227 **IDENTIFYING THE PROTEIN KINASES IN THE CARDIAC MYOCYTE KINOME**

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Background Protein kinases regulate every aspect of cell function, including the cell fate decisions of cardiac myocytes that lead to cardiac pathologies. They are attractive therapeutic targets because of their enzymatic activities and substrate-binding/catalytic sites that are readily targeted by small molecules. There are over 500 protein kinases in the mammalian kinome. The most well-studied cardiac protein kinases were mostly identified in the context of cancer or inflammation, and many kinases that are highly expressed in heart remain poorly investigated. The aim is to unlock the potential of protein kinases as therapeutic targets for heart diseases by defining the cardiac myocyte kinome (i.e. the panoply of protein kinases expressed in cardiac myocytes).

Methods and Results We have mined microarray data from neonatal and adult rat ventricular myocytes (NRVMs and ARVMs, respectively) for mRNA expression levels of all protein kinases listed in the human/mouse kinome. We have identified significant expression of 296, including some that have never previously been studied in heart. mRNA expression levels of 253 are within a 1.5-fold range in the two cell types. Thus, although many argue that studies in NRVMs are not reflective of the adult state, for study of most protein kinases, neonatal rat ventricular myocytes are a reasonable experimental model to use. Thirty-one protein kinases are more highly expressed in NRVMs, including cyclin-dependent kinases required for cell cycle progression. Nevertheless, mRNA expression in ARVMs is still significant. Twelve protein kinases are more highly expressed in ARVMs including some that have not been well-characterised in any tissue and for which there are few/no studies in the heart. Expression at the protein level has been confirmed for some novel cardiac kinases (e.g. MAP4K3, MAP4K4, MAP4K5). mRNA data for human heart biopsies are largely in accord with the data for rat cardiac myocytes. The most highly expressed protein kinase in ARVMs is Pink1 (associated with neurological disorders), which is also highly expressed in human heart biopsies.

Conclusion Cardiac myocytes express many protein kinases, some of which have never previously been studied in the context of their likely contribution to cardiac function. These data will provide a resource and will lay a solid foundation for identifying the most suitable targets in the cardiac myocyte kinome for the amelioration of heart failure.