

Determining Growth Models for Human Lymphoblastic Leukemia Cells for Expansion in a Centrifugal Bioreactor for Utilization in Cancer Immunotherapy

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606,520

Projected USA Cancer Deaths 2020

~10,000,000

Cancer Deaths Worldwide

No Cure

Currently exists

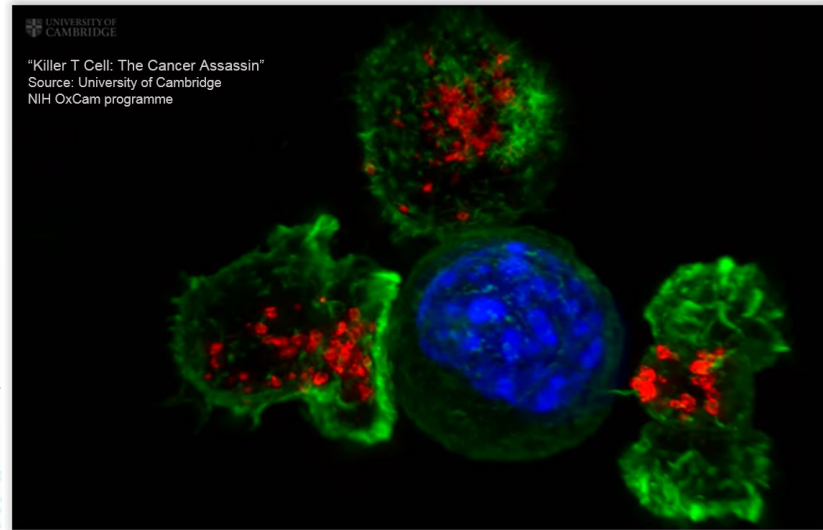
Immunotherapy

-Pros

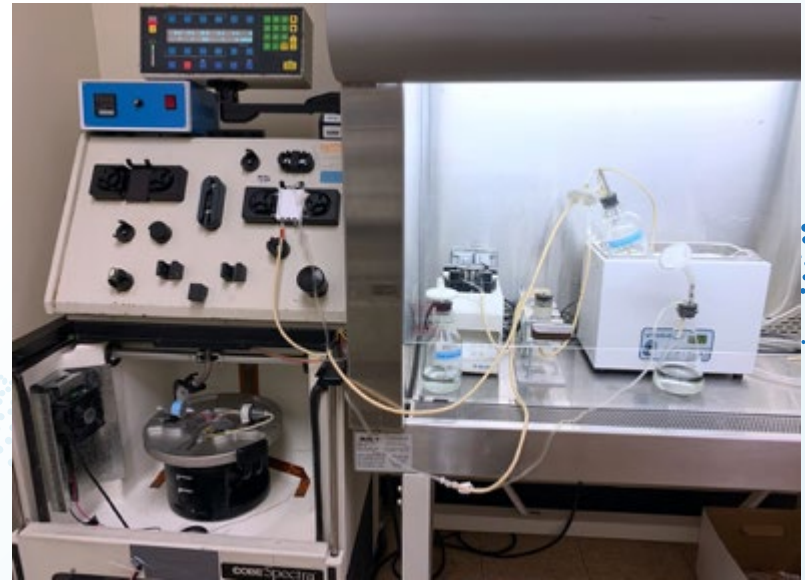
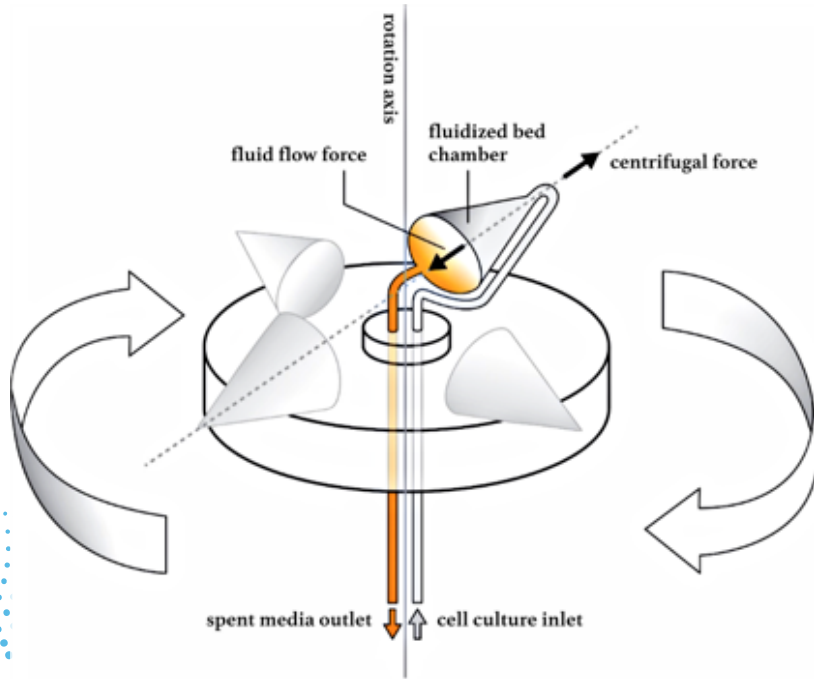
- Targeted cancer therapy
- Uses existing immune system

