



# Luc Hondeghem

MD, PhD

I was active in cardiac electrophysiology for fifteen years at UCSF, and for five years as a Director at the Stahlman Cardiovascular Research Laboratories of Vanderbilt University. I returned to Belgium in 1990 and founded an electrophysiological laboratory (Hondeghem Pharmaceutical Consulting). The laboratory conducted over 25,000 experiments. All were aimed at developing effective and safe cardiac antiarrhythmic agents to cure cardiac diseases. To my regret, some companies deemed detecting cardiac problems more important than curing them. I participated in 82 publications and 33 books, of which my most recent is "Big Pharma, Big Lies".

## CONTACT



luc.hondeghem@screenqt.com



[www.linkedin.com/in/luc-hondeghem](http://www.linkedin.com/in/luc-hondeghem)



Ostend, Belgium

## EDUCATION

### PhD in Pharmacology

UCSF, San Francisco

1973

### MS in Physiology

Catholic University Leuven, Belgium

1971 - Summa cum laude

### MD Medicine

Catholic University Leuven, Belgium

1970

## EXPERIENCE

1990-today

### Professor Medicine & Pharmacology | K.U. Leuven

32 years

- Teaching cardiovascular electrophysiology

1990-2003

### President | Hondeghem Pharmaceutical Consulting

13 years

- Data analysis and report writing
- Publications research

1985-1990

### Professor Medicine & Pharmacology

### Director of Stahlman Cardiovascular Research Vanderbilt University

15 years

- Endowed chair
- Start-up cardiovascular research center

1982-1987

### Established Investigator | American Heart Association

5 years

1981

### US Patent Holder

- #4,255,790 for Programmable Pulse Generating System

1973-1985

### Assistant & Associate Professor of Pharmacology | UCSF San Francisco

12 years

- Best Teaching Award students
- Best Teaching Award Academic Senate

# PUBLICATIONS

---

## Abstracts

Hondeghem LM, Jensen RA:

In vitro effects of quinidine, diphenylhydantoin and lidocaine on impulse conduction at the Purkinje-myocardial fiber junction  
Fifth International Congress on Pharmacology p105 (#626) 1972

Hondeghem LM, De Geest H:

Additive effects on atrial rate of acetylcholine released by vagal nerve stimulation  
FASEB 32:799 (#3280) 1973

Grant AO, Hondeghem LM, Katzung BG:

Effects of dehydrobenzperidol in guinea pig papillary muscle in vitro  
ASPET Fall Meeting 16:224 (#189) 1974

Katzung BG, Hondeghem LM, Grant AO:

Selective depression of ventricular extrasystoles induced by depolarizing current of injury: Effects of epinephrine and barium  
Sixth International Congress on Pharmacol p510 (#1219) 1975

Katzung BG, Hondeghem LM, Morgenstern J:

Computer simulation of cardiac arrhythmogenesis and antiarrhythmic drug action International Society for Heart Research p50,  
1977

Hondeghem LM:

Rate and voltage dependent effects of procainamide: A test of model for antiarrhythmic drug action  
ASPET Fall Meeting 19:152 (#140) 1977

Hondeghem LM, Katzung BG:

Prediction of the rate, rhythm and voltage dependent effects of quinidine and lidocaine on the upstroke ( $V_{max}$  of the cardiac  
action potential  
Circulation 56:III-135 (#519) 1977

8Hondeghem LM, Katzung BG:

Comparison of the observed and predicted effects of quinidine and lidocaine in atrial, ventricular and Purkinje fibers  
Seventh International Congress of Pharmacology, Paris, France, 1978

Hondeghem LM, Katzung BG:

Combined effects of quinidine and lidocaine on  $V_{max}$  of the cardiac action potential

FASEB 1979

Housmans PR, Hondeghem LM, Vermeyen KM, Lewis MJ, Tjandramaga TB, Verbesselt AR, Hannegreefs GH, Brutsaert DL:

Depressed contractile sensitivity of mammalian ventricular myocardium to ouabain following chronic digoxin exposure

European Congress of Cardiology, Paris, France, 1980

Hondeghem LM, Courtney KR:

Cardiac sodium channels are different from nerve and skeletal muscle sodium channels *Biophys J* 33:211, 1981

Moyer JR, Ehring GR, Hondeghem LM:

Kinetics of interaction of a series of aprindine derivatives with the cardiac sodium channel

FASEB (#8575) 1982

Hondeghem LM, Kanaya S, Arlock P, Katzung BG:

Verapamil and diltiazem block inactivated calcium channels

*Circulation* 66:II-293 (#1173) 1982

Mason JW, Hondeghem LM, Katzung BG:

Amiodarone blocks inactivated  $Na^+$  channels

*Circulation* 66:II-2 92 (#1168) 1982

Hondeghem LM, Ayad MJ:

Depolarization induced potentiation of norepinephrine contractions can be blocked by nifedipine

*Biophysical Journal* 41:310a (#T-PM-G7) 1983

Clarkson CW, Mason JW, Matsubara T, Moyer JW, Hondeghem LM:

