

Update: CC Center for Cellular Engineering

April 23, 2021

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Director, Center for Cellular Engineering

CENTER FOR CELLULAR ENGINEERING

Mission

- **Provide cellular therapy services for Clinical Center Investigators and their patients**

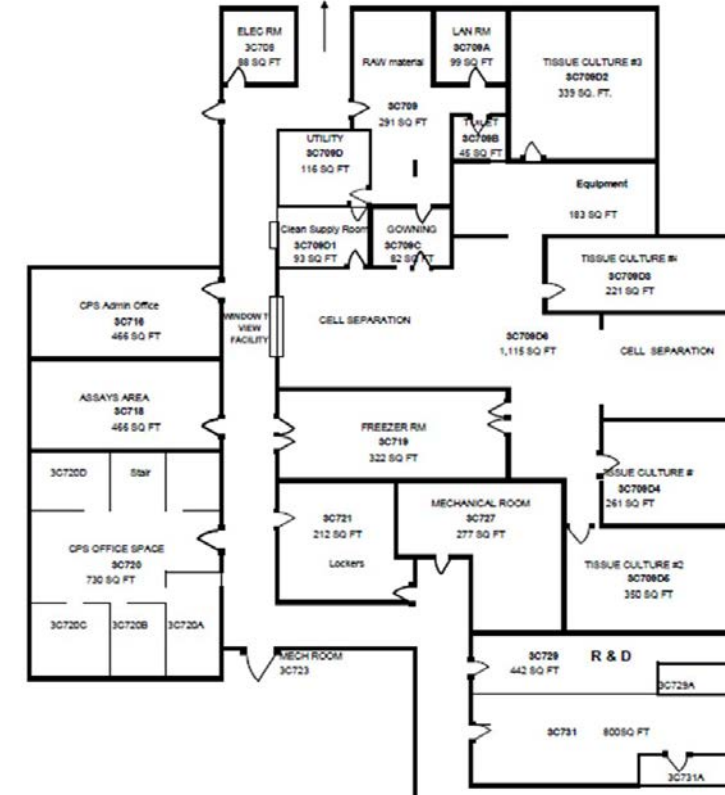
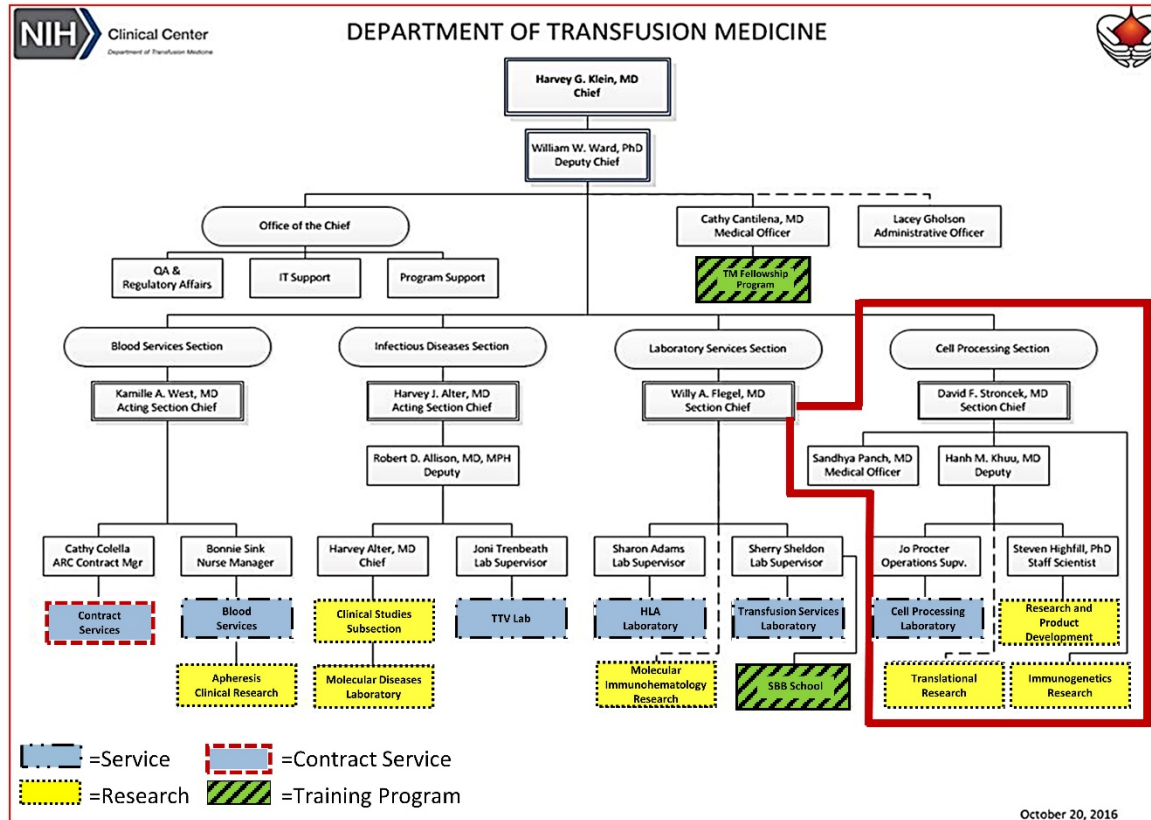
Major Activities

- ***Manufacture*** early phase cell and gene therapies
- ***Process*** hematopoietic stem cell grafts for transplantation
- ***Coordinate*** the collection and shipment of autologous cells to other facilities for manufacturing cell therapies and receiving, storing and issuing the final products
- ***Label*** cells for *in vivo* trafficking and survival studies

2017: Cell Processing Section, Department of Transfusion Medicine

One section in the DTM with 2 supervisors

One Processing Facility Built in 1997



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Overview

Business plan developed in 2017

Five CCE Sections

- Cell Therapy Manufacturing
- New Product Management
- Research & Practice Development – Organized in 2018
- Product Assurance & Characterization Testing – Organized in 2019
- Quality – Organized in 2019

