbach BA, Madsen S, Petri R, Jakobsson J, Pircs K. Impact of differential and time-dependent autophagy activation on therapeutic efficacy in a model of Huntington disease [published online ahead of print, 2020 May 6]. Autophagy. 2020;1-14. doi:10.1080/15548627.2020.1760014

[3] If the infrastructure was first established in 2020, please include this information here too.

Petri R, Brattås PL, Sharma Y, et al. LINE-2 transposable elements are a source of functional human microRNAs and target sites. PLoS Genet. 2019;15(3):e1008036. Published 2019 Mar 13. doi:10.1371/journal.pgen.1008036

Pircs K, Petri R, Madsen S, et al. Huntingtin Aggregation Impairs Autophagy, Leading to Argonaute-2 Accumulation and Global MicroRNA Dysregulation. Cell Rep. 2018;24(6):1397-1406. doi:10.1016/j.celrep.2018.07.017

Lockowandt M, Günther DM, Quintino L, Breger LS, Isaksson C, Lundberg C. Optimization of production and transgene expression of a retrogradely transported pseudotyped lentiviral vector. J Neurosci Methods. 2020 Apr 15;336:108542. doi: 10.1016/j.jneumeth.2019.108542. Epub 2020 Feb 1. PMID: 32017975.

Quintino L, Avallone M, Brännstrom E, Kavanagh P, Lockowandt M, Garcia Jareño P, Breger LS, Lundberg C. GDNF-mediated rescue of the nigrostriatal system depends on the degree of degeneration. Gene Ther. 2019 Feb;26(1-2):57-64. doi: 10.1038/s41434-018-0049-0. Epub 2018 Dec 7. PMID: 30531868; PMCID: PMC6514883.

Quintino L, Namislo A, Davidsson M, Breger LS, Kavanagh P, Avallone M, Elgstrand-Wettergren E, Isaksson C, Lundberg C. Destabilizing Domains Enable Long-Term and Inert Regulation of GDNF Expression in the Brain. Mol Ther Methods Clin Dev. 2018 Sep 4;11:29-39. doi: 10.1016/j.omtm.2018.08.008. PMID: 30324128; PMCID: PMC6187056.

Fieblinger T, Zanetti L, Sebastianutto I, Breger LS, Quintino L, Lockowandt M, Lundberg C, Cenci MA. Striatonigral neurons divide into two distinct morphological-physiological phenotypes after chronic L-DOPA treatment in parkinsonian rats. Sci Rep. 2018 Jul 3;8(1):10068. doi: 10.1038/s41598-018-28273-5. PMID: 29968767; PMCID: PMC6030109.

Davidsson M, Díaz-Fernández P, Torroba M, Schwich OD, Aldrin-Kirk P, Quintino L, Heuer A, Wang G, Lundberg C, Björklund T. Molecular barcoding of viral vectors enables mapping and optimization of mRNA trans-splicing. RNA. 2018 May;24(5):673-687. doi: 10.1261/rna.063925.117. Epub 2018 Jan 31. PMID: 29386333; PMCID: PMC5900565.

Di Maria V, Moindrot M, Ryde M, Bono A, Quintino L, Ledri M. Development and Validation of CRISPR Activator Systems for Overexpression of CB1 Receptors in Neurons. Front Mol Neurosci. 2020;13:168. Published 2020 Sep 8. doi:10.3389/fnmol.2020.00168

Canals I, Ginisty A, Quist E, Timmerman R, Fritze J, Miskinyte G, Monni E, Hansen MG, Hidalgo I, Bryder D, Bengzon J and Ahlenius H. Rapid and Efficient Induction of Functional Astrocytes from Human Pluripotent Stem Cells. Nature Methods, 2018 Sep;15(9):693-696

Fritze J, Ginisty A, McDonald R, Quist E, Stamå E, Monni E, Dhapola P, Lang S and Ahlenius H. Loss of Cxcr5 alters neuroblast proliferation and migration in the aged brain. Stem Cells. 2020 Sep;38(9):1175-1187

Davidsson, M., M. Negrini, S. Hauser, A. Svanbergsson, M. Lockowandt, G. Tomasello, F. P. Manfredsson and A. Heuer (2020). "A comparison of AAV-vector production methods for gene therapy and preclinical assessment." Sci Rep 10(1): 21532.

Fiorenzano A, Birtele M, Wahlestedt JN, Parmar M. Evaluation of TH-Cre knock-in cell lines for detection and specific targeting of stem cell-derived dopaminergic neurons Heliyon 2021

Shrigley S, Nilsson F, Mattsson B, Fiorenzano A, Mudannayake J, Bruzelius A, Ottosson DR, Björklund A, Hoban DB, Parmar M Grafts Derived from an α-Synuclein Triplication Patient Mediate Functional Recovery but Develop Disease-Associated Pathology in the 6-OHDA Model of Parkinson's Disease Journal of Parkinson's Disease, 2020

Hoban DB, Shrigley S, Mattsson B, Breger LS, Jarl U, Cardoso T, Nelander Wahlestedt J, Luk KC, Björklund A, Parmar M. Impact of α-synuclein pathology on transplanted hESC-derived dopaminergic neurons in a humanized α-synuclein rat model of PD. Proceedings of the National Academy of Sciences (PNAS) 2020

