



# Exploring the Effects of Environmental Conditions on Cardiomyocyte Differentiation

Utilizing regenerative medicine for treatment of cardiac injuries or disorders requires robust generation of cardiac cells. Traditionally, cell growth and differentiation has been performed in a standard incubator under normoxic conditions. Using the **Xcell Bio Avatar™ System**, we can control both oxygen levels *and* pressure to better mimic the environment found in the human body. Controlling the pressure the cells are under has a significant impact on cell health, growth and differentiation.

Directed differentiation of specific lineages from human pluripotent stem cells (hPSCs), including human embryonic stem cells (hESCs) and induced pluripotent stem cells (iPSCs), is the first critical

step toward constructing development or disease models, drug screening tools, or cellular therapies from hPSCs. Because postnatal cardiomyocytes have little or no regenerative capacity, very limited supplies of human cardiomyocytes are available at present.<sup>1</sup> This is a critical bottleneck in the development of new patient therapies.

Using a standard incubator vs. our AVATAR system, we divided our cell population into three categories: Normoxia + Standard Incubator, AVATAR using 5% O<sub>2</sub> and 0 PSI and finally AVATAR using 5% O<sub>2</sub> and 2 PSI. Keeping oxygen constant and fine tuning the pressure enabled us to determine the effects of pressure on the cells and assess the efficiency of cardiomyocyte generation.

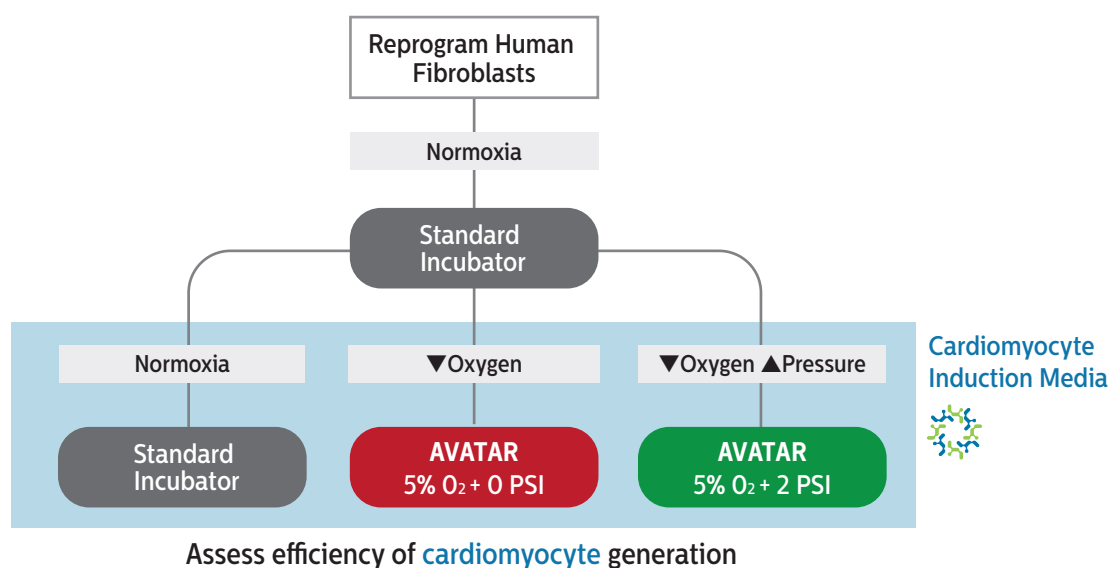
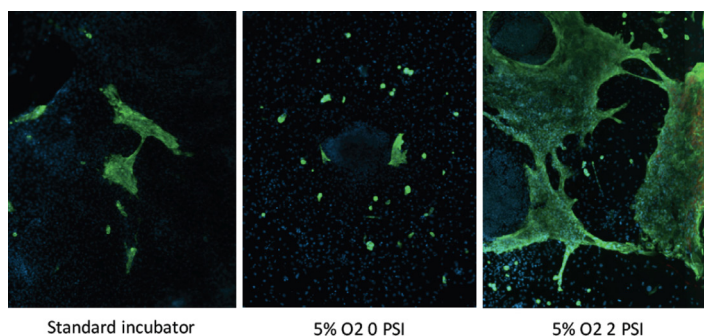


Figure 1: Experimental design to assess the efficiency of cardiomyocyte generation.

