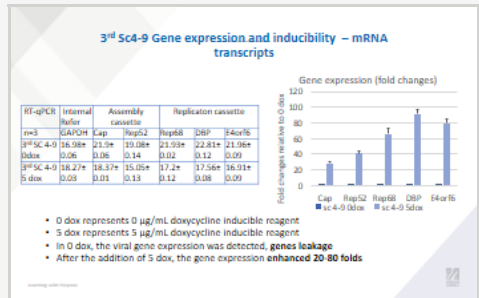
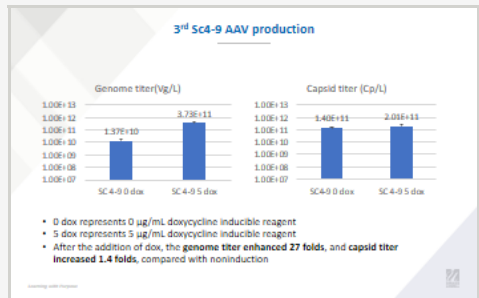


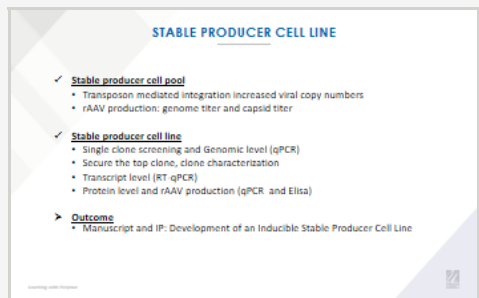
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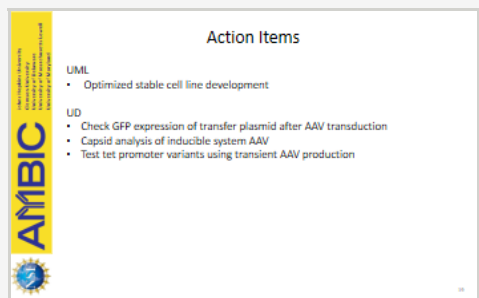
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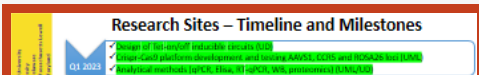
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# Research Sites – Timeline and Milestones

Q1 2023

- ✓ Design of Tet-on/off inducible circuits (UD)
- ✓ Crispr-Cas9 platform development and testing AAVS1, CCR5 and ROSA26 loci (UML)
- ✓ Analytical methods (qPCR, Elisa, RT-qPCR, WB, proteomics) (UML/UD)

Q2 2023

- ✓ Tet off/on switch for 2 AAV cassettes via Golden gate. 1, replication plasmid, 2, assembly plasmid(UD)
- ✓ Site-specific integration of replication cassette made by UD (UML)
- ✓ Testing inducible plasmids via transient (UML/UD)

Q3-4 2023

- ✓ Tet off/on switch for the 3<sup>rd</sup> AAV cassette via Golden gate, 3, transfer plasmid(UD)
- ✓ Site-specific integration of the 2<sup>nd</sup> and 3<sup>rd</sup> cassette and develop the baseline of stable cells (UML)

Q1-2 2024

- ✓ Enhancing the genome copy for transfer cassette (UML)
- ✓ Optimization of gene level and dynamics by engineered inducible variants (UD); Evaluate optimized plasmids via transient(UML/UD)
- Optimized AAV parts integration, The optimized stable cell line(UML)

Q3-4 2024

- Cell line productivity and stability evaluation(UML/UD)
- AAV production bottlenecks investigation(UD/UML)