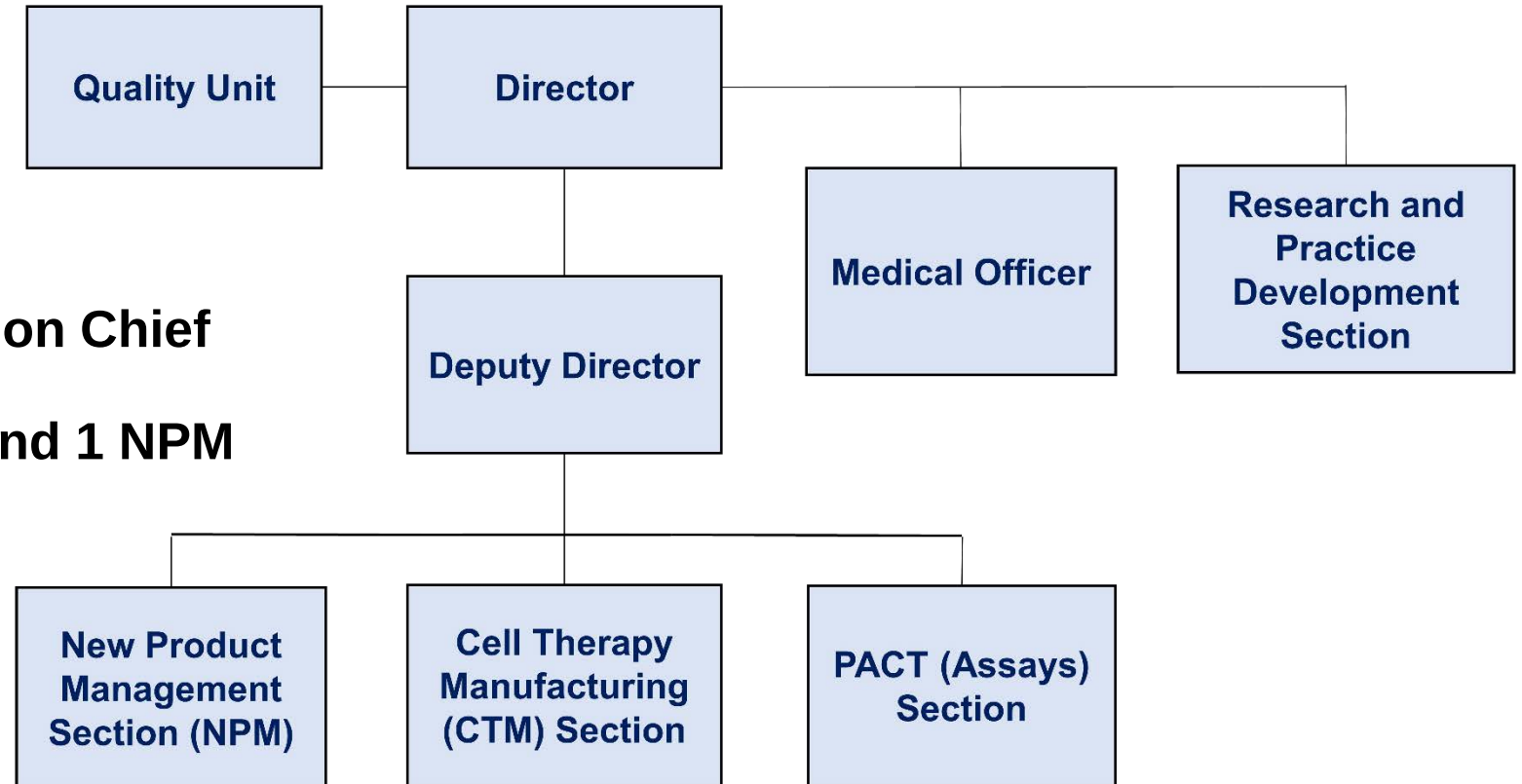
Staff Additions and Organizational Changes Since 2019

New Staff

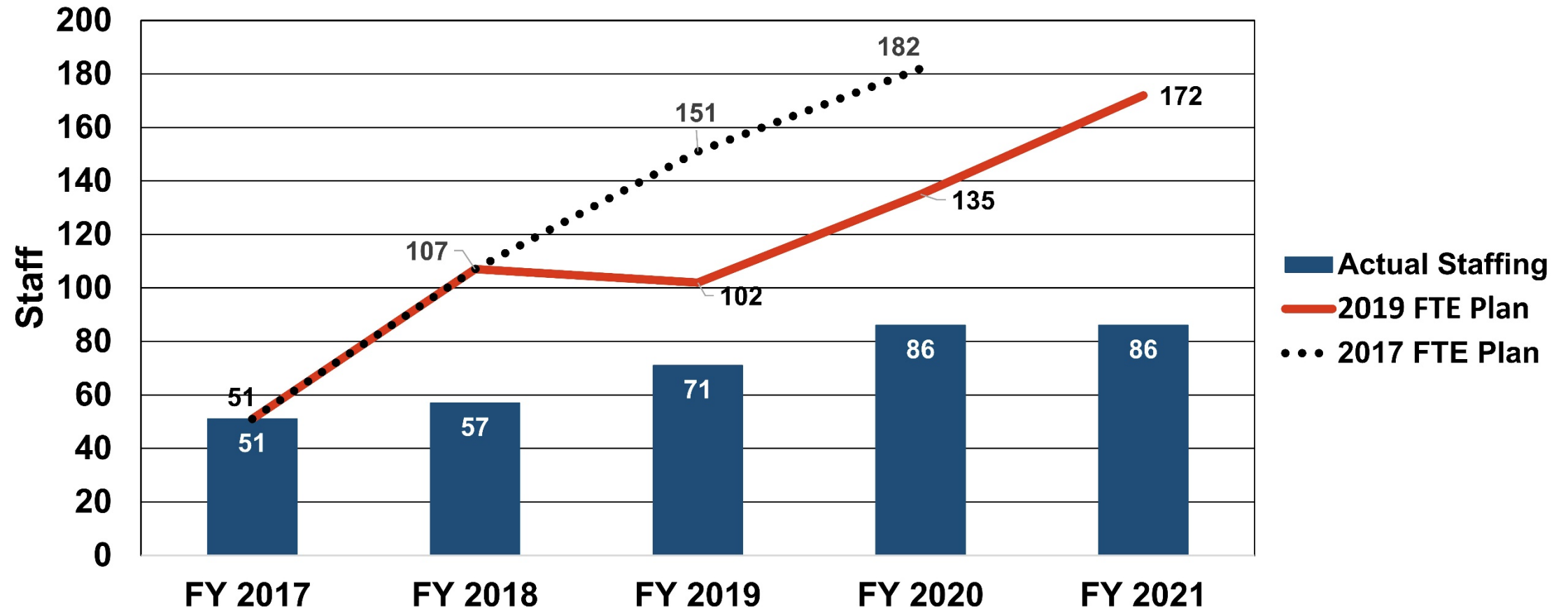
- Deputy Director
- Quality Unit Director
- PACT Section Chief
- Cell Therapy Manufacturing Section Chief
- Medical Officer
- 5 Supervisors: 3 Quality, 1 CTM and 1 NPM

