Chromatin Modification during the Formation of Self-Organized Tissue Structures

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Stem cells offer enormous potential for treating disease because of their regenerative abilities. Studies using stem cells enable scientists to learn about the cell's essential properties and to generalize qualities observed to a wide range of cell types. Stem cell research continues to advance knowledge regarding development from a single cell and how healthy cells replace damaged ones. Stem cells have been observed to form self-organizing tissues (toroids) when grown on top of a collagen hydrogel. However, stem cells do not form these self-organizing toroidal aggregates when grown inside collagen gels.The mechanisms by which these cells form toroids remains unclear. Our hypothesis is that there are epigenetic modifications that dictate toroid formation in stem cells that can be detected using the chromatin immunoprecipitation (ChIP) protocol combined with Next Generation Sequencing (NGS) bioinformatics. Application of ChIP-seq will identify the changes in gene expression that occur as a result of chromatin-modifying enzymatic activity during toroid formation. The histone variants and posttranslational modifications (PTMs) that are occurring driving toroid formation can be analyzed through the use of bioinformatics gleaned from the ChIP protocol. The bioinformatics will provide data indicating which particular histones have undergone epigenetic changes, thus indicating the sequences accessible or restricted for DNA polymerase processing and exposing the genetic underlying of toroid formation. Interestingly, cancer stem cells never form toroids when grown on top of collagen hydrogel. Further study of the mechanisms by which cells behave, and the subsequent changes in chromatin given particular tissue parameters, will illuminate new chemotherapeutic targets. Thus this work extends beyond just development and give credence and has significance in the burgeoning fields of regenerative medicine and cancer biology.