Tiklová K, *Nolbrant S, *Fiorenzano A, Björklund ÅK, Sharma Y, Heuer A, Gillberg L, Hoban DB, Cardoso T, Adler AF, Birtele M, Lundén-Miguel H, Volakakis N, Kirkeby A, *Perlmann T,*Parmar M. Single cell transcriptomics identifies stem cell-derived graft composition in a model of Parkinson's disease Nature Communications 2020

Palma-Tortosa S, Tornero D, Grønning Hansen M, Monni E, Hajy M, Kartsivadze S, Aktay S,Tsupykov O, Parmar M, Deisseroth K, Skibo G, Lindvall O, Kokaia Z. Activity in grafted human iPS cell–derived cortical neurons integrated in stroke-injured rat brain regulates motor behavior Proceedings of the National Academy of Sciences (PNAS) 2020

Davidsson M, Wang G, Aldrin-Kirk P, Cardoso T, Nolbrant S, Hartnor M, Mudannayake J, Parmar M, Björklund T. A systematic capsid evolution approach performed in vivo for the design of AAV vectors with tailored properties and tropism Proceedings of the NationalAcademy of Sciences (PNAS) 2019

Adler A*, Cardoso T*, Nolbrant S, Mattsson S, Hoban D, Jarl U, Nelander Wahlestedt J, Grealish S, Björklund A, Parmar M. hESC-derived dopaminergic transplants integrate into basal ganglia circuitry in a preclinical model of Parkinson´s disease. Cell Reports 2019

Cardoso T, Adler AF, Mattsson B, Hoban DB, Nolbrant S, Wahlestedt JN, Kirkeby A, Grealish S, Björklund A, Parmar M. Target-specific forebrain projections and appropriate synaptic inputs of hESC-derived dopamine neurons grafted to the midbrain of parkinsonian rats. J Comp Neurology, 2018

AAV Production Everywhere: A Simple, Fast, and Reliable Protocol for In-house AAV Vector Production Based on Chloroform Extraction.
Negrini M, Wang G, Heuer A, Björklund T, Davidsson M.
Curr Protoc Neurosci. 2020 Sep;93(1):e103. doi: 10.1002/cpns.103.
PMID: 32865885

Seeding of protein aggregation causes cognitive impairment in rat model of cortical synucleinopathy.

Espa E, Clemensson EKH, Luk KC, Heuer A, Björklund T, Cenci MA.
Mov Disord. 2019 Nov;34(11):1699-1710. doi: 10.1002/mds.27810. Epub 2019 Aug 26.
PMID: 31449702

Vector-mediated l-3,4-dihydroxyphenylalanine delivery reverses motor impairments in a primate model of Parkinson's disease.
Rosenblad C, Li Q, Pioli EY, Dovero S, Antunes AS, Agúndez L, Bardelli M, Linden RM, Henckaerts E, Björklund A, Bezard E, Björklund T.
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PMID: 31243443

A novel adeno-associated virus capsid with enhanced neurotropism corrects a lysosomal transmembrane enzyme deficiency.
Tordo J, O'Leary C, Antunes ASLM, Palomar N, Aldrin-Kirk P, Basche M, Bennett A, D'Souza Z, Gleitz H, Godwin A, Holley RJ, Parker H, Liao AY, Rouse P, Youshani AS, Dridi L, Martins C, Levade T, Stacey KB, Davis DM, Dyer A, Clément N, Björklund T, Ali RR, Agbandje-McKenna M, Rahim AA, Pshezhetsky A, Waddington SN, Linden RM, Bigger BW, Henckaerts E.
Brain. 2018 Jul 1;141(7):2014-2031. doi: 10.1093/brain/awy126.
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Molecular barcoding of viral vectors enables mapping and optimization of mRNA trans-splicing.
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Chemogenetic modulation of cholinergic interneurons reveals their regulating role on the direct and indirect output pathways from the striatum.
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Itzia Jimenez-Ferrer, Filip Bäckström, Alfredo Dueñas-Rey, Michael Jewett, Antonio Boza-Serrano, Kelvin C. Luk, Tomas Deierborg and Maria Swanberg
The MHC class II transactivator modulates seeded alpha-synuclein pathology and dopaminergic neurodegeneration in an in vivo rat model of Parkinson's disease
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Gsta4 Prevents Dopamine Neurodegeneration in a Rat Alpha-Synuclein Model of Parkinson's disease
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Striatonigral neurons divide into two distinct morphological-physiological phenotypes after chronic L-DOPA treatment in parkinsonian rats. 2018;8(1):10068.

Relevant review articles:

Cenci MA, Bjorklund A. Animal models for preclinical Parkinson's research: An update and critical appraisal. Prog Brain Res. 2020;252:27-59.

Espa E, Clemensson EKH, Luk KC, Heuer A, Bjorklund T, Cenci MA. Seeding of protein aggregation causes cognitive impairment in rat model of cortical synucleinopathy. Mov Disord. 2019;34(11):1699-710.

Sebastianutto I, Cenci MA. mGlu receptors in the treatment of Parkinson's disease and L-DOPA-induced dyskinesia. Curr Opin Pharmacol. 2018;38:81-9.

Cenci MA, Jorntell H, Petersson P. On the neuronal circuitry mediating L-DOPA-induced dyskinesia. J Neural Transm (Vienna). 2018;125(8):1157-69.

Cenci MA, Crossman AR. Animal models of l-dopa-induced dyskinesia in Parkinson's disease. Mov Disord. 2018;33(6):889-99.