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My most cited papers (original articles) based on data obtained in May 2024 from my author page at Google Scholar
https://scholar.google.com/citations?user=W8CXjsMAAAAJ&hl=en&oi=ao

My most cited original articles related to dopamine cell replacement in Parkinson´s disease

1. Li JY, Englund E, Holton JL, Soulet D, Hagell P, Lees AJ, Lashley T, Quinn NP, Rehncrona S, **Björklund A**, Widner H, Revesz T, Lindvall O, Brundin P. (2008) Lewy bodies in grafted neurons in subjects with Parkinson's disease suggest host-to-graft disease propagation. *Nature Medicine* 14(5):501-3. **2080 total citations.**

This paper, published jointly with a similar study from Jeffrey Kordower´s lab, provided the first compelling evidence that alpha-synuclein pathology can transfer between cells. The transfer of pathology from the host brain to the grafted dopamine neurons reported in this paper generated much attention in the PD field and has remained highly cited (>100 times/year).

2. Lindvall, O., Brundin, P., Widner, H., Rehncrona, S., Gustavii, B., Frackowiak, R., Leenders, K.L., Sawle, G., Rothwell, J.C., Marsden, C.D., **Björklund, A**. (1990) Grafts of fetal dopamine neurons survive and improve motor function in Parkinson's disease. *Science* 247:574-577. **1413 total citations.**

The first report of successful grafting of fetal dopamine neurons in a PD patient. A seminal study in the dopamine cell replacement field that helped to launch the Lund PD transplantation program.

3. Piccini P, Brooks DJ, **Björklund A**, Gunn RN, Grasby PM, Rimoldi O, Brundin P, Hagell P, Rehncrona S, Widner H, Lindvall O (1999) Dopamine release from nigral transplants visualized in vivo in a Parkinson's patient. *Nature Neurosci* 2:1137-1140. **900 total citations.**

This imaging study demonstrated for the first time the ability of the grafted dopamine neurons to restore dopamine release in the grafted striatum. It was performed on one of the most carefully studied patients in the Lund cohort, Patient 4. *This patient had a transplant only on one side, making it possible to use the contralateral non-grafted side as an internal control. His transplant remained viable until his death, 24 years after grafting, as reported in PNAS in 2016.*

4. **Björklund, A.**, Dunnett, S.B., Stenevi, U., Lewis, M.E., Iversen, S.D. (1980) Reinnervation of the denervated striatum by substantia nigra transplants: functional consequences as revealed by pharmacological and sensorimotor testing. *Brain Research* 199:303-333. **685 total citations.**

Our pioneering study on fetal dopamine neuron grafting in the rat PD model was published as a short communication in 1979 (Björklund A & Stenevi U, Brain Research 177:555-560, *1979). A year later we published this more comprehensive account of our initial findings, now in a collaboration with Susan Iversen and her PhD student Stephen Dunnett in Cambridge, UK. These two papers have remained as standard references in the field.*

5. Widner, H., Tetrud, J., Rehncrona, S., Snow, B., Brundin, P., Gustavii, B., **Björklund, A.**, Lindvall, O., Langston, J.W. (1992) Bilateral fetal mesencephalic grafting in two patients with parkinsonism

induced by 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP). *New Engl. J. Med*. 327: 1556-1563. **609 total citations.**

This paper resulted from a collaboration with Bill Langston who, a few years earlier, had identified a group of drug addicts in the San Fransisco area that developed severe parkinsonism resulting from the administration of MPTP. Due to their severe striatal DA depletion and stable clinical condition they turned out to be ideal subjects, providing compelling proof of the ability of fetal DA neuron grafts to restore striatal DA neurotransmission and recovery of mobility and motor function.

6. **A Björklund,** U Stenevi, RH Schmidt, SB Dunnett, FH Gage (1983) Intracerebral grafting of neuronal cell suspensions. I. Introduction and general methods of preparation. Acta physiologica scandinavica. Supplementum 522, pages 1-7. **553 total citations.**

In this paper, published as the introductory article in a supplement to Acta Physiologica Scandinavica in 1983, we give a detailed account of the cell suspension method that has since become the standard method for intracerebral neural grafting. In the subsequent seven papers in this supplement, we published the first comprehensive reports of the survival and function of nigral dopaminergic neurons grafted to the rat striatum, and septal cholinergic neurons grafted to the hippocampus.

