Optimizing MSC Production

THE CHALLENGE

Manufacturing of cell therapies is a time consuming and expensive proposition. Optimizing manufacturing processes involves establishing culture parameters to reduce time and expense while providing a phenotype that delivers the intended efficacy. One of the more critical elements of cell manufacturing remains the growth supplements required for optimal growth. Traditionally, fetal bovine serum has been the work-horse of cell culture, albeit carrying with it ethical and safety issues. Alternatively, human derived supplements from processed blood have been growing in usage across the field.

Traditionally known for their role in thrombosis, platelets have more recently been recognized as key mediators of the regenerative processes at wound sites. The growth factors and cytokines released during lysis of platelets modulate the local immune response as well as seed the provisional matrix, launching an accelerated recovery of the local tissues (Figure 1). Given this role in human biology, it's no surprise that a processed platelet lysate imparts reliable growth promoting characteristics to cell culture media.

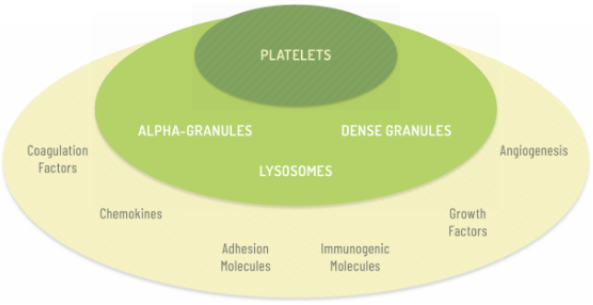


Figure 1: Composition of platelets

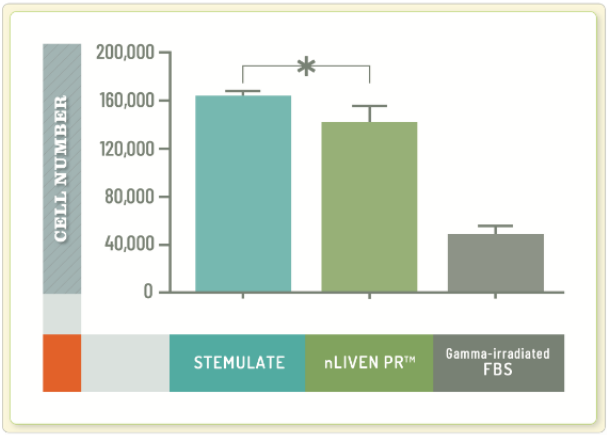
OUR GOAL

Sexton is committed to providing tools to the cell and gene therapy industry that improve our customer's outcomes and reduce risks. Stemulate®, Sexton's pooled human platelet lysate and nLiven PR, processed with pathogen reduction technology to further reduce risks (visit our website to read more about our validated PR process), offer a strong history of use for the production of multiple cell-types to accomplish that objective.

MSC EXPANSION

Referenced in nearly 100 publications and presentations, Stemulate and nLiven have now been established as excellent growth supplements for MSCs derived from a range of tissues including adipose (Figure 2), bone marrow, cartilage, dental pulp and umbilical cord.

Consistently outperforming irradiated FBS, our standard and PR treated pooled platelet lysates allow users to reproducibly manufacture MSCs often with reduced concentrations and faster doubling times, conveying a subsequent reduction in time and costs. By utilizing a growth supplement that results in a faster doubling time, a reduced overall cost can be achieved, both through reducing clean room manufacturing times to obtain target dose and also through reduction in reagent use.



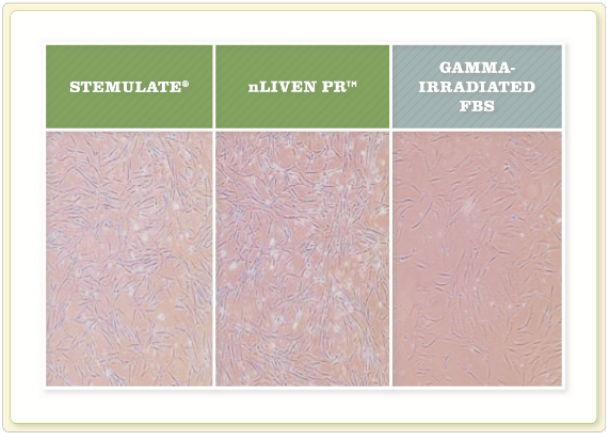


Figure 2: Adipose MSCs

CONSISTENCY

Manufactured using large lot sizes, our proprietary process ensures a safe and consistent product is delivered with each lot. Perhaps due to the programed nature of protein expression in platelets compared to the inherently variable nature of blood biochemistry, evaluations across multiple lots of Stemulate and nLiven demonstrate highly consistent protein concentrations of key growth factors (e.g. EGF levels in Stemulate® as seen in Figure 3). This product consistency correlates with a significant reduction in variability of performance during manufacture of MSCs. (Figure 4)

Figure 3: EGF levels across 11 lots of Stemulate

Figure 4: BM-MSCs expanded with ten lots of Stemulate

EASE OF ADOPTION

With both a research grade and clinical grade Stemulate® available, users can rely on Sexton hPL from early research and development to full scale clinical production. Both grades support robust expansion of MSCs with industry leading lot-to-lot consistency.

Released against additional criteria and more stringent requirements, the clinical grade material utilizes the same manufacturing processes as the research Stemulate. This facilitates users to easily transition from research to clinical grade material without the added cost and time spent on re-validation.

IMPROVING OUTCOMES THROUGH PROCESS

Media optimization for expansion of MSCs ponders a number of key variables with a view to defining a robust and reproducible expansion process for manufacture of efficacious MSCs. Equally, users must consider the impact of this process on their overall COGS. Attaining a process that offers reduced doubling time of desired cell populations whilst minimizing raw material use inherently eases the overall cost of manufacturing a cellular product

Furthermore, consistency in the composition and performance of starting materials is not only beneficial for cell manufacturing performance but also an explicit goal of cGMP manufacturing. Reduction of variability in manufacturing components provides not only improved yields but also reduced failures and subsequent investigations.

CONCLUSION

In summary, optimization of an appropriate reagent at an early stage of development will allow seamless transition to later stage clinical manufacture. At the outset, considering the critical attributes of an ancillary material and its subsequent effects on the manufacturing process, both from a biological and efficacy standpoint, but also from a COGS and business perspective, can allow for selection of the correct raw material for a user's process. In Stemulate and nLiven, Sexton Biotechnologies provides supplements allowing for the clinical development and manufacture of safe, efficacious and reproducible MSCs with potential economic incentive.

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