-Cons

- High number of cells needed
- Patient specific
- Expensive

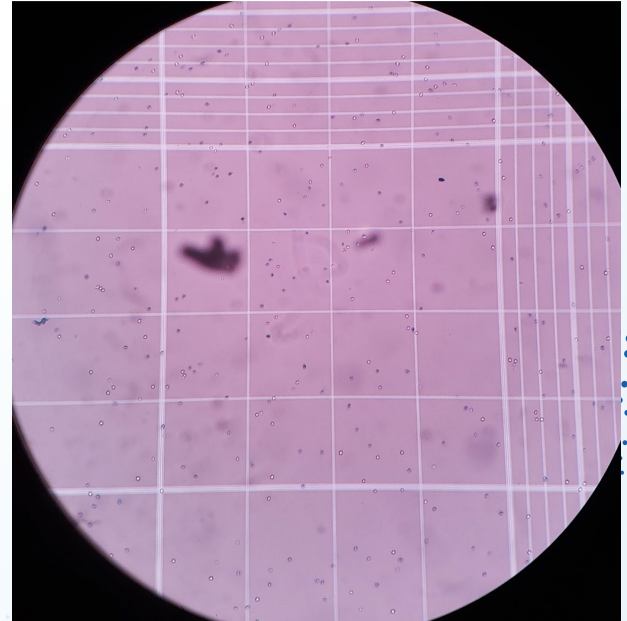


Centrifugal Bioreactor



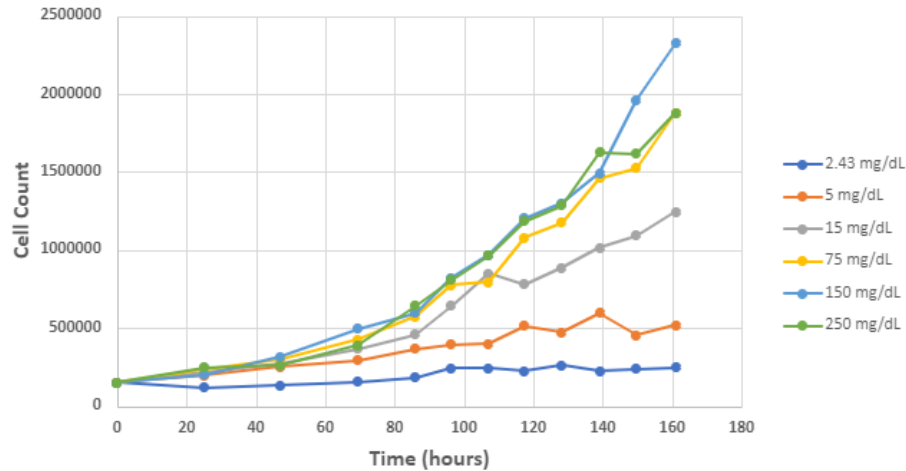
Initial modeling

- Human Lymphoblastic Leukemia cells
 - Similar behaviour
 - Model through kinetic studies
 - Growth studies
 - Inhibition Studies