Slow inactivation in guinea pig ventricular myocardium

*Biophysical Journal* 41:309a (#T-PM-G6) 1983

Clarkson CW, Thigpen T, Shnider SM, Hondeghem LM:

Bupivacaine toxicity: Fast inactivation block and slow diastolic recovery

*Circulation* 68:III-296 (#1184) 1983

Moyer JW, Hondeghem LM:

Characterization of activation and inactivation block in a series of aprindine derivatives using voltage clamp techniques  
FASEB 1983

Matsubara T, Hondeghem LM:

Mechanism for preferential effectiveness of lidocaine against ventricular arrhythmias *Circulation* 68:III-295 (#1180) 1983

Hondeghem L:

Antiarrhythmic drug action on  $V_{max}$  of cardiac cells  
Research Committee Meeting of AHA, Boston, 1984

Clarkson CW, Hondeghem LM, Matsubara T, Levinson G:

Possible mechanism of bupivacaine toxicity: Fast inactivation block with slow diastolic recovery  
*Anesthesia and Analgesia* 63:199, 1984

Clarkson CW, Hondeghem LM:

Evidence that quinidine, lidocaine and bupivacaine interact with a single common receptor site in cardiac sodium channels.  
*Circulation* 70:II-273,1984

Hondeghem LM, Clarkson CW:

Modulated receptor theory and cardiac toxicity of local anesthetics  
*Molecular and Cellular Mechanisms of Anesthesia*, Calgary 1984

Davis JC, Matsubara T, Moraday F, Scheinman MM, Hondeghem LM:

Modulation of lidocaine's use-dependent block and recovery from block by pH  
*Am J Cardiol* 5:467, 1985

Clarkson CW, Follmer CH, Yeh JZ, Ten Eick RE, Hondeghem LM:

Evidence for two components of sodium channel block by lidocaine in single isolated cardiac myocytes  
*Circulation* 72:II-152, 1985

Kopelman HA, Bajaj AK, Wikswo JP Jr, Hondeghem LM, Woosley RL, Roden DM:

Frequency- and direction-dependent effects of single and combination antiarrhythmic drugs on conduction velocity in vivo  
American College of Cardiology, 35th Annual Scientific Session. *J Am Coll Cardiol* 1986:7:82A

Roden DM, Bennett PB, Hondeghem LM:

Quinidine blocks cardiac potassium channels in a time- and voltage-dependent fashion *Biophys J* 49:352, 1986

Stroobandt R, Bennett PB, Hondeghem LM, Kesteloot H:

Transcainide, a new antiarrhythmic drug

*Eur Conf Clin Cardiol*, 1986.

Bennett PB, Woosley B, Hondeghem LM:

Competitive interactions of lidocaine (L) and one of its metabolites, glycine xylidide (GX) with cardiac sodium channels

*Circulation* 74:II-20, 1986

Roden DM, Bennett PB, Snyders D, Hondeghem LM:

Quinidine reduces IK and delays its activation

*Circulation* 74:II-255, 1986

Snyders DJ, Hondeghem LM, Katzung BG:

Sigmoidal time course of IK activation in cardiac myocytes

*Circulation* 74:II-255, 1986

Snyders DJ, Bennett PB, Hondeghem LM:

Quinidine block of cardiac sodium channels

Meeting of the working group of cardiac cellular electrophysiology, Bern, Switzerland, September 1986

Kesteloot H, Stroobandt R, Bennett PB and Hondeghem LM:

Transcainide, a new antiarrhythmic drug

Japan 1986

Bennett PB, Hondeghem LM:

Frequency-independent block of cardiac sodium channels by a potent lidocaine analog, transcainide

*Biophys J* 51:435, 1987

Snyders DJ, Hondeghem LM:

Voltage- and temperature-dependent recovery of quinidine-blocked cardiac sodium channels

*Biophys J* 51:260, 1987

Bennett PB, Kabalka G, Kennedy TT, Woosley RL, Hondeghem LM:

An amiodarone derivative with reduced toxicity and Na-channel blocking properties *Circulation* 76:IV-150, 1987

Snyders DJ, Hondeghem, LM:

Use-dependent unblocking of quinidine-blocked sodium channels: slowed activation and inactivation.

*Circulation* 76:IV-150, 1987

Balsler JR, Hondeghem LM, Roden DM:

Quinidine Block of IK Accumulates at Negative Potentials

*Circulation* 76:IV-149, 1987

Balsler JR, Hondeghem LM, Roden DM:

Amiodarone reduces time dependent IK activation

*Circulation* 76:IV-151, 1987

Anno T, Johns J, Snyders D, Bennett P, Hondeghem L:

O-Demethyl encainide (ODE) interacts with cardiac sodium channels in a temperature-and voltage-dependent fashion.

*Biophys J* 53:536, 1988

Johns J, Hondeghem L:

Voltage- and time-dependent effects of verapamil upon the Ca<sup>++</sup> Current and [Ca<sup>++</sup>]<sub>i</sub> transient in cardiac myocytes.

*Biophys J* 53:159, 1988

Balsler JR., Hondeghem LM, Roden DM:

Drug block of the delayed rectifier IK in heart: multiple state-dependent mechanisms.

