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Summary

The hurdle in the translational nature of stem cells research is the heterogeneity of the differentiated population of cells. Theoretically, it is envisaged that when pluripotent stem cells (PSCs) are treated with certain factors, the cells will differentiate into the appropriate differentiated cells. However, in reality, due to the known and unknown differences in the environment of the cells, populations thus arising are heterogeneous in nature. However, traditionally these issues were addressed using various cocktails of growth factors. Alternatively, I wanted to explore the nature of cells to ECM binding on differentiation and whether it was possible to bring about the various aspects of stem cells research, such as its maintenance and differentiation, with artificially created bioengineered ECM matrix. In my experiments, I have tried to address these particular issues using certain biomaterials prepared indigenously in my laboratory.

Firstly, I used N-cadherin-Fc to observe it`s effects. It was observed that it was possible to bring about growth factor free neuronal conversion from mouse iPS cells. This occurred due to the down-regulation of Rho-Rock signaling, which led to a decrease in dissociation induced apoptosis. Furthermore, when cells were dissociated from embryoid body and transferred on N-cadherin-Fc, N-cadherin homophilic interaction was observed whereby neuronal cells were enriched to about 95%. Since, the N-cadherin homophilic interaction excludes E-cadherin, approximately 100% of the undifferentiated cells could be removed. In addition, it was also

observed that N-cadherin mimicking differentiation was possible using SWELYYPLRANL/CBP peptide fused onto elastin like polypeptides (ELPs), denoted as E-CBP here.

Secondly, we prepared an integrin dependent RGD as well as integrin independent CBP on a common backbone of elastin like polypeptides (E12), ERE-CBP. On culturing of mouse iPS cells on the matrix resulted in its binding and propagation. When compared with control matrix (gelatin) the cells on the ERE-CBP containing matrix were able to maintain better pluripotency. Moreover, without pathway inhibitors, long term maintenance of mouse iPS cells was possible on ERE-CBP matrix.

Thirdly, I wanted to observe it would be possible for laminin mimicking differentiation using different laminin domains, IKVAV (I), YIGSR (Y), and RNIAEIIKDI (p20), fused on to ELPs, such as EY, EIEY, Ep20, EIEY:2Ep20. Among various combinations EIEY:2Ep20 showed best neurosphere binding and conversion. Apart from that, on this combination matrix it was possible to carry out neuronal differentiation on par with that on Laminin.

Hence it can be concluded that it is possible to carry out neural differentiation with triple laminin peptides fused to ELPs in place of laminin. Additionally, it is possible to carry out differentiation and maintenance of PSCs with bio-engineered ECM in lieu of the growth cocktails. Hence, I am hypothesizing that for the optimum and maximum output in differentiation it is necessary to consider the defined bio-engineered ECM as well as growth cocktails.