Embryonic stem cells are commonly differentiated as 3D spheroids referred to as “embryoid bodies” (EBs). Although EBs can yield derivatives of all 3 germ lineages (ectoderm, endoderm and mesoderm), directed differentiation to any one lineage or specific cell phenotype is often difficult to attain in practice. By spatiotemporally engineering the molecular and cellular elements of the microenvironment of EBs, it may be possible to improve the efficiency and efficacy of directed differentiation strategies. The objective of this proposal is to incorporate “layer-by-layer” technologies being developed by Dr. GE’s lab with microsphere-mediated embryoid body differentiation technologies being developed by Dr. McDevitt’s laboratory. In addition, genetically modified ES cell lines being developed by Dr. Wang’s lab will be used to assess mesoderm differentiation. The interdisciplinary and complementary sets of expertise should lead to a fruitful collaboration and generate sufficient preliminary data to pursue subsequent extramural funding opportunities for the team of investigators.