*Clinical Research* 36:260A, 1988

Snyders DJ, Hondeghem LM:

Use-dependent unblocking of cardiac sodium channels: evidence for an RD state

XII Workshop on Cardiac electrophysiology, Leuven Belgium, 1988

Bennett PB, Hondeghem LM:

Modulated receptor hypothesis: single channel applications.

XII Workshop on Cardiac electrophysiology, Leuven Belgium, 1988

Anno T, Hondeghem LM:

Isoproterenol-enhanced slow inactivation block of cardiac sodium channels in the presence of flecainide.

International congress on Molecular and cellular mechanisms of antiarrhythmic agents, Nashville, 1988

Hondeghem LM:

Demonstration of an analytical solution of the modulated receptor hypothesis as a graphical educational tool

International congress on Molecular and cellular mechanisms of antiarrhythmic agents, Nashville, 1988

Hagiwara H, Hare GMT, Johns JA, Hondeghem LM, Sugiura M, Inagami T:

Sustained endothelin-induced vasoconstriction associated with transiently elevated calcium

42nd Annual Fall Conference and Scientific Sessions, AHA 1988

Johns JA, Hondeghem LM:

Two mechanisms of the positive staircase phenomenon

Circulation 1988

Bennett PB, Hondeghem LM:

Inhibition of sodium conductance by quinidine: single channel blocking mechanisms. Circulation 1988

Murray KT, Anno T, Bennett PB, Hondeghem LM:

Voltage clamp of cardiac sodium current in 145 mM sodium at 37°C

J Molec and Cell Cardiol 1989

Anno T, Hondeghem LM:

Voltage-dependent recovery from flecainide block is due to activation unblocking

Biophys J 55:289, 1989

Bennett PB, Balsler JR, Hondeghem LM:

A model of the sodium channel: Macroscopic and single behavior

Biophys J 55:318, 1989

Bennett PB, Valenzuela C, Hondeghem LM:

Modulation of cardiac Na, Ca, and K currents by amiodarone and des-oxo-amiodarone Biophys J 55:295, 1989

Murray KT, Hondeghem LM:

Voltage clamp of cardiac sodium current at 37°C: reduction by mexiletine

Biophys J 55:312, 1989

Hondeghem LM:

Modulated receptor hypothesis: from single channel to QRS

International Satellite Symposium of 53rd Annual Meeting of the Japanese Circulation Society, 1989

Valenzuela C, Bennett PB, Hondeghem LM:

Stereospecific block of cardiac Na channels by bupivacaine

Biophys J, 1990

Anno T, Bennett PB, Hondeghem LM, Snyders DJ:

Activation unblock of cardiac Na channels without opening

Biophys J, 1990

## **Brief Communications**

Hondeghem LM:

The effects of lidocaine on the excitability of canine Purkinje fibers in the presence of 2, 4-dinitrophenol

Proc West Pharmacol Soc 17:1-3, 1974

Hondeghem LM:

Selective depression of the ischemic and hypoxic myocardium by lidocaine

Proc West Pharmacol Soc 18:27-30, 1975

Hondeghem LM:

Effects of quinidine, lidocaine and phenytoin on the excitability of the ischemic rabbit heart

Proc West Pharmacol Soc 19:320-322, 1976

Hondeghem LM, Katzung BG:

A unifying molecular model for the interaction of antiarrhythmic drugs with cardiac sodium channels: Application to quinidine and lidocaine

Proc West Pharmacol Soc 20:253-256, 1977



Moyer JW, Hondeghem LM:

Rate, rhythm and voltage dependent effects of aprindine: A test of a model of the mechanisms of action of antiarrhythmic drugs  
Proc West Pharm Soc 21:57-61, 1978

Ehring GR, Hondeghem LM:

Rate, rhythm and voltage dependent effects of phenytoin: A test of a model of the mechanisms of action of antiarrhythmic drugs  
Proc West Pharm Soc 21:63-65, 1978

Hondeghem LM, Ehring GR, Moyer JW:

Observations on the nature of the voltage shift of antiarrhythmic drugs  
Proc West Pharmacol Soc 2 1:67-69, 1978

Ehring GR, Hondeghem LM:

Structural similarities and cardiac electrophysiological differences between lidocaine and procainamide  
Proc West Pharmacol Soc 23:163-166, 1980

Moyer JW, Hondeghem LM:

Effects of the combination of quinidine and lidocaine on the upstroke velocity of the cardiac action potential  
Proc West Pharmacol Soc 23:159-161, 1980

Hondeghem LM, van Bogaert PP, Brutsaert DL:

On the voltage clamping of isolated single cardiac myocytes  
Proc West Pharmacol Soc 24:255-277, 1981

Ehring GR, Hondeghem LM:

Antiarrhythmic structure-activity relationships in a series of lidocaine-procainamide derivatives  
Proc West Pharmacol Soc 24:221-224, 1981

Ehring GR, Moyer JW, Hondeghem LM:

Implications from electrophysiological differences resulting from small structural changes in antiarrhythmic drugs  
Proc West Pharmacol Soc 25:65-67, 1982