## Controlled Differentiation

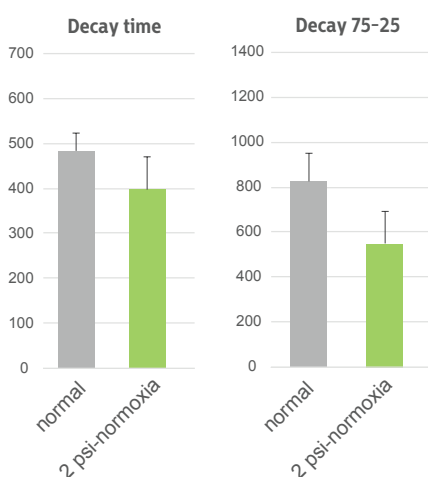
Figure 2 shows the effects of 5% O<sub>2</sub> and with no pressure, and 5% O<sub>2</sub> with 2 PSI of pressure. There is a clear impact on cell differentiation with the addition of increased pressure showing more widespread expression of mature cardiac markers.



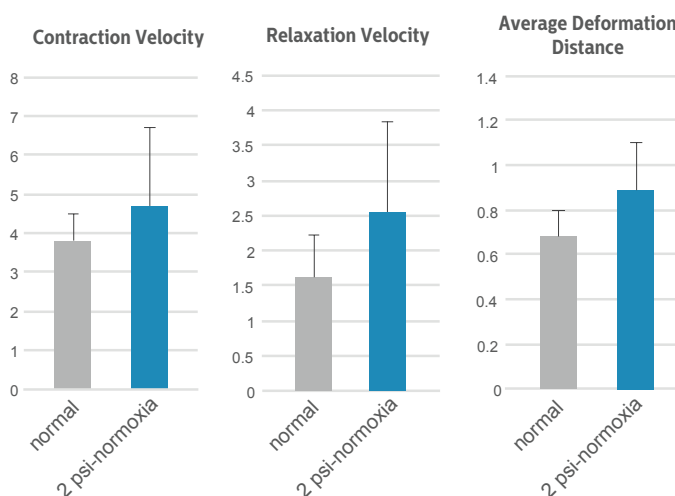
**Figure 2:** Positive effects of pressure on cardiomyocyte growth and differentiation

## Improvements in Late Stage Maturation

For late stage cardiomyocyte maturation, the AVATAR system showed clear improvements in both the calcium relaxation kinetics as well as the contractility parameters by controlling pressure, leading to improved late stage cell health and viability.



**Figure 3:** Calcium reaction kinetics decreases from normoxia to 2psi + normoxia.



**Figure 4:** Contractility parameters - Addition of the AVATAR system showed increases in contraction velocity, relaxation velocity and average deformation distance.

## The AVATAR Advantage

- Fine tune BOTH oxygen and pressure to rapidly expand patient-derived tumor, immune and stem cell populations
- Improve cell transfection efficiency, viability and expansion
- Control cell state by tailoring the gene, protein, and metabolic profiles of your cells



### References

1. Directed cardiomyocyte differentiation from human pluripotent stem cells by modulating Wnt/ $\beta$ -catenin signaling under fully defined conditions *Xiaojun Lian, Jianhua Zhang, Samira M. Azarin, Kexian Zhu, Laurie B. Hazeltine, Xiaoping Bao, Cheston Hsiao, Timothy J. Kamp, and Sean P. Palecek*



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