KPCRTF State Funded Projects Reporting Template

University of Louisville
Development of First GMP Facility Dedicated to Production of CAR-T Cells in Kentucky
Program Director: Dr. Robert Emmons

Reporting Period: ___End of Fiscal Year 2021 Report _____

Below please provide a brief summary of the status of the Project listed as well as for each Objective listed below. Include any barriers, how and if they were overcome, and successes achieved.

During our first year of state funding, we have established a fully functional and regulatory compliant GMP facility at the UofL and begun production runs for the CD4 CAR-T clinical trial. We expect fast expansion to a novel CD19 clinical trial. Matching funds have been obtained through generous philanthropy and we expect further expansion through industry partners in the coming months. This work could not have proceeded without State support and we are deeply grateful.

Primary Objectives:
#1 – Standardize the Good Manufacturing Practice (GMP) operation to ensure CAR-T cell manufacturing quality and safety needed for future Investigative New Drug (IND) applications and for pediatric patients to be enrolled into clinical trials.

a. Start-up test for expansion of CAR-T cells using CliniMACS Prodigy bioreactor.

1. Miltenyi Prodigy was purchased and installed in cleanroom #1 "The Evan Dunbar Lab" manufacturing suite in the Brown Cancer Center GMP Facility.

2. Miltenyi Biotec completed onsite Installation Qualification and Operational Qualification (IQ/OQ) of Prodigy.

#2 – Optimize the manufacturing engineering runs for the dual targeted CAR-T cells for AML and CD19/VAC CAR-T cells for CD19+ lymphoid malignancies and submit both pediatric IND applications for the FDA.

a. Engineering run for the dual targeted (CD33 and CD123) CAR-T cells for AML and CD19/VAC CAR-T cells for B cell malignancies.

b. As previously discussed, a novel fourth generation CD19 CAR-T has been developed by ICell and we have a signed agreement between our two entities, we are in the stages of reviewing preclinical data to initiate the IND preparation to begin soon. The CAR -T will be utilized to target pediatric and adult ALL.

c. Developing the novel CAR-T therapy IND for the adult and pediatric clinical trials.

Dr. Tse from our Pediatric Cancer group will provide update on the progress of his group's development of the novel CAR-T in his interim report.

Secondary Objectives:

1. Reactivation and staffing of a previously dormant GMP facility on the UofL campus suitable to produce CAR-T cells for clinical trial available for testing in pediatric patients at the UofL and UK.

Created a new Environmental Monitoring Program and SOP, to routinely monitor the environmental quality and resident Bioburden within the GMP Facility.

Received/Installed all Processing Equipment in Cleanroom #2 (The Dr. Stephanie Altobellis Lab).

Created an Inventory spreadsheet and hand counted all consumables to keep a running tally moving forward.

All supplies in Inventory Room have been labeled with lot #s and expiration dates and this info was transposed to the newly created Inventory spreadsheet.

BSC recertification was performed in March.

Completed Semi-Annual Facility Clean.

Flow Cytometer preventive maintenance was performed in February.

Miltenyi Prodigy -IQ/OQ validation completed.

Purchase, Install, and Qualification of Controlled Rate Freezer for cryopreservation of CAR-T products

Purchase, Install, and Qualification of Endotoxin Testing Instrument of CAR-T products

Created two new Quality Control SOPs for Real-Time PCR and Flow Cytometric Analysis.

Revised all twenty-three pre-existing SOPs and in addition created twenty-two new equipment SOPs.

All 67 pieces of equipment now have an individual equipment folder that will store all equipment calibration information, preventive maintenance, manuals, and user log forms.

ISO Cleanroom Facility recertification performed in March.

Weekly, Monthly, Quarterly Cleaning of the GMP Facility and QC/Inventory room 132.

Weekly Review of SMART-VUE alarms.

Initiated visitor log forms, production facility access log forms and restricted access approval forms.

Quarterly Doors and Seals, Weekly Pest Control, Daily and Weekly Facility Inspections were completed.

Created new Quality Assurance SOP for Human Cell and Tissue Product Processing.

Created a new safety SOP for general laboratory safety to be used as a training tool for all new personnel and visitors.

Documented personnel training on all newly revised and newly created SOPs.

Documented Annual Water Quality for incoming potable water.

Began utilization of CXAlloy as Electronic Management Software to schedule all Base Building, Facility, and Equipment-related activities.

Trained Physical Plant personnel on the GMP Facility HVAC unit and Base Building procedures described in CXAlloy.

Created hard copy storage of all CXAlloy Base Building completed procedures for Preventive Maintenance.

2. Completion of preparations for the engineering run of the AML dual target CAR-T (CD33 and CD123) and CD19/VAC that will lead to the FDA IND submission for pediatric patients in the Commonwealth of Kentucky.

   Please see above for current status of fourth generation CD19 CAR preparation.

3. Procurement of matching funds from private and community donors to support the CAR-T cell program.

   A) We have obtained a 1-million-dollar grant from Tom Dunbar to support the UofL GMP facility which will now be called the Dunbar CarT facility
   B) We are actively seeking other donors and have also obtained smaller donations to fund the facility (we can summarize these if necessary).
   C) During Q1 of 2021, we received both pledge funds and donations from seven sources to the CAR-T Facility, specific amounts are available upon request.
   D) We have received a four hundred-thousand-dollar pledge from the Dunbar family in honor of Tom Dunbar, we expect to receive the pledged funds in 4th quarter of 2021.

4. Enrollment of patients into the CD4-CAR-T protocol using CD4-CAR-T product produced by our GMP facility.

Currently awaiting enrollment and treatment of patient three of the CD4 protocol at Stony Brook. Once completed enrollment will be opened to patient accrual at the University of Louisville and other sites. University of Louisville IBC and IRB approval received. We anticipate publication of the results after completion of patient 3 at Stony Brook.

Deliverables (check appropriate time period when each deliverable is completed)	**Month 1-3**	**Month 4-6**	**Month 7-9**	**Month 10-12**	**Month 13-15**	**Month 16-18**	**Month 19-21**	**Month 22-24**	√
Notify DPH when IRB approval is received or if not required	X								
Reactivation and staffing of previously dormant GMP facility		X							
Complete preparations for the engineering run of the AML dual target CAR-T									
FDA IND Submission									
Procurement of matching funds from private and community donors	X	X	X	X					
Enrollment of patients into the CD4-CAR-T protocol using CD4-CAR-T product	X								

Quarterly Reports are due:

- October 15, 2020
- January 15, 2021
- April 15, 2021
- July 15, 2021
- October 15, 2021
- January 15, 2022
- April 15, 2022
- July 15, 2022

Reports should be returned to:
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