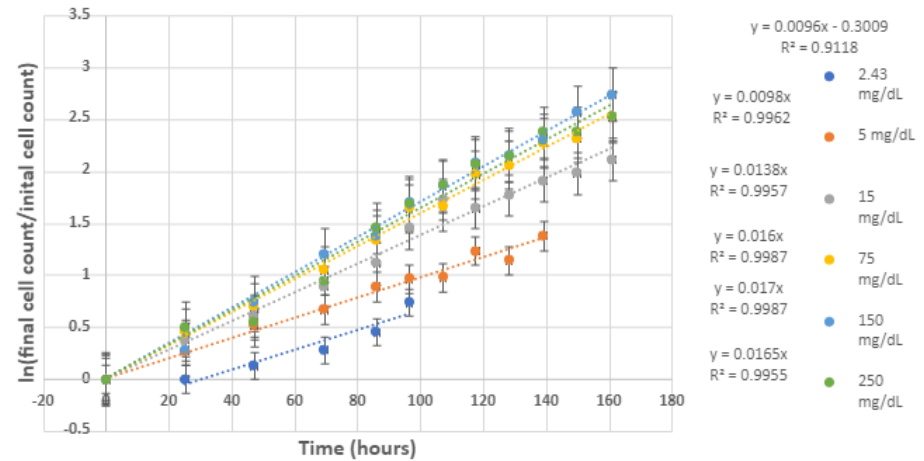


Growth Studies

Average Cell Counts over Time

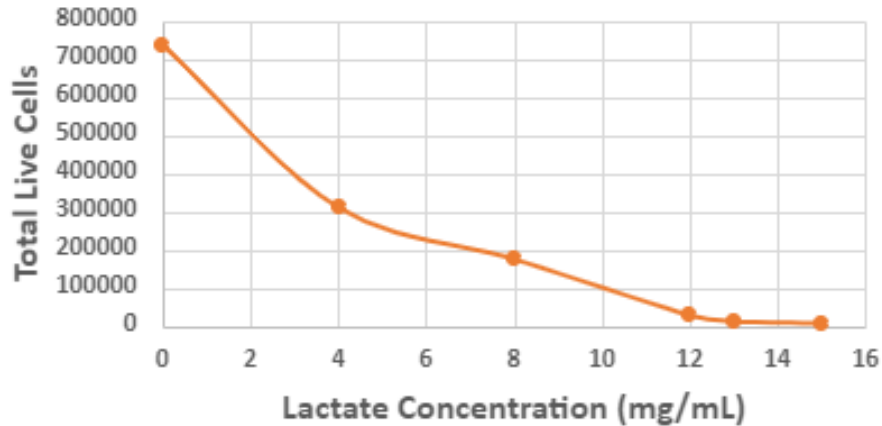


Linearized Growth Plot

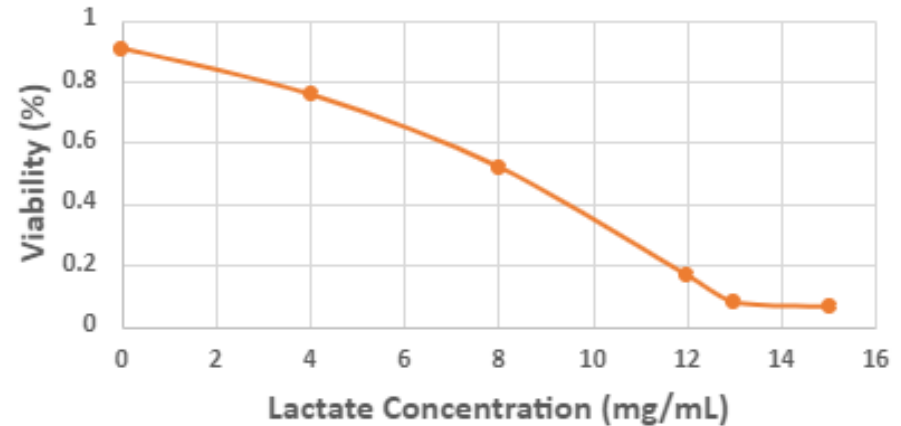


Inhibition Studies, Lactate

Effect of Lactate on # of Live Cells

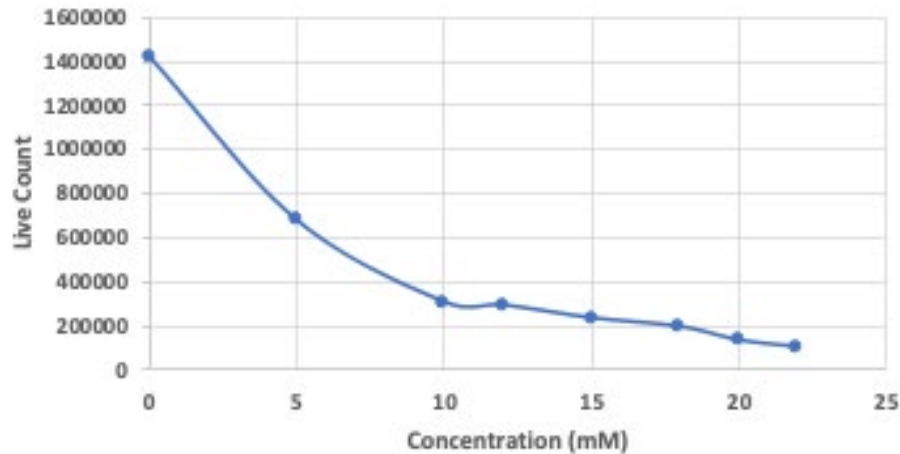


Effect of Lactate on Viability

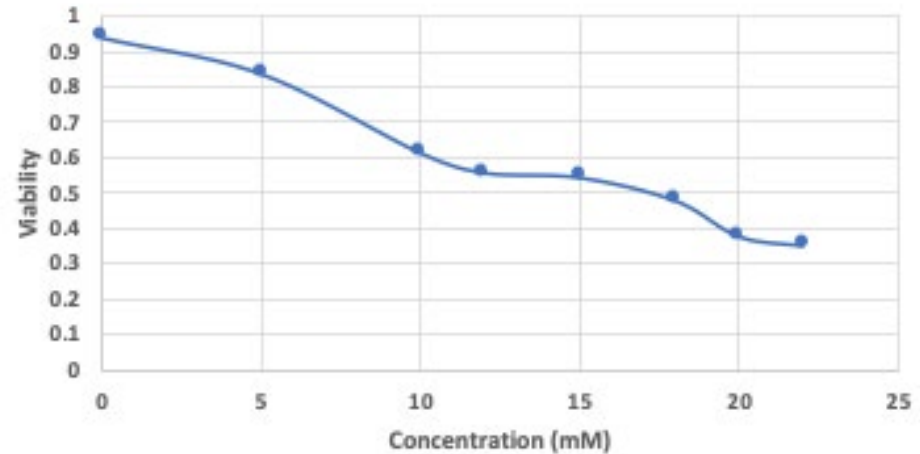


Inhibition Studies, Ammonium

Live Total at each Concentration



Viability at each Concentration



Mathematical Modeling

- Model Ideal growth rate
 - Monod Equation
- Apply to CBR environment
- From our studies :
 - $\mu_{\max}$ and C_m
 - $C_{L\max}$ (16)
 - $C_{A\max}$ (22)

