

58. The path from “Eureka!” to a living drug: translating a stem cell-derived product to the clinic

1 unit Mark Tomishima, November 21, 2025

1. *The past:* The history of cell therapy for Parkinson’s disease
 - a. Discovery of MPTP
 - b. Fetal cell trials in the 1980s
 - c. Challenges for using primary cell source
2. Pluripotent stem cell-based strategies for cell therapy
 - a. PSCs bypass a number of challenges
 - b. But PSCs create new challenges
 - i. Developmental biology of midbrain dopamine neurons
 1. Neural fate – dual SMAD inhibition
 2. Floorplate (ventral neural) – Shh signaling
 3. WNT signaling (anterior-posterior patterning)
3. *The present:* The NYSTEM grant and the development of MSK-DA01
 - a. Clinical reagents change biology in culture
 - b. Reoptimizing biology to make the right product
 - c. Manufacturing in a cleanroom (CTCEF in Zuckerman)
 - d. Bemdaneprocel in the clinic
 - e. The birth of BlueRock
4. *The future:* Cell therapy genome engineering
 - a. Cargo expression and philosophy
 - b. STEL (Sustained Transgene Expression Locus) expression rationale and screening
 - c. SLEEK: SeLection by Essential-gene Knock-in (selection without antibiotic use)
 - d. GAPZAP cell development (cells containing novel kill switch)

Discussion paper:

Human pallial MGE-type GABAergic interneuron cell therapy for chronic focal epilepsy

Bershteyn M, Bröer S, Parekh M, Maury Y, Havlicek S, Kriks S, Fuentealba L, Lee S, Zhou R, Subramanyam G, Sezan M, Sevilla ES, Blankenberger W, Spatazza J, Zhou L, Nethercott H, Traver D, Hampel P, Kim H, Watson M, Salter N, Nesterova A, Au W, Kriegstein A, Alvarez-Buylla A, Rubenstein J, Banik G, Bulfone A, Priest C, Nicholas CR.

Cell Stem Cell. 2023 Oct 5;30(10):1331-1350.e11. doi: 10.1016/j.stem.2023.08.013. PMID: 37802038.

Review paper:

History and current status of clinical studies using human pluripotent stem cells

Kobold S, Bultjer N, Stacey G, Mueller SC, Kurtz A, Mah N.

Stem Cell Reports 2023 Apr 6;18(8):1592–1598. doi: 10.1016/j.stemcr.2023.03.005