My most cited original articles related to the anatomy and function of the dopamine and noradrenaline neuron systems in the brain.

1. Lindvall, O., **Björklund, A**. (1974) The organization of the ascending catecholamine neuron systems in the rat brain as revealed by the glyoxylic acid fluorescence method. *Acta Physiol. Scand*. *Supplement 412*. **1647 total citations.**

My most important anatomical paper that remains well cited still today, 50 years after its publication. It was the first to give a more complete picture of the projections and terminations of the dopamine and noradrenaline systems in the rat brain. All thanks to the high sensitivity of the glyoxylic acid histofluorescence method that we had developed during the past years (see paper 3, below).

2. **Björklund, A.,** Moore, R.Y., Nobin, A., Stenevi, U. (1973) The organization of tubero-hypophyseal and reticulo-infundibular catecholamine neuron systems in the rat brain. *Brain Research* 51:171-191. **714 total citations.**

The first more systematic attempt to map the origin, course and termination of the dopamine neurons residing in the paraventricular/arcuate nuclei. It continues to be quoted rather frequently, 47 years after its publication (4-8 times/year over the last 5 years).

3. Lindvall, O., **Björklund, A**. (1974) The glyoxylic acid fluorescence histochemical method: a detailed account of the methodology for the visualization of central catecholamine neurons. *Histochemistry* 39:97-127. **610 total citations.**

The most sensitive version of the histofluorescence techniques that remained in use throughout the 1980s when they were replaced by the more versatile immunofluorescence methods. It was well quoted during its time, until the end of the 1980s, but has since dwindled.

4. Lindvall, O., **Björklund, A.,** Moore, U., Stenevi, U. (1974) Mesencephalic dopamine neurons projecting to neocortex. *Brain Research.* 81:325-331. **576 total citations.**

*The first anatomical description of the meso-cortical dopamine system derived from the A10 cell group in the ventral tegmental area (VTA**),** made possible due to the improved sensitivity of the glyoxylic acid histofluorescence method (paper 3, above).*

5. **Björklund, A.,** Lindvall, O. (1975) Dopamine in dendrites of substantia nigra neurons: suggestions for a role in dendritic terminals. *Brain Research.* 83:531-537. **538 total citations.**

Possibly the very first study highlighting the role of dopamine in the dendrites of nigral dopaminergic neurons, revealed by the glyoxylic acid method (paper 3, above).

My most cited original articles related to PD disease modelling and L-DOPA-induced dyskinesia

1. Kirik D, Rosenblad C, Burger C, Lundberg C, Johansen TE, Muzyczka N, Mandel RJ, **Björklund A.** (2002) Parkinson-like neurodegeneration induced by targeted overexpression of alpha-synuclein in the nigrostriatal system. *J Neurosci.* 22(7):2780-91. **896 total citations.**

The AAV-alpha-synuclein model was developed simultaneously in our lab and in Ron Klein´s lab in Florida, with similar findings published within 2 weeks from each-other. The viral vector model has become a widely used standard tool in the PD field, and this pioneering study has been well cited over the years (30-40 times/year over the last years).

2. Kirik, D., Rosenblad, C., **Björklund A (**1998) Characterization of behavioral and neurodegenerative changes following partial lesions of the nigrostriatal dopamine system induced by intrastriatal 6-hydroxydopamine in the rat. *Exp Neurol.* 152: 259-277. **806 total citations.**

This was the first serious attempt to stadardize the intrastriatal, partial 6-OHDA lesion model in rats. It is now commonly used as an alternative to the standard MFB lesion model, and as a result this paper remains well cited.

3. Cenci, M.A., Lee, C.S., **Björklund, A**. (1998) L-dopa-induced dyskinesia in the rat is associated with striatal overexpression of prodynorphin- and glutamic acid decarboxylase mRNA. *Eur J Neurosci.* Vol. 10: 2694-2706. **721 total citations.**

The dykinesia model developed and validated in this paper has become a standard tool for studies on the mechanism of L-DOPA induced dyskinesia and has thus remained well cited over the years.