Organization Changes

- Independent Quality Unit
- CCE Advisory Group



Staffing: Actual, 2017 Business Plan and 2019 Business Plan



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Lab and Office Space Added

Molecular QC Laboratory

Building 10, 2nd floor, Room 2C328

Approximately 400 sq ft

Testing for vector copy number, recombinant vector and vector insertion site

Opened in November 2018

Product Development Laboratory

Building 10, Rooms 5B10, 5B14 and 5B16

Approximately 2,500 sq ft

Culture room, general lab space and office space

Opened in July

Offices

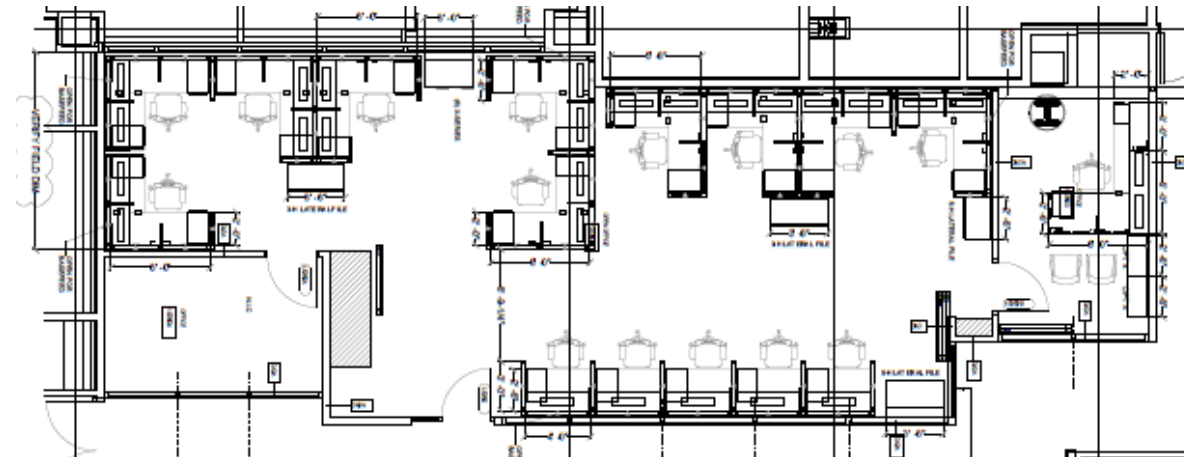
Building 10, SE Atrium, Level 1

Near Terrace GMP facility

2 offices and 15 workstations

Occupied in February 2020

SE Atrium Offices



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3T Cell Processing Lab

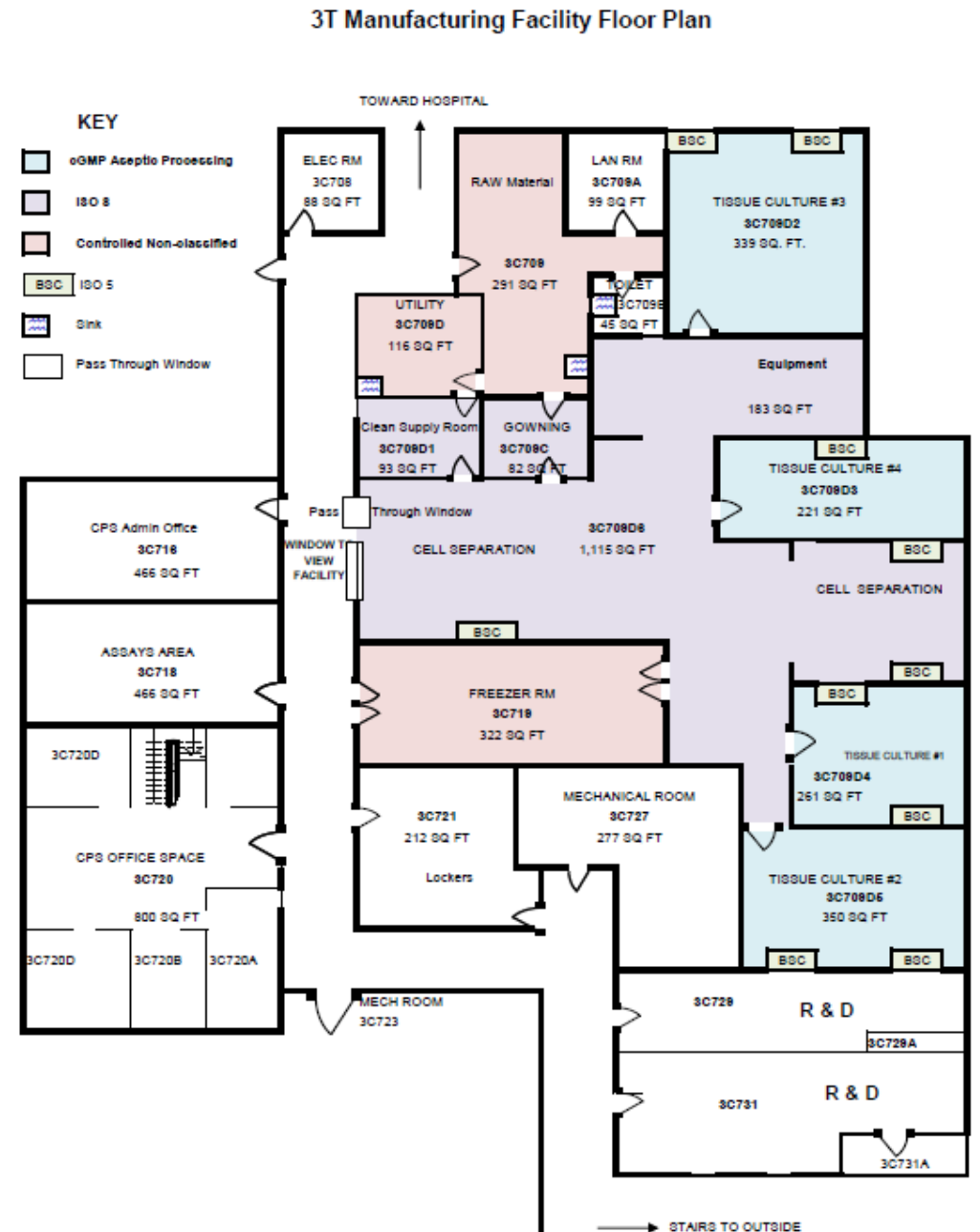
Opened in 1997

4 Culture Rooms

Outdated Design and Construction

- HVAC system lacks terminal HEPA filters
- Walls and ceiling are drywall with epoxy paint
- Casework in the laboratory

