The Epigenetic Regulation of Mesenchymal and Stem Cell Like Properties

Alvina Zia1,2, Maria Castaneda2, Petra den Hollander2, Sendural A. Mani2

Houston Baptist University1, Houston, TX
Department of Translational Molecular Pathology, The University of Texas MD Anderson Cancer Center2, Houston, TX

Background

Epithelial-Mesenchymal Transition (EMT) is a biological program that induces epithelial cells to morph into a mesenchymal stem cell-like phenotype. Recently, our lab identified that cell division is critical for the gain of stem cell properties during EMT but not for mesenchymal properties. Epigenetic programming is critical for both cell division and EMT regulation. Epigenetic regulators include various histone or chromatin remodeling proteins such as EZH2, HDACs, and DNMTs.

Hypothesis

Due to the link of epigenetic regulation in both EMT and cell division, we hypothesize that a particular class of epigenetic inhibitors will be able to unlink the gain of mesenchymal and stemness properties.

Methods

- EMT-enriched cell line: SUM159 cell line
- Epithelial cell line: MCF10A. EMT was induced using TGF-B1 for 6 days.
- Inhibitors Tazemetostat, Vorinostat, and Decitabine were utilized on cells.
- ICS were determined using IncuCyte
- Protein analysis by Western Blot
- Stemness analysis by Mammosphere assay

Results

- Figure 4: Dose response curve of cell viability upon drug treatment in MCF10A + 6 days TGF-B1, with calculated IC50 and IC10.
- Figure 5: Western blot analysis of drug treated MCF10A and SUM159. Decitabine provided conflicting results, with more studies required. Vorinostat was capable of inhibiting mesenchymal properties, but Tazemetostat has no effect on mesenchymal properties acquisition. 4

Conclusions

- Figure 7: A) Figure depicts the EMT process. Epithelial cells convert to mesenchymal-like cells with acquisition of stem cell like properties. B) When cell division is inhibited in the EMT process what results are cells that possess mesenchymal properties but not stem cell like properties. C) The addition of Decitabine concluded that further study will be needed to determine its effect on mesenchymal properties, but it is capable of inhibiting the acquisition of stem cell like properties. D) The addition of Vorinostat concluded that the drug indeed inhibits the acquisition of mesenchymal properties as well as the inheritance of stem cell like properties. E) The addition of Tazometostat concluded that the drug has no real effect on mesenchymal properties, but capable of inhibiting acquisition of stemness properties. This drug’s results proved to be most similar to the effect of inhibiting cell division during EMT.

References

6. Images Created with BioRender.com

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