## Wnt signaling mediates self-organization and axis formation in embryoid bodies.

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**Public Summary:**
Embryonic stem cells (ES cells) are pluripitent because they form all three germ layers and all cell types. This can be accomplished when ES cells differentiate as aggregates, termed embryoid bodies. Differentiation of cells depends on signals that provide instructive and positional cues, but do such gradients exist in embryoid bodies? We report here the establishment of polarity and the formation of a specialized are called the primitive streak-like region in the embryoid body, dependent on local activation of Wnt signals. In this region, cells undergo an epithelial-to-mesenchymal transition and differentiate into mesendodermal progenitors. Exogenous Wnt3a protein posteriorizes the embryoid body, resulting in predominantly mesendodermal differentiation. Conversely, inhibiting Wnt signaling promotes anterior character and results in neurectodermal differentiation. The activation of Wnt signaling and primitive streak formation requires external signals but is self-reinforcing after initiation. Our findings show that the Wnt pathway mediates the local execution of a gastrulation-like process in the embryoid body, which displays an unexpected degree of self-organization.

**Scientific Abstract:**
Embryonic stem cells (ESCs) form descendants of all three germ layers when differentiated as aggregates, termed embryoid bodies. In vivo, differentiation of cells depends on signals and morphogen gradients that provide instructive and positional cues, but do such gradients exist in embryoid bodies? We report here the establishment of anteroposterior polarity and the formation of a primitive streak-like region in the embryoid body, dependent on local activation of the Wnt pathway. In this region, cells undergo an epithelial-to-mesenchymal transition and differentiate into mesendodermal progenitors. Exogenous Wnt3a protein posteriorizes the embryoid body, resulting in predominantly mesendodermal differentiation. Conversely, inhibiting Wnt signaling promotes anterior character and results in neurectodermal differentiation. The activation of Wnt signaling and primitive streak formation requires external signals but is self-reinforcing after initiation. Our findings show that the Wnt pathway mediates the local execution of a gastrulation-like process in the embryoid body, which displays an unexpected degree of self-organization.