Hondeghem LM, Ayad M:

Nifedipine blocks the voltage dependent potentiation of norepinephrine in vascular smooth muscle  
Proc West Pharmacol Soc 231-233, 1983

Hondeghem LM, Matsubara T:

Quinidine and lidocaine: Activation and inactivation block

Proc West Pharmacol 27:19-21, 1984

Clarkson CW, Hondeghem LM:

Electrophysiological evidence that local anesthetics and antiarrhythmic drugs bind to a specific receptor site in cardiac sodium channels: Displacement of bupivacaine by lidocaine

Proc West Pharmacol 27:23-25, 1984

Hondeghem LM, Clarkson CW:

Is tetrodotoxin block of cardiac sodium channels voltage-dependent?

Proc West Pharmacol 28:9-10, 1985

Snyders DJ, Hondeghem LM:

Drug-associated sodium channels inactivate and reactivate at more negative potentials than drug-free channels

Proc West Pharmacol 30:149-151, 1987

Bennett PB, Kabalka G, Woosley RL, Hondeghem LM:

Block and enhancement of cardiac ion channel currents by des-oxo-amiodarone

Proc West Pharmacol, 1988

Hondeghem LM:

Antiarrhythmic and pro-arrhythmic activities of class I and class III agents

JMCC 26:CXLII, S33, 1994

Hondeghem LM:

Molecular basis of arrhythmogenic effects of antiarrhythmic agents

65 Jahrestagung der Deutschen Gesellschaft für Kardiologie- Herz und Kreislaufforschung.

Mannheim, 1999

## **Book Chapters**

Hondeghem LM, Mason JW:

Agents used in cardiac arrhythmias

Chapter 12:138-154, Lange Medical Publications, 1982 (1st edition)

Hondeghem LM, Miller RD:

Local anesthetics

Chapter 23:264-269, Lange Medical Publications, 1982 (1st edition)

Hondeghem LM, Clarkson CW, Matsubara T:

Bupivacaine: Fast in slow out (FISO)

Report to Anesthetic and Life Support Drugs Advisory Committee,

Department of Health and Human Services, October 4th, 1983

Hondeghem LM, Mason JW:

Agents used in cardiac arrhythmias

Chapter 13:158-174, Lange Medical Publications, 1984 (2nd edition)

Hondeghem LM, Miller RD:

Local anesthetics

Chapter 24:293-298, Lange Medical Publications 1984 (2nd edition)

Hondeghem LM, Katzung BG:

Mechanism of action of antiarrhythmic drugs

Chapter 21:459-476

In: Physiology and pathophysiology of the heart

Ed: N Sperelakis. Martinus Nyhoff Publishers, 1984

Clarkson CW, Inazawa M, Kanaya S, Hondeghem LM, Katzung BG:

Evidence for a modulated receptor mechanism of calcium channel blockade

Chapter 11:137-151

In: Calcium antagonists: Mechanism of action on cardiac muscle and vascular smooth muscle

Ed: N Sperelakis. Martinus Nyhoff Publishers, 1984

Hondeghem LM, Clarkson CW:

Modulated receptor theory and cardiac toxicity of local anesthetics in Molecular and Cellular Mechanisms of Anesthesiology

Ed: SH Roth and KW Miller. Plenum Medical Book Company, 1984

Covino BG, Graboys TB, Hondeghem LM, Merin RG, Strichartz GR, Vandam LD:

Guidelines for cardiotoxicity of local anesthetics in man

FDA subcommittee report 1985

Katzung BG, Hondeghem LM, Clarkson CW, Matsubara T:

Mechanisms for selective actions and interactions of antiarrhythmic drugs.

Chapter 23:199-205

In: Cardiac electrophysiology and arrhythmias

Ed: DP Zipes and J Jalife. Grune & Stratton 1985

Clarkson CW, Hondeghem LM:

Effects of antiarrhythmic drugs on conduction and automaticity

Chapter 30:407-420

In: Regulation of the Heart

Ed: H Rupp. Thieme-Stratton Inc NY, 1986

Hondeghem LM, Katzung BG:

Control of vascular smooth muscle contractility and the action of calcium channel  
blockers

Chapter 4:38-52

In: Regulation of the Heart

Ed: H. Rupp. Thieme-Stratton Inc. NY, 1986

Hondeghem LM:

Interaction of class I drugs with the cardiac sodium channel

Chapter 8:157-174

In: Handbook of experimental pharmacology: Antiarrhythmic drugs

Ed: EM Vaughan Williams and TJ Campbell

Springer-Verlag, 1989

Hondeghem LM, Mason JW:

Agents used in cardiac arrhythmias

Chapter 13:151-168

Lange Medical Publications, 1987 (3rd edition)

Hondeghem LM, Miller RD:

Local anesthetics

Chapter 24:289-294, Lange Medical Publications, 1987 (3rd edition)

Hondeghem LM, Katzung BG:

Mechanism of action of antiarrhythmic drugs

Chapter 24:509-525

In: Physiology and pathophysiology of the heart

Ed: N Sperelakis. Martinus Nyhoff Publishers 1989

Mason JW, Hondeghem LM:

