Gene expression of stretch activated channels and mechanoelectric feedback in the heart

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In the heart, mechanical forces on the myocardium can induce electrical disturbances (mechano-electric feedback or MEF). It seems likely that MEF involves stretch sensitive non specific cation channels (SACs) and mechanosensitive potassium channels in the myocardial cell membrane (Hu and Sachs, 1997; Kim, 1992).

Using patch clamp techniques we have characterised a mechanosensitive potassium channel in isolated rat ventricular myocytes. The channel is highly selective for K^+, has a conductance of c.100 pS, and responds strongly to suction applied to the patch electrode. We propose that this channel is *TREK-1*, a member of the 4T2P gene family (Lesage and Lazdunski, 2000) since *TREK-1*, when expressed in heterologous systems, has been shown to have the combination of properties that matches our functional measurements in cardiac cells (Maingret *et al,* 1999), and RT-PCR has shown the gene for *TREK-1* to be expressed in the heart (Aimond *et al,* 2000).

In order to control dispersion of repolarisation, the cardiac action potential has a very different morphology in different parts of the heart, a crucial determinant of this action potential heterogeneity being the variation in the expression level of the voltage dependent potassium channels. Here we report that the gene expression level of TREK-1 is also spatially heterogenenous in adult rat ventricle. Using real-time RT-PCR against GAPDH as a comparator gene, *TREK-1* expression was found to be 0.34 ± 0.14 in endocardial cells compared to 0.02 ± 0.02 in epicardial cells ($p < 0.05$). In agreement with this differential gene expression, whole cell TREK-1 current density, activated by chloroform, was larger in endocardial cells (0.8 ± 0.27 pA/pF) compared to epicardial cells (0.21 ± 0.06 pA/pF) ($p < 0.05$).

We hypothesise that this differential expression of *TREK-1* may be related to the distribution of stress across the ventricular wall and may play a role in synchronisation of repolarisation during contraction of the ventricle.

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