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PROTEOMIC ANALYSES OF PITX2 LACK OF FUNCTION IN VENTRICULAR MYOCARDIUM

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The heart is the first organ to display morphologic asymmetry during development. However, a left-right differential gene expression program starts earlier in the lateral plate mesoderm. The final effector of this left-right signalling pathway is the bicoid-related homeodomain transcription factor *Pitx2*. Implication of this factor in heart development has been proposed by analyses of *Pixt2abc* null mice, which display several cardiac malformations. However, the functional and temporal contribution of this transcription factor during heart development is poorly understood. In this work, by using two-dimensional gel electrophoresis (2-DE), we compared the proteome of mice lacking all *Pitx2* isoforms in the ventricular myocardium and outflow tract versus control mice. More than 200 proteins were resolved in each gel. Twenty-two proteins with significative change in expression were detected. Twelve of them were down-regulated in Pitx2 conditional mutant mice whereas ten proteins were up-regulated. Identification of these proteins by mass spectrometry suggests that several cellular processes may be altered in these conditional mutant mice. These cellular processes are metabolism (increase of glycolisis, TCA cycle and BCAA metabolism, and partial inhibition of β-oxidation), energy production (inhibition of oxidative phosphorylation), and cell stress (increase of anti-oxidative defence). The combination of these alterations suggest that specific delection of all isoforms of *Pitx2* in ventricular myocardium and outflow tract could drive to cardiac physiopathology characterised by ischemia and oxidative stress.