COST EFFECTIVENESS ANALYSIS OF EXPANSION OF BONE MARROW MESENCHYMAL STEM CELLS AND ADIPOSE STEM CELLS WITH PLUS™ HUMAN PLATELET LYSATE

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INTRODUCTION

Challenges in mesenchymal stem cells (MSCs) manufacturing

Scaling up production | Intrinsic biological variability | Use of xenogeneic materials | Management of production costs

Ethical, safety and regulatory considerations discourage the use of animal origin supplementation, such as fetal bovine serum (FBS). Human platelet lysate (hPL) has been gaining popularity as a xeno--free supplement for MSCs expansion.

Collection of bone marrow derived MSCs (BM-MSCs) is an expensive, invasive process. Other sources of adult stem cells,such as adipose tissue for collection of adipose stem cells (ASCs), are seen as more sustainable for being derived from biological waste.

Computational models can help identify manufacturing strategies and parameters to reduce costs and process variability.

COMPUTATIONAL METHODOLOGY

Open source simulation tool | Manufacturing facility parameters | Biological variability | Manufacturing costs per dose

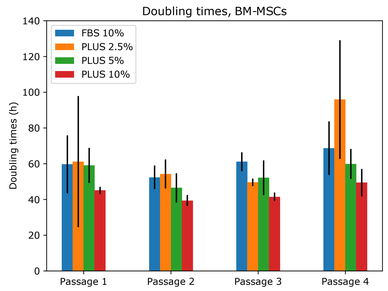
Open source tool developed in Python
Biological variability from random sampling by Monte Carlo Method

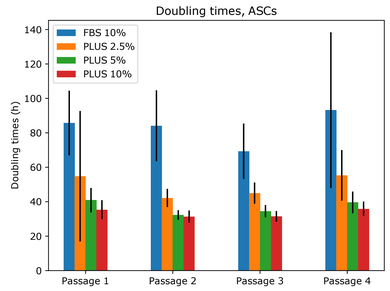
MODEL PARAMETRIZATION

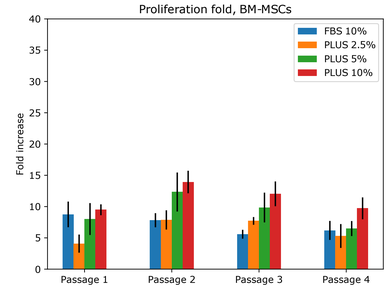
Expansion of 50 MSC donors per source for 4 passages
Use planar flasks with areas up to 6360 cm^2 (cellstacks10)
Simulate a GMP facility with 4 manufacturing clean rooms and 8 incubators

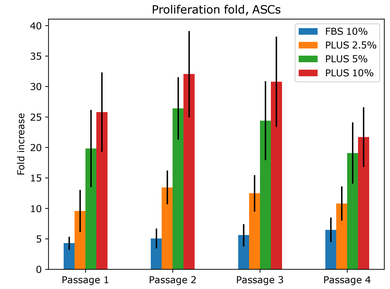
Parameter	Value
Seeding density	1500 $cells.cm^{-2}$
Basal medium/ml	$ 0.04
FBS/ml	$ 1.30
PLUS™ (hPL)/ml	$ 3.00
Labor rate/day	$ 100
Total building costs	$ 1.55M
Vessel costs/unit	Up to $142

EXPERIMENTAL RESULTS

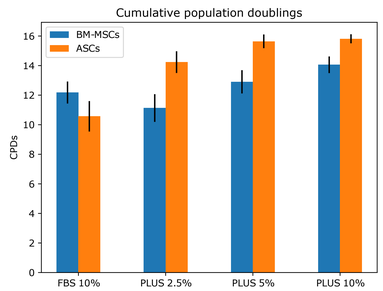


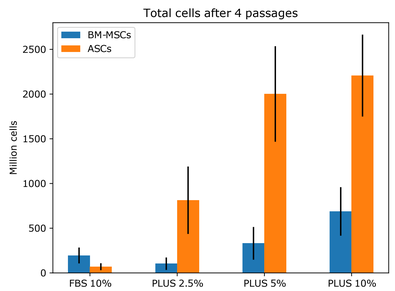


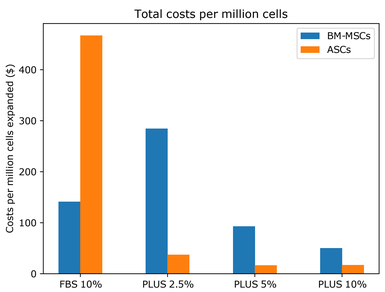


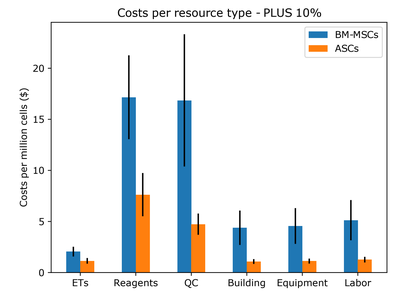


SIMULATION RESULTS









DISCUSSION

Culture medium

Medium supplemented with PLUS™ (hPL) has a price per ml up to 2x higher than with FBS, but enables up to 32x higher cell yield after 4 passages and cost savings per million cells produced of up to 164x.
Experiments show higher growth rates and fold increase with PLUS™ for both cell sources.

Source of MSCs

Under the xeno-free conditions enabled by PLUS™, ASCs are more cost-effective to expand than BM-MSCs.
The most cost-effective concentration of PLUS™ for BM-MSCs expansion is 10%, while for ASCs 5% is more cost-effective.
The incorporation of the isolation and downstream process steps may confirm if adipose tissue is a viable alternative source to bone marrow from the economic standpoint.

CONCLUSIONS AND FUTURE WORK

Given real biological data, the bioeconomics model was able to predict the most cost effective culture medium, favoring the investment in PLUS™ over the traditional supplementation with FBS. Also, under xeno-free conditions, expansion of ASCs is more cost effective than BM-MSC.

The model can be used to evaluate the cost effectiveness of xeno-free conditions for expansion of cells in 3D culture, as well as incorporate isolation and downstream processes. Another future goal is to simulate the costs of a clinical trial for MSCs - this data could be used for process planning before IND application for a prospective clinical indication.

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