THE F-CURRENT IN NON-PACEMAKER CELLS: ROLE AND PHARMACOLOGICAL IMPLICATIONS

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Pacemaker channels play a major role in the generation of sinoatrial rhythmic activity. However, their expression is not confined to specialized myocardial cells, such as primary and subsidiary pacemakers. Electrophysiological and molecular data collected over the last ten years, demonstrated that f-channels are present also in non-pacemaker cardiomyocytes. These channels are highly expressed in fetal and neonatal cardiomyocytes and even in embryonic stem (ES) cells and ES-derived cardiomyocytes. In the adult heart, I_f current densities and/or mRNA levels of its molecular correlate (i.e. hyperpolarization-activated cyclic nucleotide-gated (HCN) channels) are increased during the development of cardiac hypertrophy and failure. Over-expression of f-channels in non-pacemaker cells are one of the consequence of the process of cardiac remodeling and it has been suggested that this phenomenon may represent an arrhythmogenic mechanism in heart failure, a condition associated with high risk for sudden cardiac death. However, it remains controversial whether I_f over-expression might play a role for the increased propensity of arrhythmias in diseased states because I_f current activation was obtained at more negative potentials in working myocardium than in pacemaker cells. The availability of selective f-channel blockers such as ivabradine will help in the near future to assess the potential arrhythmogenic role of I_f in heart disease.