Differential Adhesion Molecule Expression during Murine Embryonic Stem Cell Commitment to the Hematopoietic and Endothelial Lineages.

Journal: PLoS One

Publication Year: 2011

Authors: Basha L Stankovich, Esmeralda Aguayo, Fatima Barragan, Aniket Sharma, Maria G Pallavicini

PubMed link: 21909405

Funding Grants: Stem Cell Research Training Grant

Public Summary:
Mouse embryonic stem cells (ESC) make cell fate decisions based on intrinsic and extrinsic factors. The decision of ESC to differentiate to multiple lineages in vitro occurs during the formation of embryoid bodies (EB) and is influenced by cell-environment interactions. However, molecular mechanisms underlying cell-environmental modulation of ESC fate decisions are incompletely understood. Since adhesion molecules (AM) influence proliferation and differentiation in developing and adult tissues, we hypothesized that specific AM interactions influence ESC commitment toward hematopoietic and endothelial lineages. Expression of AM in the adherens, tight and gap junction pathways in ESC subpopulations were quantified. E-cadherin (E-cad), Claudin-4 (Cldn4), Connexin-43 (Cx43), Zona Occludens-1 (ZO-1) and Zona Occludens-2 (ZO-2) transcript levels were differentially expressed during early stages of hematopoietic/endothelial commitment. Stable ESC lines were generated with reduced expression of E-cad, Cldn4, Cx43, ZO-1 and ZO-2 using shRNA technology. Functional and phenotypic consequences of modulating AM expression were assessed using hematopoietic colony forming assays, endothelial sprouting assays and surface protein expression. A decrease in E-cad, Cldn4, Cx43 and ZO-1 expression was associated with less commitment to the hematopoietic lineage and increased endothelial differentiation as evidenced by functional and phenotypic analysis. A reduction in ZO-2 expression did not influence endothelial differentiation, but decreased hematopoietic commitment two-fold. These data indicate that a subset of AM influence ESC decisions to commit to endothelial and hematopoietic lineages. Furthermore, differentially expressed AM may provide novel markers to delineate early stages of ESC commitment to hematopoietic/endothelial lineages.

Scientific Abstract:
Mouse embryonic stem cells (ESC) make cell fate decisions based on intrinsic and extrinsic factors. The decision of ESC to differentiate to multiple lineages in vitro occurs during the formation of embryoid bodies (EB) and is influenced by cell-environment interactions. However, molecular mechanisms underlying cell-environmental modulation of ESC fate decisions are incompletely understood. Since adhesion molecules (AM) influence proliferation and differentiation in developing and adult tissues, we hypothesized that specific AM interactions influence ESC commitment toward hematopoietic and endothelial lineages. Expression of AM in the adherens, tight and gap junction pathways in ESC subpopulations were quantified. E-cadherin (E-cad), Claudin-4 (Cldn4), Connexin-43 (Cx43), Zona Occludens-1 (ZO-1) and Zona Occludens-2 (ZO-2) transcript levels were differentially expressed during early stages of hematopoietic/endothelial commitment. Stable ESC lines were generated with reduced expression of E-cad, Cldn4, Cx43, ZO-1 and ZO-2 using shRNA technology. Functional and phenotypic consequences of modulating AM expression were assessed using hematopoietic colony forming assays, endothelial sprouting assays and surface protein expression. A decrease in E-cad, Cldn4, Cx43 and ZO-1 expression was associated with less commitment to the hematopoietic lineage and increased endothelial differentiation as evidenced by functional and phenotypic analysis. A reduction in ZO-2 expression did not influence endothelial differentiation, but decreased hematopoietic commitment two-fold. These data indicate that a subset of AM influence ESC decisions to commit to endothelial and hematopoietic lineages. Furthermore, differentially expressed AM may provide novel markers to delineate early stages of ESC commitment to hematopoietic/endothelial lineages.