4. Carta M, Carlsson T, Kirik D, **Björklund A (**2007) Dopamine released from 5-HT terminals is the cause of L-DOPA-induced dyskinesias in parkinsonian rats. *Brain,* 130: 1819-1833**. 716 total citations.**

This study launched the idea that L-DOPA-derived dopamine, released in a dysregulated manner as a "false transmitter" from serotonin terminals, is a key mechanism for the development and maintenance of L-DOPA-induced dyskinesia. This idea has since then gained support from in vivo imaging and postmortem studies and remains relevant.

5. Kirik, D, Annett, LE, Burger, C, Muzyczka, N, Mandel, RJ, **Björklund A** (2003) Nigrostriatal a-synucleinopathy induced by viral vector-mediated overexpression of human a-synuclein: A new primate model of Parkinson's disease. *Proc Natl Acad Sci U S A.* 100:2884-2889. **488 total citations.**

The first study to explore the use of AAV vector mediated overexpression of alpha-synuclein in a primate (marmosets), showing the versatility of the AAV vector approach for PD disease modeling in non-human primates.

My most cited original articles related to neuroprotection and intracerebral delivery of neurotrophic factors

1. Fischer, W., Wictorin, K., **Björklund, A**., Williams, L.R., Varon, S., Gage, F.H. (1987) Amelioration of cholinergic neuron atrophy and spatial memory impairment in aged rats by nerve growth factor. *Nature* 329: 65-68. **1231 total citations.**

The first study to report on the neuroprotective effect of NGF on the firebrain cholinergic system in aged rats. It was performed in collaboration with Rusty Gage, started when he was a postoc in my lab and completed after his move to UCSD. The NGF was produced in Silvio Varon´s lab at UCSD.

2. Decressac M, Mattsson B, Weikop P, Lundblad M, Jakobsson J, **Björklund A** (2013) TFEB-mediated autophagy rescues midbrain dopamine neurons from α-synuclein toxicity. *Proc Natl Acad Sci, USA,* May 7;110(19):E1817-26. doi: 10.1073. **774 total citations.**

In this study we have explored the role of autophagy in the neurodegenerative process induced by overexpression of human wildtype alpha-synuclein in the rat AAV-synuclein model. The striking results seen here highlight transcription factor EB (TFEB) as a therapeutic target, and are also in support of strategies aimed at the development of disease modifying therapies for PD based on modulation of the autophagy/lysosomal pathway.

3. Kirik D., Rosenblad C., **Björklund A.,** Mandel R. J. (2000) Long-term rAAV-mediated gene transfer of GDNF in the rat Parkinson's model: intrastriatal but not intranigral transduction promotes functional regeneration in the lesioned nigrostriatal system. *J Neurosci.* 20, 4686-4700. **490 total citations.**

Our first study using AAV vector delivery of GDNF in the rat PD model. The study was performed during Ron Mandel´s stay in our lab as visiting scientist in 1999. The study used an AAV2-GDNF vector that Ron brought with him from his previous employer, the Somatix company. It was designed to explore the importance of the site of GDNF delivery – striatal vs. nigral – for the preservation of the entire nigro-striatal pathway and the preservation and recovery of motor function in the intrastriatal 6-OHDA lesion model of PD.

4. Sauer, H., Rosenblad, C., **Björklund, A**. (1996) Glial cell-line neurotrophic factor but not Transforming growth factor-ß3 prevents delayed degeneration of nigral dopaminergic neurons following striatal 6-hydroxydopamine-lesion. *Proc Natl Acad Sci,* USA, 92: 8935–8939. **431 total citations.**

We were among the first to investigate the neuroprotective effect of recombinant GDNF on lesioned nigral dopamine neurons. While the competing labs used MPTP lesioned mice and rats with surgical knife cuts of the NSP, our study was performed in the more progressive rat model using intrastriatal 6-OHDA lesions.