Walls and Floor Need Repair



2J Cell Processing Lab

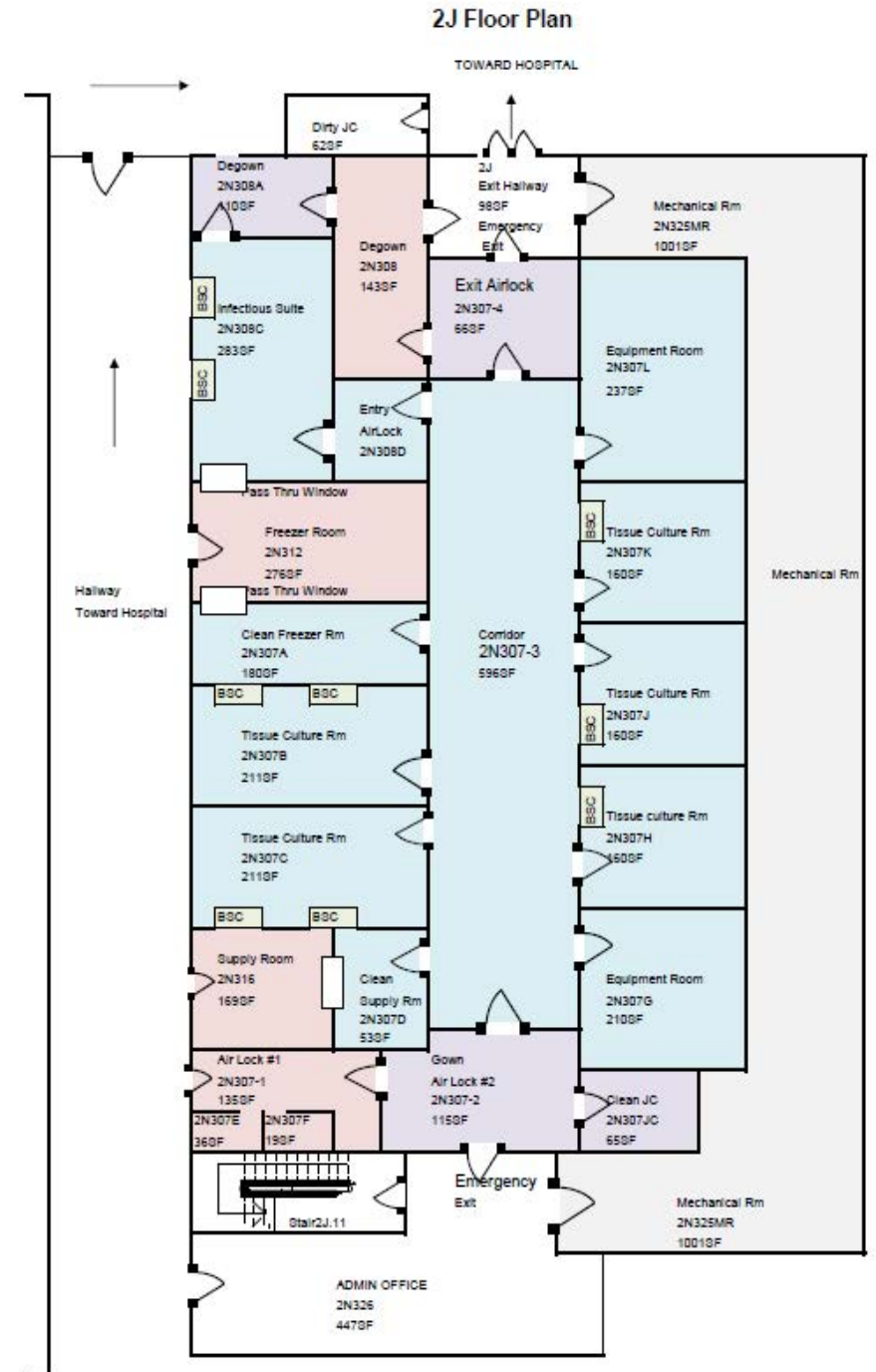
Opened in 2018

8 Culture Rooms

- Converted an equipment storage room to a culture room in 2020

Limitations

- Shared entrance/exist corridor
- Walls and ceiling are drywall with epoxy paint
- Located on the 2nd floor of a 13 story building and is at risk of flooding



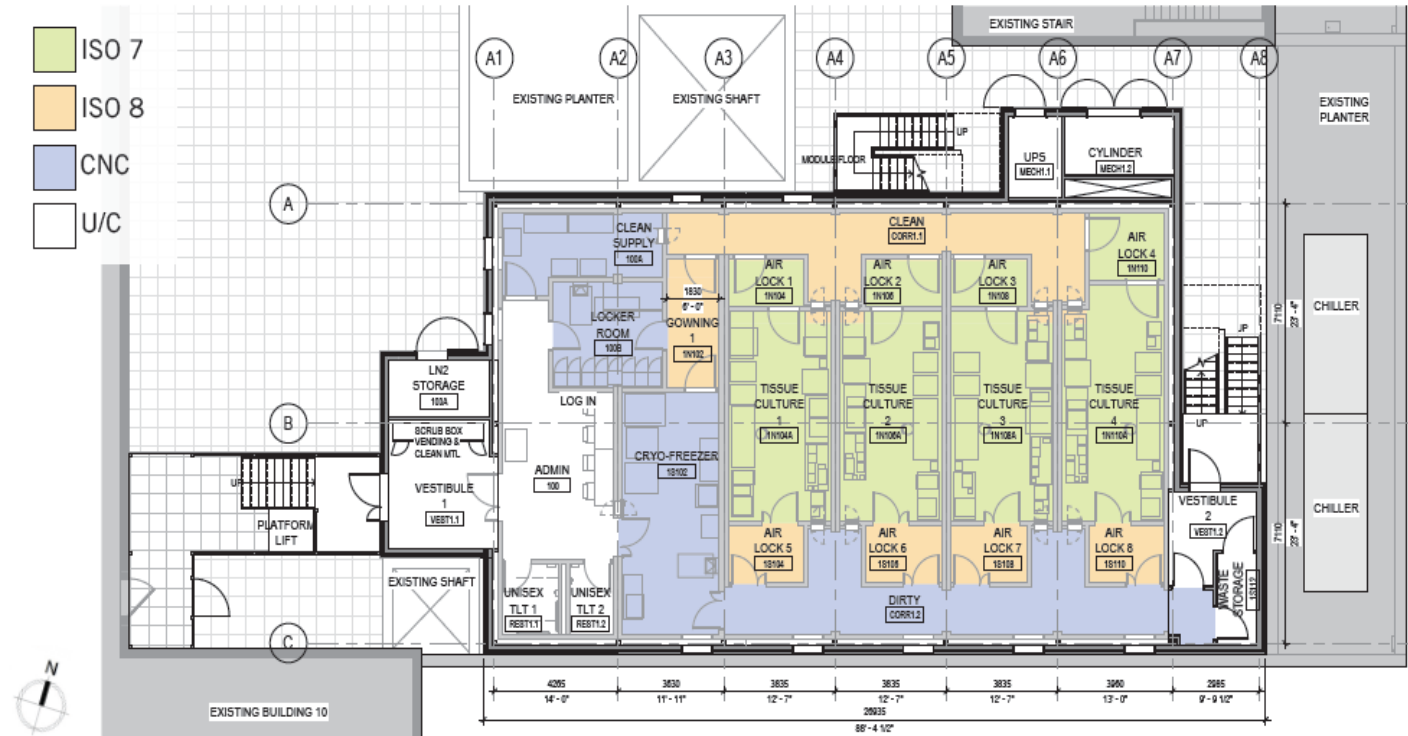
T10B Cell Processing Lab

Opening in 2021

4 Culture Rooms

21st Century Design

- Separate entrance and exit corridors
- Each culture room has an entrance and exit airlock
- Laminate walls



12E Facility

Opening in 2023

State of the Art Design and Construction

- 7 culture rooms
- 2 cell processing rooms
- An assay lab
- Office Space



Summary of Facility and Culture Room Availability

Event	Date	Facilities Available for Processing	Total Culture Rooms Available
3T open	Pre-2018	3T	4
2J opened	January 2018	3T and 2J	12
Terrace opens and 3T closes for renovations	Fall 2021	2J and Terrace	12
3T opens for limited processing	Winter 2022	3T, 2J and Terrace	16
12E opens and 3T closes	Late 2023	2J, Terrace and 12E	19

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Cell Processing Activity

43 Active Protocols

- 16 Complex Cell and Gene Therapy
- 20 Hematopoietic Stem Cell (HSC) Transplants
- 7 Collaborative Manufacturing

