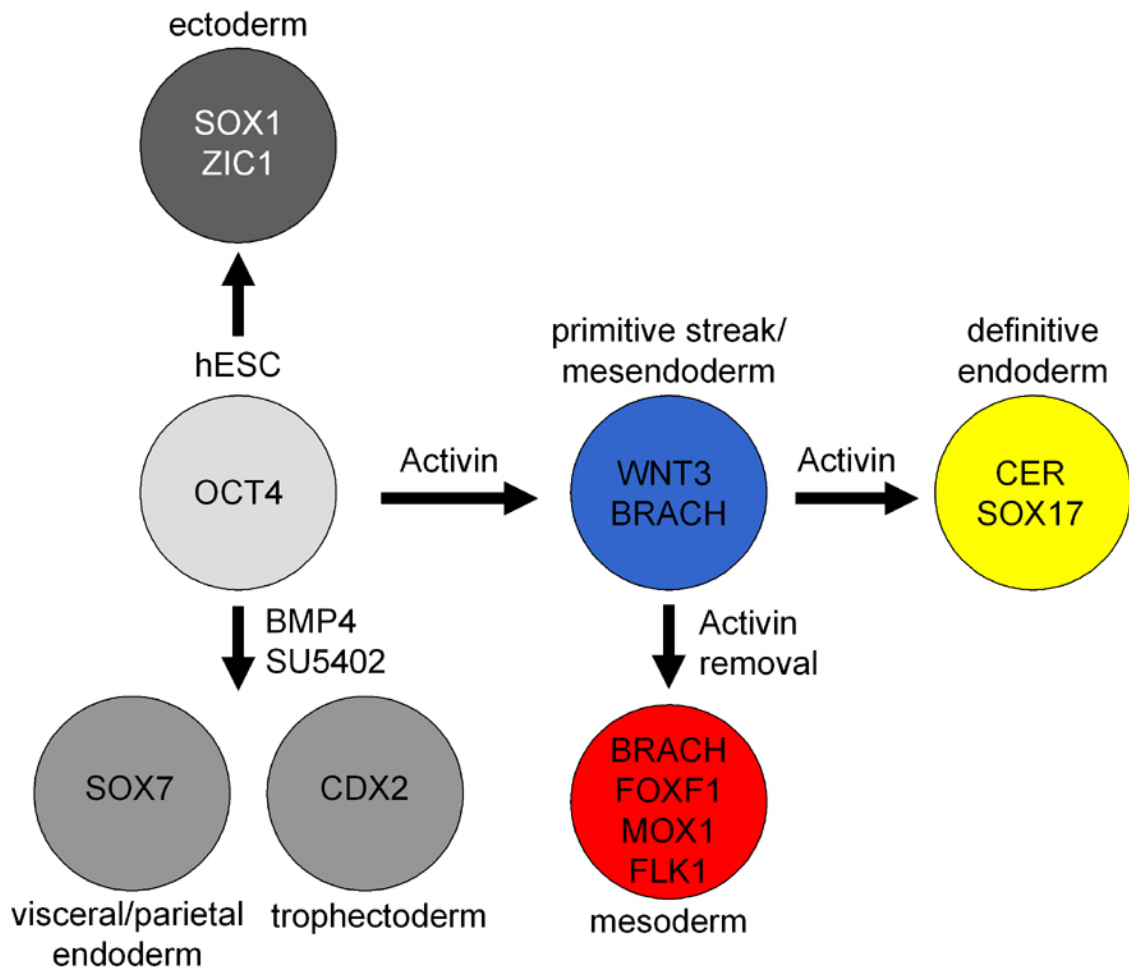


Supplementary Fig. 8 Model summarizing transitions during hESC differentiation.



Differentiation of hESCs through a process that closely recapitulates gastrulation can be orchestrated by the application of high dose activin A in the context of low serum supplementation. Maximal expression of primitive streak-expressed genes (WNT3, BRACH) occurs at 24-36 hours. If maintained in high dose activin A, the primitive streak-like cells are efficiently converted into cells that express definitive endoderm markers (SOX17, CER). In contrast, if exogenous activin A is removed, cells express mesoderm markers (BRACH, FOXF1, MOX1, FLK1). Treatment of hESCs with BMP4/SU5402 induces gene expression associated with primitive endoderm (visceral endoderm and parietal endoderm) and trophoctoderm.