Principles of cardiac electrophysiology

Chapter 30:102-110

In: Textbook of Internal Medicine

Ed: William N. Kelley

J.B. Lippincott Co, 1988

Hondeghem LM, Mason JW:

Agents used in cardiac arrhythmias

Chapter 14:165-182

Appleton and Lange Medical Publications, 1989 (4th edition)

Hondeghem LM, Miller RD:

Local anesthetics

Chapter 25:315-322

Appleton and Lange Medical Publications, 1989 (4th edition)

Snyders DJ, Bennett PB, Hondeghem LM:

Mechanisms of drug-channel interaction

Chapter 82: 2165-2193

Ed.: Fozzard, Haber, Jennings, Katz and Morgan.

The Heart and cardiovascular system

Raven Press 1992

Hondeghem LM, Bennett PB:

Models of antiarrhythmic drug action

Chapter 11:201-239

In: Molecular and cellular mechanisms of antiarrhythmic agents.

Ed: Hondeghem LM

Futura Publishing Co, 1989

Hondeghem LM:

Molecular interactions of antiarrhythmic agents with their receptor site

Chapter 114: 1330-1335

In: Cardiac Electrophysiology, from cell to bedside.

Ed: Zipes DP, Jalife J, Saunders Co

Hondeghem LM, Anno T, Bennett PB, Johns JA, Murray KT, Snyders DJ:

Modulated receptor: voltage- and time-dependence of sodium channel block. In "Current topics in antiarrhythmic agents: mode of action and clinical usage." (Proceedings of the meeting in Nagoya, Japan, March 1989)

Excerpta Medica, Tokyo

Hondeghem LM, Mason JW:

Agents used in cardiac arrhythmias

Chapter 14:190-210

Appleton and Lange Medical Publications, 1992 (5th edition)

Hondeghem LM, Miller RD:

Local anesthetics

Chapter 25:315-322

Appleton and Lange Medical Publications, 1992 (5th edition)

Hondeghem LM, Roden DM:

Agents used in cardiac arrhythmias

Chapter 14:363-370

Appleton and Lange Medical Publications, 1995 (6th edition)

Hondeghem LM, Miller RD:

Local anesthetics

Chapter 25:395-403

Appleton and Lange Medical Publications, 1995 (6th edition)

Hondeghem LM:

Use dependence and reverse use dependence of antiarrhythmic agents: pro-and antiarrhythmic actions

Chapter 6: 92-105

In:Antiarrhythmic Drugs

Ed: Breidhardt, Borggreffe, Camm, Shenasa

Springer 1995

Hondeghem LM:

Receptor physiology and its relationship to antiarrhythmic drugs

Chapter 23: 347-354

In:Cardiac Arrhythmia: Mechanisms, diagnosis and management

Ed: Podrid, Kowey

Williams & Wilkins 1995

Hondeghem LM, Roden DM:

Agents used in cardiac arrhythmias

Chapter 14:216-241

Appleton and Lange Medical Publications, 1998 (7th edition)

Hondeghem LM, Roden DM:

Agents used in cardiac arrhythmias

Chapter 14: 219-244

Appleton and Lange Medical Publications, 2000 (8th edition)

Hondeghem LM:

Frequency dependence of class I and class III antiarrhythmic agents explaining their antiarrhythmic and proarrhythmic properties.

In "Monophasic Action Potentials"

Chapter 24: 381-394

Ed: Franz. Futura Pub. 2000

Hondeghem LM:

TRLad: foundation for proarrhythmia (triangulation, reverse use dependence and instability).

Pages 235-250 in "The hERG Cardiac Potassium Channel: structure, function and long QT syndrome". Novartis Foundation

Symposium 266 pp 235-250

John Wiley & Sons, Ltd 2005

Hondeghem LM:

QT Prolongation is a Poor Predictor of Proarrhythmia Liability: Beyond QT Prolongation!

Heart Rate and Rhythm: Molecular basis, pharmacological modulation, and clinical implication. Ed. Onkar N. Tripathi, Ursula Ravens, Michael C. Sanguinetti (Eds) Springer (in Press)

## Reviewed Publications

Hondeghem LM:

Orthosympathetic and parasympathetic interactions on heart rate

MS Thesis, University of Leuven, Belgium, 1971

Hondeghem LM:

A morphological, electrophysiological and pharmacological study of the Purkinje-myocardial junction

PhD Thesis, University of California, San Francisco, 1973

Hondeghem LM, Jensen RA:

Purkinje-myocardial conduction delay: An alternative explanation

J Molec and Cell Cardiol 6:485-490, 1974

Hondeghem LM, Grant AO, Jensen RA:

Antiarrhythmic drug action: Selective depression of hypoxic cardiac cells

Am Heart J 87:602-606, 1974

Hondeghem LM, Stroobandt R:

Purkinje fibers of sheep papillary muscle: Occurrence of discontinuous fibers

Am J Anatomy 141:251-262, 1974

Hondeghem LM, Mouton E, Stassen T, De Geest H:

