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Quantifying Movement Characteristics of Mesenchymal Stem Cells for Tissue Engineering

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Introduction

Throughout the human body, cartilage surrounds the bones providing vital support and cushion. Loss of cartilage from degenerative joint diseases such as osteoarthritis and rheumatoid arthritis affect close to 64 million Americans, roughly 18.9% of the population (Centers for Disease Control and Prevention). Articular cartilage damage may also result from joint injury caused by playing sports, falls from heights, or automobile accidents. Currently, the treatment options are limited; through surgery the cartilage can be smoothed or realigned, the joint fused, or totally replaced, however the resulting quality is generally beneath the level prior to injury or disease. The growing field of regenerative medicine seeks to develop better treatment options using the natural systems of the body and tissue engineering to create treatment options that restore function comparable to the natural standard. One avenue focuses on inducing the migration of cells into a tissue scaffold. This research aims to support the advancement of artificial articular cartilage by quantifying the movement characteristics of mesenchymal stem cells, which may be used in computational models to aid in the development of artificial tissues.

Materials and Methods

Videos capturing the movement of mesenchymal stem cells were obtained from Dr. Mary Murphy at the University of Galway. Individual cells were manually tracked using ImageJ, an open-source image analysis program developed at the National Institutes of Health. It can be used in biological-image analysis to track the xy coordinates relative to location on the screen. These data were uploaded into a MATLAB program created by the authors to calculate movement characteristics and to graph the direction and magnitude of movement and compared to MATLAB generated random walk data. The movements were analyzed to calculate the straightness index, mean squared displacement (MSD) curves, and the relative and global turning angle distributions (TADs). The straightness index is defined as the net distance moved over the total distance traveled, giving an indication of how straight the cell moved. The global TAD is the distribution of the angle taken with reference to the starting point and can give an idea of overall cell movement bias. The relative TAD is taken in relation to the previous movement vector and can reveal persistence at each point. The MSD curve is the mean squared displacement over each time interval and indicates the total

distance traveled from the starting point. It can be compared to Brownian motion generated from the random walks, which would be expected to produce a straight line over many trials to indicate if the cells are migrating a longer or shorter distance than random movement predicts.

Results/Conclusions/Discussions

Generally, across all experimental data sets, the MSD curves exhibited a much greater average slope and upward tendency than the random walk data, even including a slight drop towards the end of each experimental curve. This would seem to indicate a more super-diffusive pattern, or that the cells moved more than expected based on a Brownian motion prediction. The straightness index for the experimental data was also generally much higher than the random walk data, a mean of about .2932 compared to a mean of approximately 0, indicating that the cells experienced greater directional bias than expected from simple random motion. The relative TAD distribution was consistently smaller for the experimental data as well, suggesting that a cell has a higher probability of continuing at a certain angle based on its velocity vector as opposed to following a fully random movement pattern, further revealing a directional bias. Overall, all of these factors indicate that the movement pattern was more direct on average than would be expected of random motion by exhibiting greater distance traveled and greater directional consistency. Thus, it would be reasonable to conclude based on these results that the motion is not random. However, the window in which these cells were analyzed was very small, thus the cells studied are those that remained within the frame and may not necessarily be representative of all cells in the sample. In the future we intend to obtain new cell movement videos and track them over larger distances. Adding these to the existing data set could create a better understanding of overall movement characteristics. If these results remain consistent in supporting biased motion, next steps could include experimental measuring of their diffusion coefficient as well as more in depth research into the factors influencing their movement. Applying this knowledge could contribute to the development of more effective methods to integrate stem cells into a tissue scaffold and a more enduring product.

References

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