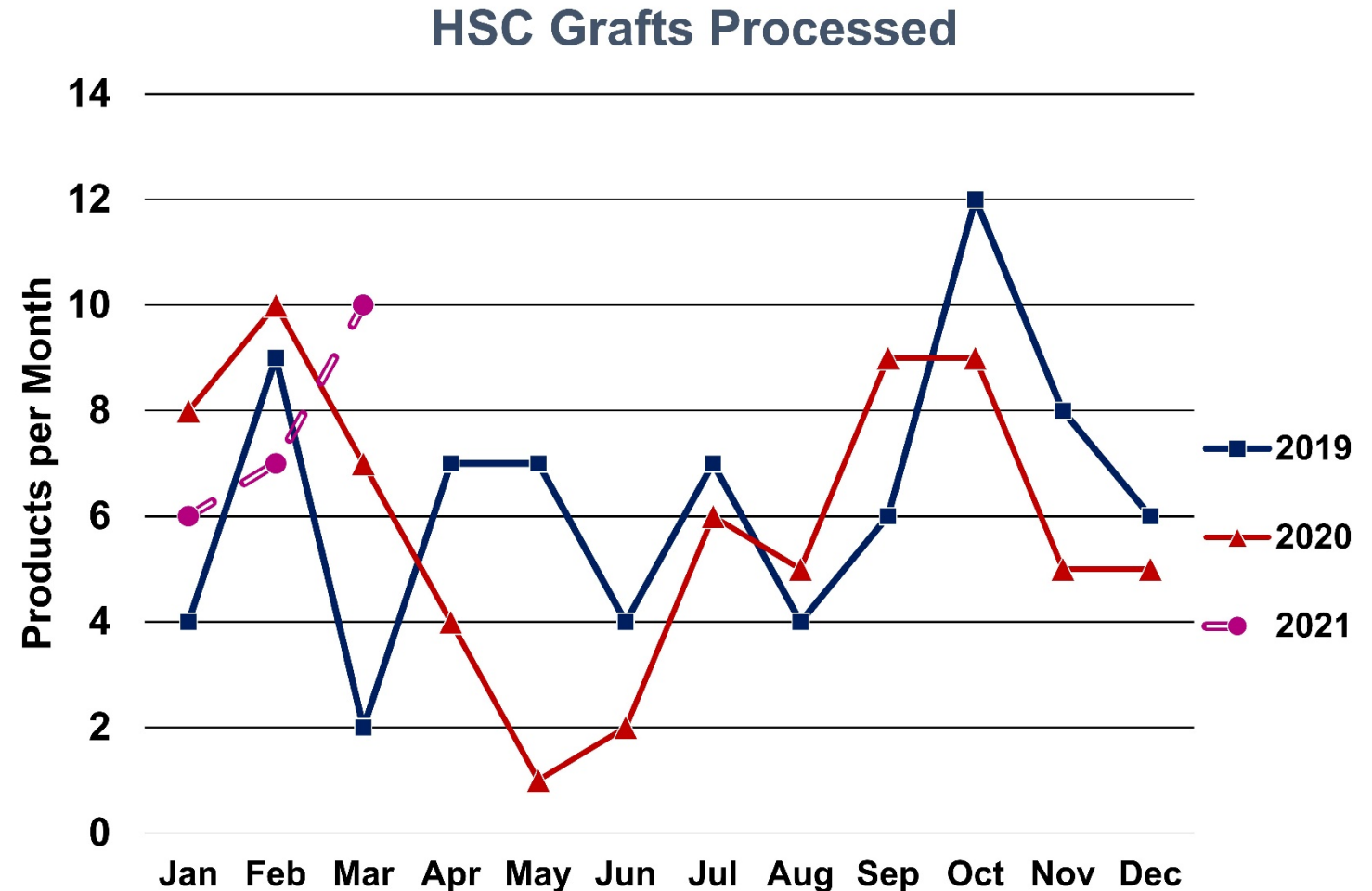
14 New Protocols in Product Development

Hematopoietic Stem Cell (HSC) Transplant Activity

Diagnosis of Patients Transplanted

- Leukemia/Lymphoma
- Aplastic Anemia
- Sickle Cell Disease
- Immune Deficiencies

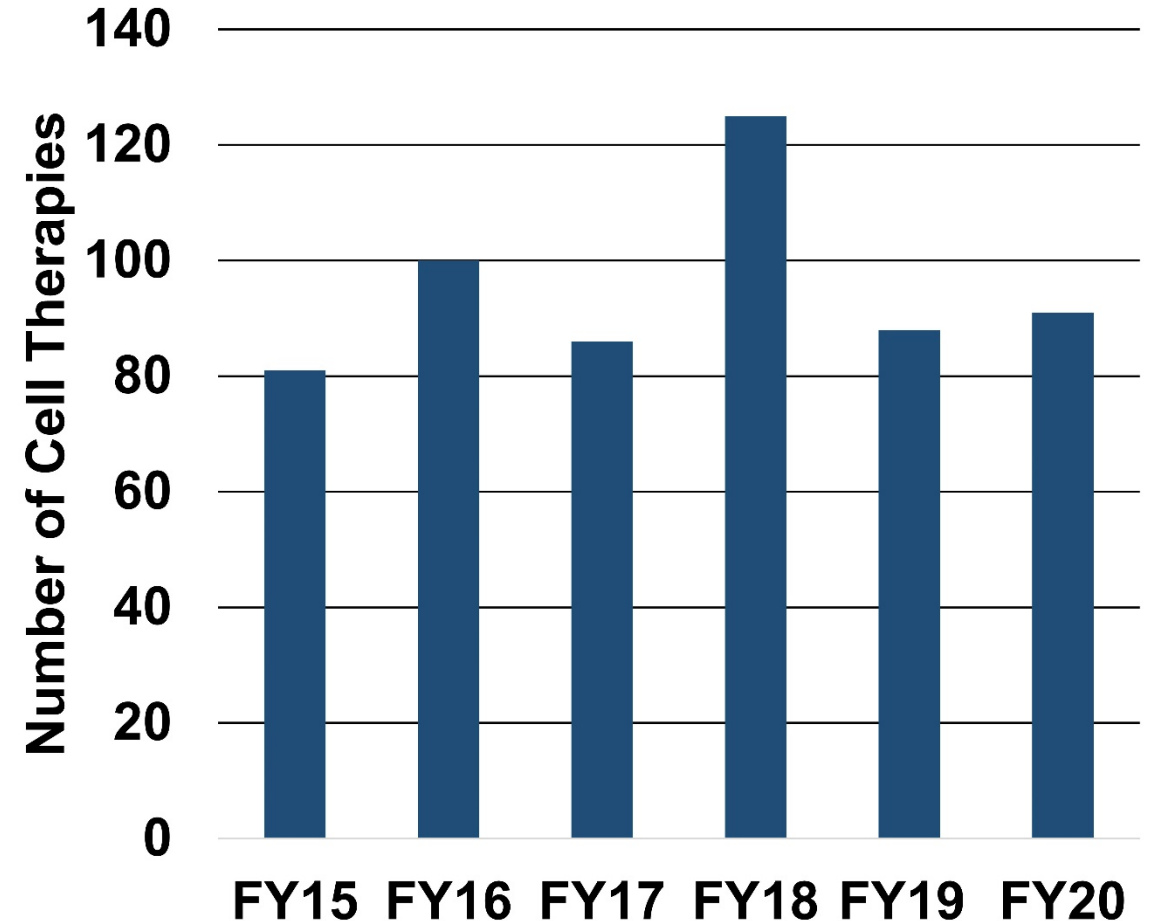
2019 = 76 Transplants
2020 = 71 Transplants