Additive effects of acetylcholine released by vagal nerve stimulation on atrial rate of reserpinized dogs. J Appl Physiol 38:108-113, 1975

Katzung BG, Hondeghem LM, Grant AO:

Cardiac ventricular automaticity induced by current of injury

Pflugers Arch 360:193-197, 1975



Hondeghem LM:

Effects of lidocaine, phenytoin and quinidine on the ischemic canine myocardium

J Electrocardiology 9:203-209, 1976

Hondeghem LM, Katzung BG:

Time and voltage dependent interactions of antiarrhythmic drugs with cardiac sodium channels

Biochimica et Biophysica Acta 472:373-398, 1977

Hondeghem LM, Cotner CL:

Measurement of  $V_{max}$  of the cardiac action potential with a sample/hold peak detector

Am J Physiol 234:H312-H314, 1978

Grant AO, Hondeghem LM, Katzung BG:

Effects of droperidol on depolarization induced automaticity, maximum upstroke velocity ( $V_{max}$ ) and the kinetics of recovery of

$V_{max}$  in guinea pig ventricular myocardium

JPET 205:193-203, 1978

Hondeghem LM, Cotner CL:

Reproducible and uniform cardiac ischemia: Effects of antiarrhythmic drugs

Am J Physiol 235:H574-H580, 1978

Hondeghem LM:

Validity of  $V_{max}$  as a measure of the sodium current in cardiac and nervous tissues

Bioph J 23:147-153, 1978

Hondeghem LM, Katzung BG:

Experimental test of a model of antiarrhythmic drug action: Effects of quinidine and lidocaine on myocardial conduction

Circulation 61:1217-1224, 1980

Hondeghem LM, Lam C:

Selective depression of 2,4-dinitrophenol treated canine Purkinje fibers by lidocaine

Naunyn-Schmiedeberg's Arch 313:11-16, 1980

Hondeghem LM, Ehring GR:

An advanced microprocessor-based programmable stimulator

Medical Electronics 74:89-92, 1982

Kohlhardt M, Seifert C, Hondeghem LM:

Tonic and phasic INa blockade by antiarrhythmics: Different properties of drugs binding to fast channels as judged from Vmax studies with propafenone and derivatives in mammalian ventricular myocardium

Pflugers Arch 396:199-209, 1983

Kanaya S, Arlock P, Katzung BG, Hondeghem LM:

Diltiazem and verapamil preferentially block inactivated cardiac calcium channels

J Molec Cell Cardiol 15:145-148, 1983

Mason JW, Hondeghem LM, Katzung BG:

Amiodarone blocks inactivated cardiac sodium channels

Pflugers Arch 396:79-81, 1983

Hondeghem LM, Katzung BG:

Antiarrhythmic agents: The modulated receptor mechanism of action of sodium and calcium channel-blocking drugs

Ann Rev Pharmacol Toxicol 24:387-423, 1984

Mason JW, Hondeghem LM:

Quinidine

Annals of New York Academy of Sciences 432:162-176, 1984

Clarkson CW, Matsubara T, Hondeghem LM:

Slow inactivation of Vmax in guinea pig ventricular myocardium

Am J Physiol 247:H645-H654, 1984

Mason JW, Hondeghem LM, Katzung BG:

Block of inactivated sodium channels and of depolarization-induced automaticity in guinea pig papillary muscle by amiodarone

Circ Res 55:277-285, 1984

Clarkson CW, Hondeghem LM:

Mechanism for bupivacaine depression of cardiac conduction: Fast block of sodium channels during the action potential with slow recovery from block during diastole

Anesthesiology 62:396-405, 1985

Clarkson CW, Hondeghem LM:

Evidence for a specific receptor site for lidocaine, quinidine and bupivacaine associated with cardiac sodium channels in guinea pig ventricular myocardium

Circ Res 56:496-506, 1985

Hondeghem LM:

Maximal upstroke velocity as an index of available sodium conductance: comparison of maximal upstroke velocity and voltage clamp measurements of sodium current in rabbit Purkinje fibers

Circ Res 54:636-651, 1984

Davis JC, Matsubara T, Scheinman MM, Katzung B, Hondeghem LM:

Use-dependent effects of lidocaine on conduction in canine myocardium: In Vivo application of the modulated receptor hypothesis

Circulation 74:I-205-214, 1986

Bennett PB, Stroobandt R, Kesteloot H, Hondeghem LM:

Sodium channel block by a potent, new antiarrhythmic agent, transcaïnide, in guinea pig ventricular myocytes

J Cardiovasc Pharmacol 9:661-667, 1987

Hondeghem LM, Ayad MJ, Robertson RM:

Verapamil, diltiazem and nifedipine block the depolarization induced potentiation of norepinephrine contractions in rabbit aorta and porcine coronary arteries

JPET 239:808-813, 1986

Hondeghem LM:

Antiarrhythmic agents: Modulated receptor applications

Circulation 75:514-520, 1987

Stroobandt K Bennett PB, Hondeghem LM, Kesteloot H:

Evaluation of the efficacy and tolerance of the antiarrhythmic agent transcaïnide (R 54718)

