

## **Engineered cell derived matrices for stem cell differentiation**

The microenvironment of the stem cell niche plays a pivotal role in regulating lineage specific differentiation of stem cells. The biomechanical properties of the stem cell niche which direct the stem cell fate is greatly dependent on the composition and organization of the insoluble extra cellular matrix (ECM) components and soluble growth factors. The intact ECM organization and composition is also required to maintain the genomic stability of growing stem cells. Though the protocols for tuning adult stem cells into cells of interest is easy and well documented, their differentiation potential is limited to only specific cell types. Lack of sorting protocols for mixed populations, and uncertainty in spontaneous differentiation of embryonic stem cells (ESCs) and induced pluripotent stem cells (iPSCs) confine the usage of these potential models in clinical applications. Hence, to maximize ESC/iPSC usage in clinical applications, protocols restricting ESC/iPSCs spontaneous differentiation and directing them into specific lineage is desirable.

Features of our invention:

- Our invention relates to synthesis of multi-sheet ECM structures from fibroblast derived matrices for tissue engineering and regenerative medicine applications.
- We have shown the usage of fibroblast engineered matrices for inducing germ layer differentiation in naive pluripotent stem cells.
- We provide methods of making different fibroblast derived matrices of varying biophysical properties suitable for expansion of embryonic stem cells (ESCs) and for inducing regulated germ layer differentiation in ESCs. We provide the method of encouraging production of endogenous growth factors by differentiating ESCs. These matrices can also be used as homing ECM for stem cells during their isolation process, and as a scaffold for stem cell expansion without any added growth factors.

Advantages:

Extracellular matrix scaffolds produced are capable of:

- Improved output in maintaining stem cell viability.
- Improved output in directing stem cells into specific lineage.
- Inducing production of endogenous growth factors by differentiating stem cells.
- Inducing production of altered Matrix metalloproteases (MMPs) during differentiating stem cells.