Total Number of Cell Therapies Manufactured Each Year

Types of Cells Manufactured

- Chimeric Antigen Receptor (CAR) T-cells
- T-Cell Receptor (TCR) engineered T-cells
- Dendritic cells
- Interferon treated monocytes
- Virus-specific T-cells
- Gene-corrected hematopoietic stem cells
- Retinal pigmented epithelial cells



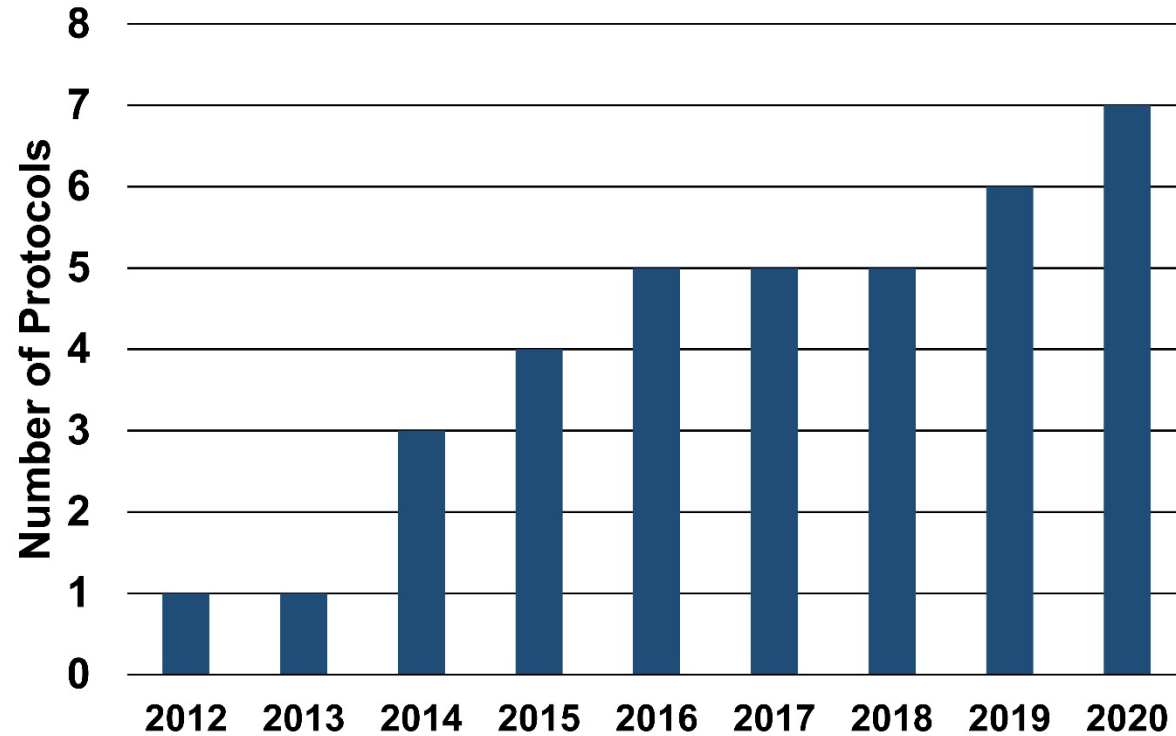
Growth of CAR T-Cell Manufacturing

2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
12-C-0012 (CD19-CAR T)	12-C-0012 (CD19 CAR T)	12-C-0012 (CD19-CAR T)	12-C-0012 (CD19-CAR T)	12-C-0012 (CD19-CAR T)					
		14-C-0059 (GD2-CAR T)	14-C-0059 (GD2-CAR T)	14-C-0059 (GD2-CAR T)					
		14-C-0168 (BCMA-CAR T)	14-C-0168 (BCMA-CAR T)	14-C-0168 (BCMA-CAR T)	14-C-0168 (BCMA-CAR T)				
			15-C-0029 (CD22-CAR T)	15-C-0029 (CD22-CAR T)	15-C-0029 (CD22-CAR T)	15-C-0029 (CD22-CAR T)	15-C-0029 (CD22-CAR T)	15-C-0029 (CD22-CAR T)	15-C-0029 (CD22-CAR T)
Types of CAR T-Cells Manufactured • CD19 (2 types) • CD22 • CD19/CD22 • CD19/CD20 • Anti-BCMA (2 types) • CD30 • Anti-SLAMF7			16-C-0054 (CD19-CAR T)	16-C-0054 (CD19-CAR T)					
					17-C-0048 (CD30-CAR T)	17-C-0048 (CD30-CAR T)	17-C-0048 (CD30-CAR T)	17-C-0048 (CD30-CAR T)	17-C-0048 (CD30-CAR T)
					10-C-0054 (CD19-CAR T)	10-C-0054 (CD19-CAR T)	10-C-0054 (CD19-CAR T)	10-C-0054 (CD19-CAR T)	10-C-0054 (CD19-CAR T)
						18-C-0059 (CD19/22-CAR T)	18-C-0059 (CD19/22-CAR T)	18-C-0059 (CD19/22-CAR T)	18-C-0059 (CD19/22-CAR T)
						18-C-0125 (BCMA-CAR T)	18-C-0125 (BCMA-CAR T)	18-C-0125 (BCMA-CAR T)	18-C-0125 (BCMA-CAR T)
							19-C-0102 (SLAMF7-CAR T)	19-C-0102 (SLAMF7-CAR T)	19-C-0102 (SLAMF7-CAR T)
								20-C-0008 (CD19/CD20-CAR T)	