Eur J Clin Pharmacol 32:449-456, 1987

Matsubara T, Clarkson CW, Hondeghem LM:

Lidocaine blocks open and inactivated cardiac sodium channels

Naunyn-Schmiedeberg's Arch Pharmacol 336:224-231, 1987

Ehring GR, Moyer JW, Hondeghem LM:

Quantitative structure activity studies of antiarrhythmic properties in a series of lidocaine and procainamide derivatives  
JPET 244:479-492, 1988

Hondeghem LM, Matsubara T:

Quinidine blocks cardiac sodium channels during opening and slow inactivation in guinea pig papillary muscle  
Br J Pharmacol 93:311-318, 1988

Roden DM, Bennett PB, Snyders DJ, Balser JR, Hondeghem LM:

Quinidine delays IK activation in guinea pig ventricular myocytes  
Circ Res 62:1055-1058, 1988

Clarkson CW, Follmer CH, Ten Eick RE, Hondeghem LM, Yeh J:

Evidence for two components of sodium channel block by lidocaine in isolated cardiac myocytes.  
Circ Res 63:869-878, 1988

Clarkson CW, Matsubara T, Hondeghem LM:

Evidence for voltage-dependent block of cardiac sodium channels by tetrodotoxin in guinea pig ventricular muscle  
JMCC 20:1119-1131, 1988

Hondeghem LM:

Antiarrhythmic agents: Modulated receptor applications  
Circulation: Preludes and Progress (Monograph 2) 155-161, 1988

Bennett PB, Woosley RL, Hondeghem LM:

Competition between lidocaine and one of its metabolites, glycylylidide, for cardiac sodium channels  
Circulation 78:692-700, 1988

Johns JA, Anno T, Bennett PB, Snyders DJ, Hondeghem LM:

Modulation of O-demethylencaïnide block of sodium channels by temperature  
J Cardiovasc Pharmacol 13:826-835, 1989

Snyders DJ, Hondeghem LM:

Effects of quinidine on the sodium current of guinea-pig myocytes: evidence for a drug-associated rested state with altered kinetics.  
Circ Res 66:565-579, (Feb) 1990

Anno T, Hondeghem LM:

Interactions of flecainide with guinea pig cardiac sodium channels: Importance of activation unblocking to the voltage dependence of recovery.

Circ Res 66:789-803, (March) 1990

Hansen DE, Craig CS, Hondeghem LM:

Stretch-Induced Arrhythmias in the isolated canine ventricle: Evidence for the importance of mechanical-electrical feedback.

Circulation 81:1094-1105, (March) 1990

Hondeghem LM, Snyders DJ:

Class III antiarrhythmic agents have a lot of potential but a long way to go: Reduced effectiveness and dangers of reverse use-dependence

Circulation 81:686-690, (Feb) 1990

Murray KT, Anno T, Bennett PB, Hondeghem LM:

Voltage Clamp of Cardiac Sodium Current in 145 mM Sodium at 37°C.

Biophys J 57:607-613, (March) 1990

Balsler JR, Bennett PB, Hondeghem LM:

Suppression of time-dependent outward current on guinea pig ventricular myocytes: actions of quinidine and amiodarone

Circ Res 69:519-529, 1991

Hondeghem LM:

Ideal Antiarrhythmic Agents: Chemical defibrillators

J Cardiovasc Electrophysiol 2:169-177, 1991

Hondeghem LM:

Development of Class III antiarrhythmic agents

J Cardiovasc Pharmacol 20:S17-S22, 1992

Hondeghem LM:

Computer aided development of antiarrhythmic agents with class IIIa properties

J Cardiovasc Electrophysiol 5:711-721, 1994

Valenzuela C, Snyders DJ, Bennett PB, Tamargo J, Hondeghem LM:

Stereoselective block of cardiac sodium channels by bupivacaine in guinea pig ventricular myocytes.

Circulation. 1995;15;92:3014-24.

Hondeghem LM:

Classification of antiarrhythmic agents and the two laws of pharmacology

Cardiovasc Res: 45:57-60, 2000

Benardeau A, Weissenburger J, Hondeghem L, Ertel EA:

Effects of the T-Type Ca<sup>2+</sup> channel blocker mibefradil on repolarization of guinea pig, rabbit, dog, monkey, and human cardiac tissue

JPET 292:561-575, 2000

Amos GJ, Abrahamsson C, Duker G, Hondeghem L, Palmer M, Carlsson L.

Potassium and calcium current blocking properties of the novel antiarrhythmic agent H 345/52: implications for proarrhythmic potential.

Cardiovasc Res. 2001 Feb 1;49:351-360.

Hondeghem L, Carlsson L, Duker G:

Instability and triangulation of the action potential predict serious proarrhythmia, but APD prolongation is antiarrhythmic.

Circulation. 2001 Apr 17;103(15):2004-13.

Hondeghem LM, Dujardin K, De Clerck F.

Phase 2 prolongation, in the absence of instability and triangulation, antagonizes class III proarrhythmia.