$$\frac{\partial C_{\text{cell}}}{\partial t} = \mu_{\max} \cdot \frac{\left(1 - \frac{C_L}{C_{L\max}}\right)^n \cdot \left(1 - \frac{C_A}{C_{A\max}}\right)^m \cdot C_G \cdot C_{\text{Cell}}}{C_G + C_M \cdot \left(1 - \frac{C_L}{C_{L\max}}\right)^q \cdot \left(1 - \frac{C_A}{C_{A\max}}\right)^p} - (D \cdot C_{\text{Cell_out}}) \quad (1)$$

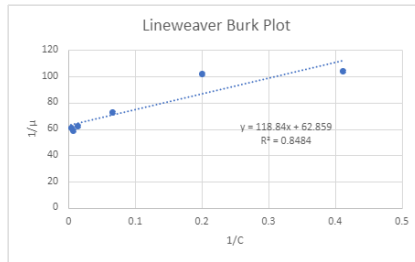
$$\frac{\partial C_G}{\partial t} = D(C_{G0} - C_G) - Y_{GC} \cdot \left(\frac{\partial C_{\text{Cell}}}{\partial t}\right) \quad (2)$$

$$\frac{\partial C_A}{\partial t} = D(C_{A0} - C_A) + Y_{AC} \cdot \left(\frac{\partial C_{\text{cell}}}{\partial t}\right) \quad (4)$$

