**425f The Effect of Multiple Passes of Edr on Suspended Animal Cells**

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When scaling up an animal cell culture, there always exist a concern over the effects of hydrodynamic forces on cell's integrity and performance throughout cultivation and downstream devices. Any alteration in metabolism caused by mechanical stresses could involve changes in the final product or its yield, affecting the global outcome of a biotechnological process. Proper scaling-up procedures ideally should prevent this from happening; however, because of our limited understanding on the effect of mechanical stress on cells, no functional relationships exists, resulting in experimental evaluation for every case, based on each company's own experience. The local energy dissipation rate (EDR) is a parameter purely based on fundamental considerations that can be used to properly quantify the hydrodynamic environment surrounding cells. The EDR is a scalar value with units of power per unit volume (W/m3 in SI units), which represents the irreversible rate of mechanical energy which ultimately is transferred to the smallest portions of the fluid and converted to heat by viscous dissipation.

In our reesearch group, we have used a microfluidic device to determine the sensitivity of animal cells to high levels of EDR under laminar flow conditions. Previous studies have focused on the effect of exposing animal cells to a single, high level of EDR; however, in a culture vessel cells are most likely exposed to short, repeated, high levels of hydrodynamic stress particularly near the impeller or at gas-liquid interface, while the remainder of the time the forces are effectively non-existent. For the present work, we cultured wild-type CHO-K1 cells and CHO-K1 cells transfected with the bcl-2 anti-apoptosis gene, in suspension in a serum-free media, and determined their behavior after being subjected to multiple exposures to high levels of EDR in terms of detection of necrosis and apoptosis (determined by using flow cytometry), as well as changes in oxygen consumption rate and growth rate.

The results are then compared to previous experiences with single hydrodynamic abuse at a range of EDR levels commonly encountered in bioprocesses.