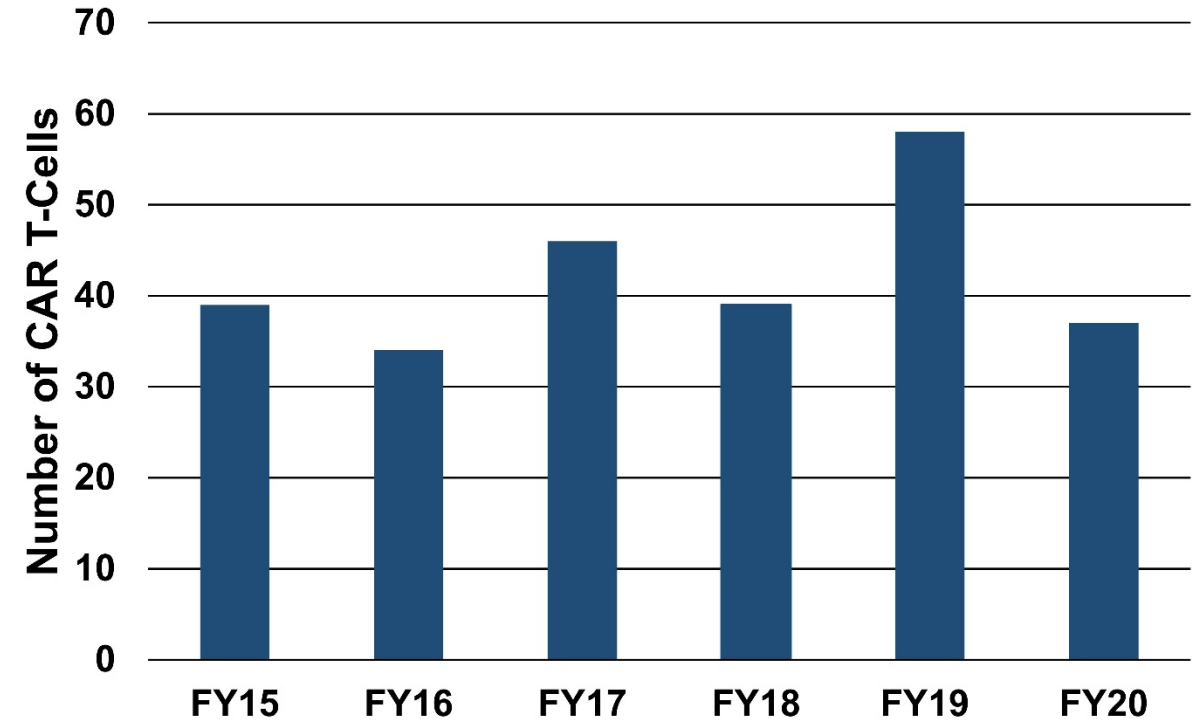
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CAR T-Cells Manufacturing

Number of CAR T-Cell Protocols



Number of CAR T-Cells Manufactured



Treatment of Age Related Macular Degeneration using Autologous Induced Pluripotent Stem Cells (iPSC) Cell-Derived Retinal Pigment Epithelial (RPE) Cells

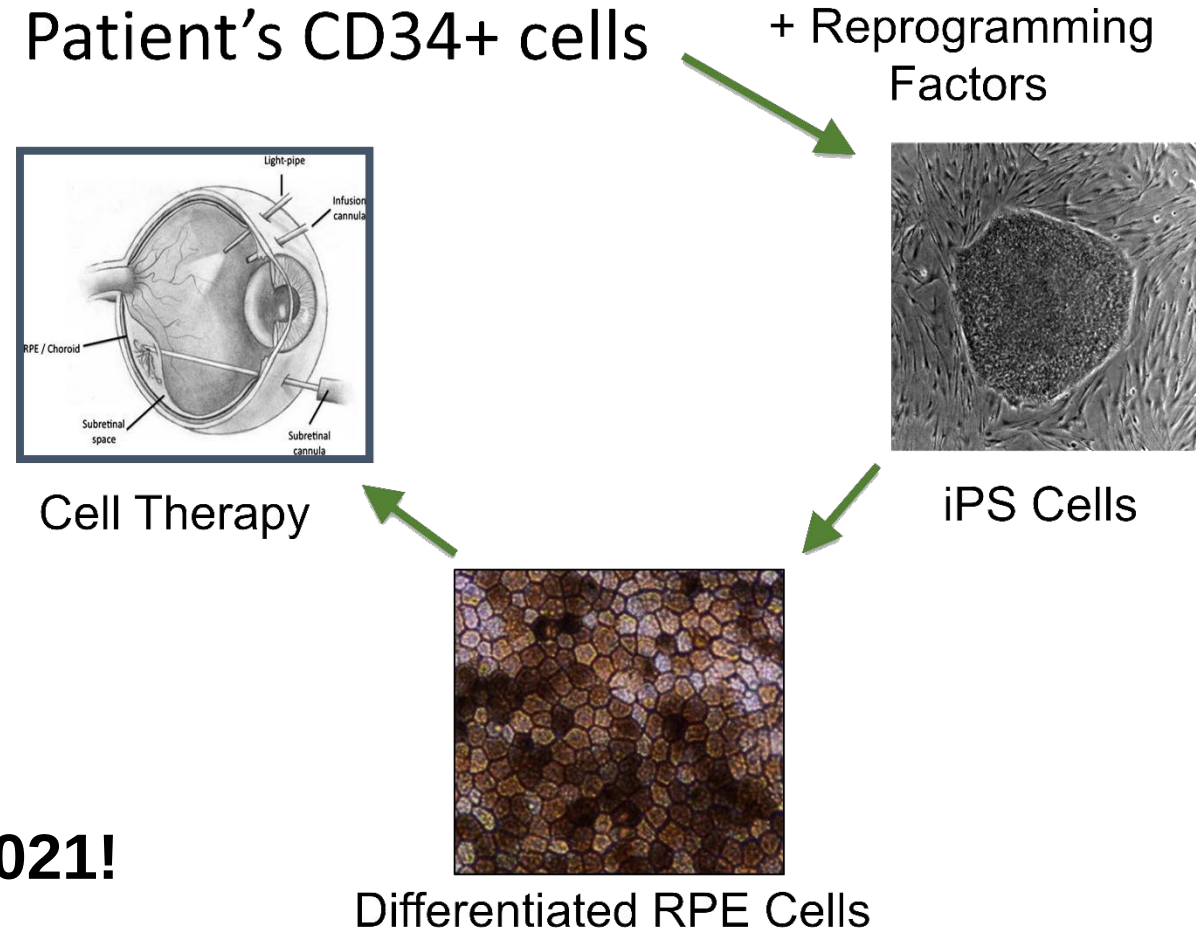
Protocol

- NIH Common Fund iPSC Project
- 5 years in development
- IND approved in December 2019
- First iPSC trial approved in the US