Cardiovasc Res. 2001 May;50(2):345-53

Hondeghem LM, Hoffmann P:

A Blinded Test in Isolated Female Rabbit Heart Reliably Identifies APD-prolongation and Proarrhythmic Drugs: Importance of Triangulation, Reverse Use Dependence and Instability. J Cardiovasc Pcol. 2003;41:14-24

Hondeghem LM, MD, PhD, Hua Rong Lu<sup>2</sup> MD, PhD, Koen van Rossem<sup>2</sup> MD, PhD Fred De Clerck<sup>2</sup> MSc, PhD:

Detection of Proarrhythmia in the Female Rabbit Heart: Blinded Validation

J Cardiovasc Electrophysiol: 2003;14:287-294

Valentin JP, Hofman P, De Clerck F, Hammond TG, Hondeghem LM:

Review of the predictive value of the Langendorff heart model (Screenit system) in assessing the proarrhythmic potential of drugs.

J Pharmacol & Toxicol Methods 2004;49:171-181

Shah RR, Hondeghem LM:

Refining detection of drug-induced proarrhythmia: QT interval and TRlaD

Heart Rhythm 2005;2:758-772

Luc M Hondeghem:

Thorough QT/QTc Not So Thorough: Removes Torsadogenic Predictors from the T-Wave, Incriminates Safe Drugs, and Misses Profibrillatory Drugs. *J Cardiovasc Electrophysiol* 2006;17:337-340

Hondeghem LM:

Estimation of Proarrhythmic Hazards by QT-prolongation/shortening: QT-obsession?  
*Drug Information Journal* 2006;40:273-279

Hondeghem LM.

Thorough QT/QTc not so thorough: removes torsadogenic predictors from the T-wave, incriminates safe drugs, and misses profibrillatory drugs. *J Cardiovasc Electrophysiol.* 2006;17:337-40.

Hondeghem LM.

Relative contributions of TRLaD and QT to proarrhythmia. *J Cardiovasc Electrophysiol.* 2007 Jun;18(6):655-7.

Hondeghem LM, De Clerck F, Camm J.

Short patent lives jeopardize drug and patient safety. *J Cardiovasc Pharmacol.* 2007;50:353-7.

Hondeghem LM.

QT and TdP. QT: an unreliable predictor of proarrhythmia. *Acta Cardiol.* 2008;63:1-7.

Hondeghem LM.

QT prolongation is an unreliable predictor of ventricular arrhythmia. *Heart Rhythm.* 2008;5:1210-2.

Hondeghem LM.

Use and abuse of QT and TRLaD in cardiac safety research: importance of study design and conduct. *Eur J Pharmacol.* 2008 14;584:1-9.

Dujardin KS, Dumotier B, David M, Guizy M, Valenzuela C, Hondeghem LM:

Ultrafast sodium channel block by dietary fish oil prevents dofetilide-induced ventricular arrhythmias in rabbit hearts. *Am J Physiol Heart Circ Physiol.* 2008;295:H1414-21.

Hondeghem LM, Dumotier B, Traebert M:

Oscillations of cardiac wave length and proarrhythmia. *Naunyn-Schmied Arch Pharmacol* 2010;382:367-376

Hondeghem LM, Dujardin K, Hoffmann P, Dumotier B, De Clerck F:

Drug-Induced QTC Prolongation Dangerously Underestimates Proarrhythmic Potential: Lessons From Terfenadine. *J Cardiovasc Pharmacol.* 2011;57:589-97.

Hondeghem LM

Low safety index of domperidone: mechanism for increased odds ratio for sudden cardiac death. *Acta Cardiol.* 2011 Aug;66(4):421-5.

Hondeghem LM

QTc prolongation as a surrogate for drug-induced arrhythmias: fact or fallacy?  
*Acta Cardiol.* 2011 Dec;66(6):685-9.

Hondeghem LM, De Clerck F

Preclinical cardiovascular safety evaluations of biologics: optimizing the approach and follow-up. *BioDrugs.* 2012 Oct 1;26(5):275-82.

Hondeghem LM

Domperidone: limited benefits with significant risk for sudden cardiac death. *J Cardiovasc Pharmacol.* 2013 Mar;61(3):218-25

Hondeghem LM

Disturbances of cardiac wavelength and repolarization precede Torsade de Pointes and ventricular fibrillation in Langendorff perfused rabbit hearts. *Prog Biophys Mol Biol* 2016 May;121(1):3-10

Hondeghem LM, Logghe NH.

Should Domperidone be Used as a Galactagogue? Possible Safety Implications for Mother and Child *rug Saf.* 2017 Feb;40(2):109-113. doi: 10.1007/s40264-016-0478-x

Hondeghem LM

Drug-Induced QT Prolongation and Torsades de Pointes: An All-Exclusive Relationship or Time for an Amicable Separation? 2018 *Jan*;41(1):11-17.  
doi: 10.1007/s40264-017-0584-4.

## Extracurricular publications

Hondeghem LM:

Programmable Pulse Generating System

US Patent 4,255,790 1981

Hondeghem LM:

MDCSTAT: statistics the easy way.

The Best of the Computer Faires (VIII): 126-129, 1983