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mTERT EXPRESSION IS INCREASED IN THE MDX MODEL OF CARDIOMYOPATHY

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Recent studies have suggested the mammalian heart has innate regenerative potential, but evidence for this remains limited and incomplete. Previously, using the murine telomerase reverse transcriptase (mTert) reporter and fate mapping mice, we demonstrated that cells expressing mTert respond to cardiac cyro-injury and contribute to the formation of new cardiomyocytes. In mdx mice (model of Duchene muscular dystrophy), cardiomyocyte loss begins in the embryo yet cardiac function remains normal until ~42-weeks. To investigate if mTert expressing cells respond to cardiomyocyte loss in this model we established mTert-GFP/DMDmdx mice and quantified mTert cells at different ages. At 13 weeks mdx mice had significantly elevated cardiac mTert-GFP cell numbers when compared to control. Suggesting that this response may be associated with cardiomyocyte renewal, increased mTert-GFP+ cells co-expressing the cardiac transcription factor NKX2.5 or markers o f mature cardiomyocytes (Troponin I) we also observed. Given the association of telomerase and stem cell biology we investigated cardiac stem cell activity in this model. A significant increase in the number of cardiac side population (CSP) cells in the hearts of 13 weeks mdx mice was observed. Suggesting this was not due to a systemic increase in SP, there was no difference in bone marrow SP or peripheral blood. Furthermore mTert was expressed a subpopulation of the CSP and this population was also increased in mdx hearts. We suggest that mTert expressing cells are involved in cardiomyocytye regeneration; mTert fate mapping studies have the potential to provide more definitive evidence of cardiomyocyte renewal in the mdx heart.