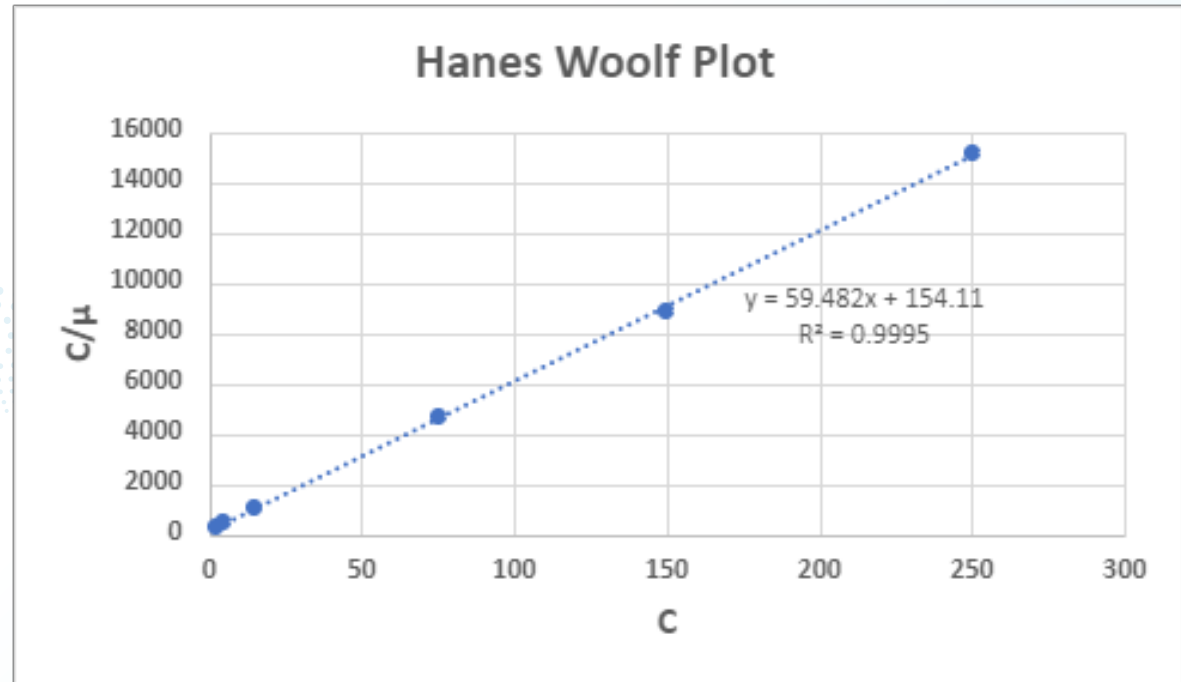
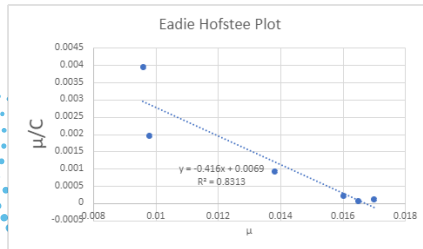
$$\frac{\partial C_L}{\partial t} = D(C_{L0} - C_L) + Y_{LC} \cdot \left(\frac{\partial C_{\text{cell}}}{\partial t}\right) \quad (5)$$

Growth Studies Modeling

$$\frac{1}{\mu} = \frac{K_m}{\mu_{max}} * \frac{1}{C_g} + \frac{1}{\mu_{max}}$$



$$\frac{C_g}{\mu} = \frac{K_m}{\mu_{max}} + \frac{C_g}{\mu_{max}}$$



$$\mu = \mu_{max} - \frac{\mu * K_m}{C_g}$$

Future Studies

- Further ammonium studies
- Determining yield coefficients
- Finalizing the modeling

Sources

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**Thank you,
Any Questions?**