Human Embryonic Stem Cells Do Not Change Their X Inactivation Status during Differentiation.

Journal: Cell Rep
Publication Year: 2017
Authors: Sanjeet Patel, Giancarlo Bonora, Anna Sahakyan, Rachel Kim, Constantinos Chronis, Justin Langerman, Sorel Fitz-Gibbon, Liudmilla Rubbi, Rhys J P Skelton, Reza Ardehali, Matteo Pellegrini, William E Lowry, Amander T Clark, Kathrin Plath
PubMed link: 27989715
Funding Grants: Discovery of mechanisms that control epigenetic states in human reprogramming and pluripotent cells, Understanding the status of the X chromosomes in human ESCs and preimplantation embryos

Public Summary:
Applications of embryonic stem cells (ESCs) require faithful chromatin changes during differentiation, but the fate of the X chromosome state in differentiating ESCs is unclear. Female human ESC lines either carry two active X chromosomes (XaXa), an Xa and inactive X chromosome with or without XIST RNA coating (XiXIST+Xa;XiXa), or an Xa and an eroded X (XeXa) where the Xi no longer expresses XIST RNA and has partially reactivated. Here, we established XiXa, XeXa, and XaXa ESC lines and followed their X chromosome state during differentiation. Surprisingly, we found that the X state pre-existing in primed ESCs is maintained in differentiated cells. Consequently, differentiated XeXa and XaXa cells lacked XIST, did not induce X inactivation, and displayed higher X-linked gene expression than XiXa cells. These results demonstrate that X chromosome dosage compensation is not required for ESC differentiation. Our data imply that XiXIST+Xa ESCs are most suited for downstream applications and show that all other X states are abnormal byproducts of our ESC derivation and propagation method.

Scientific Abstract:
Applications of embryonic stem cells (ESCs) require faithful chromatin changes during differentiation, but the fate of the X chromosome state in differentiating ESCs is unclear. Female human ESC lines either carry two active X chromosomes (XaXa), an Xa and inactive X chromosome with or without XIST RNA coating (XiXIST+Xa;XiXa), or an Xa and an eroded X (XeXa) where the Xi no longer expresses XIST RNA and has partially reactivated. Here, we established XiXa, XeXa, and XaXa ESC lines and followed their X chromosome state during differentiation. Surprisingly, we found that the X state pre-existing in primed ESCs is maintained in differentiated cells. Consequently, differentiated XeXa and XaXa cells lacked XIST, did not induce X inactivation, and displayed higher X-linked gene expression than XiXa cells. These results demonstrate that X chromosome dosage compensation is not required for ESC differentiation. Our data imply that XiXIST+Xa ESCs are most suited for downstream applications and show that all other X states are abnormal byproducts of our ESC derivation and propagation method.