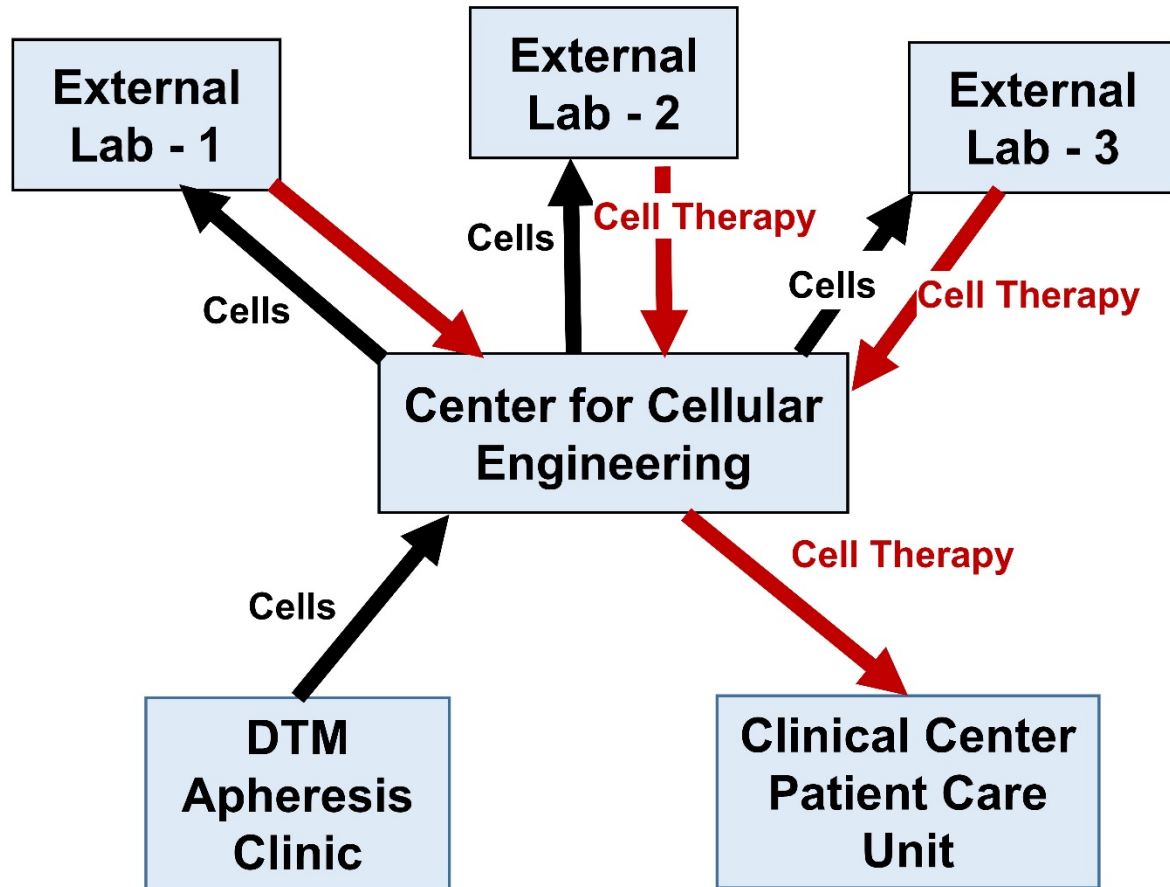
Processing

- Blood (CD34+ Cells) to iPSC (3 months)
- iPSC to RPE (2.5 months)

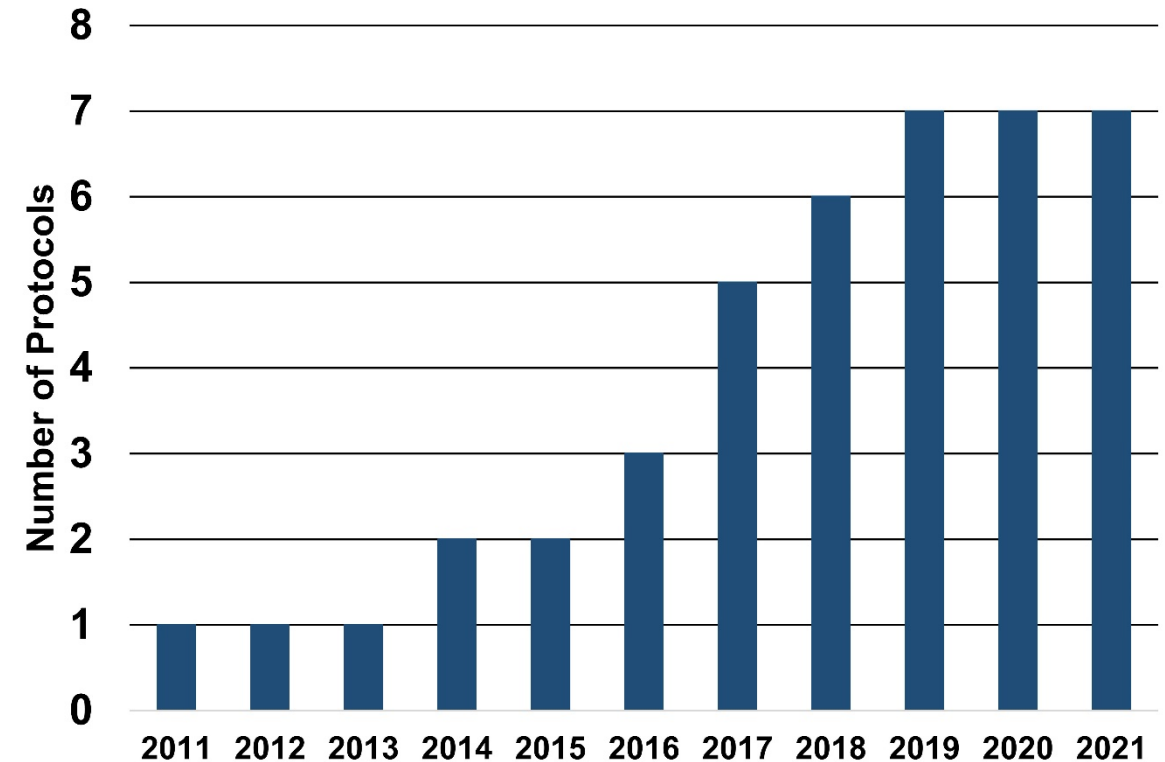
Expect to treat the first patient in June 2021!



Accommodating Protocols Involving Off Campus Manufacturing of Autologous Cells



Collaborative Protocols



15 products in 2020

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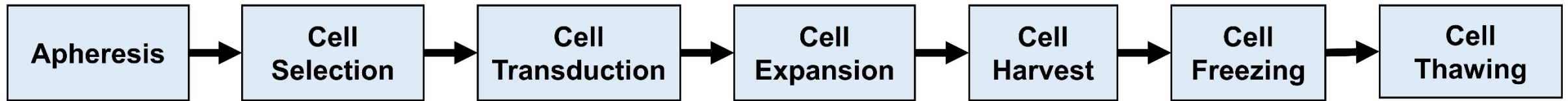
Acquisition of New Instruments for Manufacturing



Recently developed instruments have several advantages

- Purpose designed and built for GMP manufacturing of cellular therapies
- Better documentation of results
- Closed to the environment
- More automated
- Easier to use
- Less staff training time

New Instruments in the CCE



Cell selection, transduction and expansion

- Bioreactor: CliniMACS Prodigy – we are currently using this instrument for CAR T-cell production
- Bioreactor: Lonza Cocoon – purchasing

Cell Freezing

- Controlled rate freezer (ViaFreeze) – purchasing

Cell thawing

- Automated and waterless thaw devices – purchasing

Current Developments and Future Directions

Cancer Immunotherapies

- 6 new CAR T-cell protocols; 5 new products
- 2 new TCR-engineered T-cell protocols
- New DC protocol manufactured w/closed system
- H1299 Tumor cell lysate

Treatment of Immune Deficiencies

- Gene corrected autologous CGD granulocytes
- Gene editing autologous SCID CD34+ cells

Cell Labeling

- T-cells labeled with fluorescein for retinal studies

New Assays

- Vector integration site analysis

Challenges

- Meeting growing IC needs
- Hiring Staff
- Increasing regulatory/quality expectations
- Develop quality systems to manage an emerging field that does not have clearly defined regulations
- Establishing systems for handling facilities, supplies and equipment
- Evaluating and implementing closed automated processing systems
- Building, commissioning and validating new processing labs



Questions?