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Mitochondrial MTG1 is Necessary for Proper Human Cardiomyocyte Activity and Zebrafish Cardiac Development: Comment to “Novel role of mitochondrial GTPases 1 in pathological cardiac hypertrophy”

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A recent paper by Xu and colleagues published in the *Journal of Molecular and Cellular Cardiology* highlights the role of a mitochondrial ribosome-associated GTPase, MTG1, in cardiac adaptation to stress [1]. The authors found that MTG1 is elevated in hearts of dilated cardiomyopathy patients and in mice exposed to left ventricular pressure overload (AB), which led them to explore the role of MTG1 in cardiac hypertrophy and heart failure. For that purpose Xu *et al.* performed interesting MTG1 loss/gain of function studies in cultured cardiomyocytes and mice exposed to hypertrophic stress. To investigate the *in vivo* impact of MTG1 on the heart and its influence on cardiac hypertrophy, they generated MTG1 global knockout (KO) mice, which were “viable, fertile, and exhibited no pathological observable phenotype under basal conditions” [1]. This is an unexpected observation. Considering that MTG1 is essential for mitochondrial ribosome biogenesis and cell survival [2], one would have had expected embryonic lethality. In fact, the essentiality of MTG1 prevented the generation of HEK293T cell lines homozygous *MTG1*-KO [2]. The possibility exists that some compensatory mechanisms could be in place to allow the survival of global *MTG1*-KO mice. Independently, Xu *et al.* obtained interesting data to show that whereas MTG1 deficiency significantly exacerbated AB-induced cardiac hypertrophy, it was attenuated by transgenic cardiac MTG1 expression and also by regulation of the TAK1-P38-JNKs signaling pathway and oxidative stress [1]. The authors claim that their results are “the first to indicate MTG1 insufficiency leads to heart failure development” and “the first study to define a role for MTG1 in cardiac hypertrophy”. These results are consistent with our earlier findings where we identified MTG1 as necessary for proper human cardiomyocyte activity and zebrafish cardiac development [2]. Likewise, we previously reported the specific role of MTG1 in the biogenesis of the mitochondrial ribosome and its requirement for mitochondrial translation and oxidative phosphorylation function. Given the frequent clinical outcome of mitoribosome assembly and mitochondrial translation defects as pure or syndromic mitochondrial cardiomyopathies [3], our study and the study by Xu *et al.* highlight the deleterious potential of *MTG1* as a mitochondrial cardiomyopathy gene.

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