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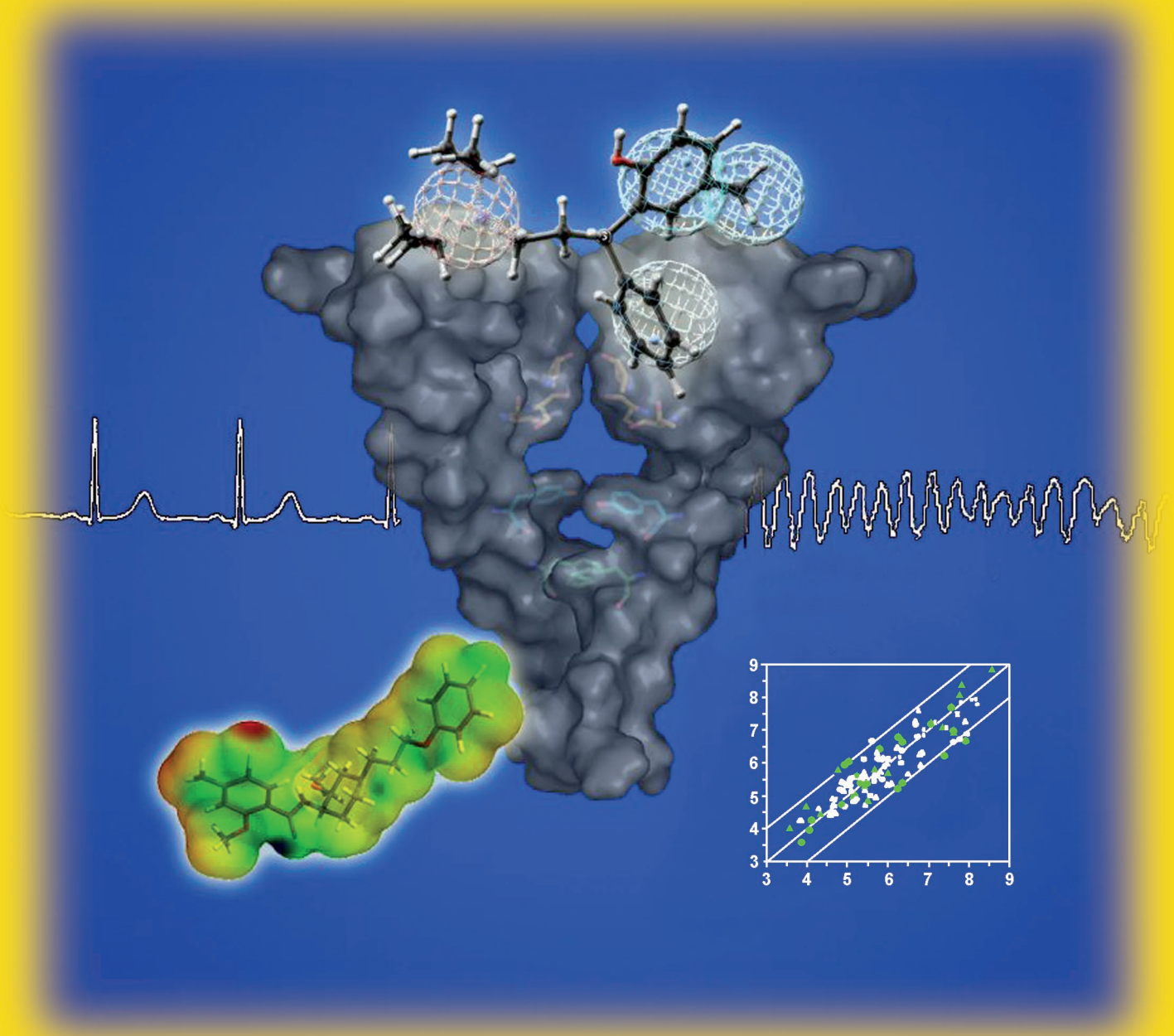
CHEMMEDCHEM

CHEMISTRY ENABLING DRUG DISCOVERY



2/2008

Review: Treatment of Dyslipidemia
(O. Rau)
Full Paper: P-Glycoprotein Binding Sites
(M. Wiese)

EU ChemSoc

WILEY-VCH

Cover Picture

Christian Kramer, Bernd Beck*, Jan M. Kriegl, and Timothy Clark*

The cover picture shows a schematic representation of the hERG-encoded potassium channel together with one pharmacophore for potent hERG inhibitors, the MEP surface of cisapride, a potent hERG inhibitor, and a plot of measured versus predicted hERG IC_{50} values. Blockade of the hERG channel leads to a prolongation of the QT interval, which might lead to torsades des pointes, an uncontrolled excitation of heartbeats. On the cover picture, an ECG plot of normal heartbeats (middle left side) and an ECG plot of torsades des pointes (middle right side) is shown in white. Torsades des pointes might lead to lethal ventricular fibrillation. Therefore the inhibition of hERG is one of the major toxicological endpoints addressed in preclinical drug development. The combination of different hERG pharmacophores, derived from highly potent structurally diverse inhibitors together with specific QSAR models, offers a novel approach to predict hERG blockade. For details, see the Full Paper by B. Beck, T. Clark, et al. on p. 254 ff.