

## PERSONAL INFORMATION

Milou-Daniel Drici

## WORK EXPERIENCE

September 2003–Present

**Professor of Clinical Pharmacology**

University of Nice Sophia Antipolis (France)

Teaching and research in drug pharmacokinetics and pharmacodynamics. A particular orientation in the cardiac safety of drugs, pertaining to ion channels, sudden death, drug-acquired long QT syndrome, and oral direct anticoagulants

September 2003–Present

**Chief of Department and Chair, Pharmacology**

University of Nice Medical Center (France)

President of the Pharmacoepidemiology and Pharmacovigilance subcommittee of IUPHAR. Pharmacovigilance activity and Pharmacoepidemiology.

Pharmaco-toxicology, Therapeutic drug monitoring methodology in clinical pharmacology.

September 2010–Present

**Director of the regional center of Pharmacovigilance**

Agence Nationale de Sécurité du Médicament and Nice University Medical Center (France)

Explore causality of drug induced adverse events in three french departments (06, 83 and 05, 3 millions inhabitants) and transmit the cases to the national registry of pharmacovigilance. Clinics of pharmacovigilance in several departments of the Nice University Medical Center

May 1997–August 2003

**Associate Professor**

CNRS-University of Nice Sophia Antipolis (France)

Basic and experimental murine pharmacology. Electrophysiology & Patch Clamp in a research laboratory to evaluate the cardiac effects of different potassium channel currents.

September 1993–December  
1994**Associate Professor**

University of Nice Medical center (France)

Director of the Clinical Pharmacology Center at Hôpital Pasteur. Principal or associate investigator of numerous phase 1, 2 and 3 clinical trials.

## EDUCATION AND TRAINING

September 1982–October 1989

**Board certified in Cardiology. Resident in Cardiology and clinical pharmacology.**

UNSA Medical Center- Nice, University of Paris VI and Aix-Marseilles- (France)

internship and rounds of residencies in cardiology, and clinical pharmacology

September 1976–September  
1982**Medical Doctor**

School of of Medicine-Timone- Aix-Marseille II (France)

medical school and rounds in differents departments (neurology, cardiology, radiology, intensive care etc...)

October 1989–October 1993

**Assistant Professor/ Fellow in Clinical Pharmacology**

Faculty of Medicine of Nice, and Nice university Medical Center (France)

Clinical Pharmacology and Therapeutics. Hypertension Clinic. Centre of Clinical Pharmacology supervision.

December 1994–April 1997

### Fellow in Clinical Pharmacology

Georgetown University, Washington, DC and F.D.A (United States)

Drug-induced Long QT syndrome : basic (Patch clamp, isolated hearts, whole animals, patients). Internal reviewing and Clinical Pharmacokinetics courses in Clinical trials at the Food and Drugs Administration.

September 1988–June 1993

### PhD - Clinical Pharmacology

University of Aix Marseilles II-School of Pharmacy (France)

Basic and clinical methodology in drug development. Ancillary properties of beta adrenergic receptor blockers.

October 1983–July 1988

### Masters in Pharmacology

University of Aix Marseilles II-School of Pharmacy and School of Medicine (France)

Cardiovascular, respiratory and renal pharmacology

General pharmacology

September 1969–June 1976

### Graduation (Baccalauréat) Série D with mention.

Lycée Est Marcel Pagnol-Marseille (France)

High School training

## ADDITIONAL INFORMATION

### Expertise

Chair of Pharmacology with research units in Therapeutic Drug Monitoring, Toxicology and Pharmacovigilance focused on the cardiac safety of drugs, with a particular scope on the electrophysiological effects of drugs on cardiac repolarisation, and on gender differences in drug pharmacodynamics.

President of the IUPHAR subcommittee of Pharmacovigilance-Pharmacoepidemiology.

Expert of cardiovascular safety of new drugs at the French Drug agency ANSM (St Denis FRANCE) with a particular focus on drugs susceptible to prolong the QT interval (pre-clinical, clinical, safety), thrombosis and sudden death.

Expertise on PK of direct oral anticoagulants.

### Publications

In the area of Cardiac safety of drugs

1. Drici MD, Baldin B. Is the clinical development of drugs appropriate in the elderly population? *Rev Prat.* 2015 May;65(5):602-4.
2. Bardy G, Fischer F, Appert A, Baldin B, Stève M, Spreux A, Lavrut T, Drici MD. Is anti-factor Xa chromogenic assay for Rivaroxaban appropriate in clinical practice? Advantages and comparative drawbacks. *Thromb Res.* 2015 Aug;136(2):396-401.
3. Stève-Dumont M, Baldin B, Legros L, Thyss A, Re D, Rocher F, Ajmia F, Spreux A, Drici MD. Are nilotinib-associated vascular adverse events an under-estimated problem? *Fundam Clin Pharmacol.* 2015 Apr;29(2):204-8.
4. Bénard-Larivière A, Miremont-Salamé G, Pérault-Pochat MC, Noize P, Haramburu F; EMIR Study Group on behalf of the French network of pharmacovigilance centres. Incidence of hospital admissions due to adverse drug reactions in France: the EMIR study. *Fundam Clin Pharmacol.* 2015 Feb;29(1):106-11.
5. Hajj A, Ksouda K, Peoc'h K, Curis E, Messali A, Deveaux LL, Bloch V, Prince N, Mouly S, Scherrmann JM, Lépine JP, Laplanche JL, Drici MD, Vorspan F. KCNH2 polymorphism and methadone dosage interact to enhance QT duration. *Drug Alcohol Depend.* 2014 Aug 1;141:34-8.
6. Tuppin P, Cuerq A, de Peretti C, Fagot-Campagna A, Danchin N, Juillièrè Y, Alla F, Allemand H, Bauters C, Drici MD, Hagège A, Jondeau G, Jourdain P, Leizorovicz A, Paccaud F. Two-year outcome of patients after a first

- hospitalization for heart failure: A national observational study. Arch Cardiovasc Dis. 2014 Mar;107(3):158-68
7. Tuppin P, Cuerq A, de Peretti C, Fagot-Campagna A, Danchin N, Juillière Y, Alla F, Allemand H, Bauters C, Drici MD, Hagège A, Jondeau G, Jourdain P, Leizorovicz A, Paccaud F. First hospitalization for heart failure in France in 2009: patient characteristics and 30-day follow-up. Arch Cardiovasc Dis. 2013 Nov; 106(11):570-85.
8. Safety of sertindole versus risperidone in schizophrenia: principal results of the sertindole cohort prospective study (SCoP). S.H.L. THOMAS, M.D. DRICI, G.C. HALL, M.A. CROCQ, B. EVERITT, M.H. LADER, C. LE JEUNNE, D. NABER, S. PRIORI, M. STURKENBOOM, F. THIBAUT, J. PEUSKENS, A. MITTOUX; P. TANGHØJ, M. TOUMI, N.D. MOORE, R.D. MANN. Acta Psychiatr Scand 2010, 1-11.
9. Cardiovascular risks of atypical antipsychotic drug treatment. M.D. DRICI, S. PRIORI. Pharmacoepidemiol Drug Saf 2007, 16(8):882-90
10. Cardiovascular safety of gadoterate meglumine (Gd-DOTA) P. BOURRINET, E. MARTEL, A.I. EL AMRANI, P. CHAMPEROUX, S. RICHARD, N. FAUCHOU, F. LE COZ, M. DRICI, B. BONNEMAIN, S. GAILLARD. Invest Radiol 2007; 42(2):63-77.
11. Sex modulates the arrhythmogenic substrate in prepubertal rabbit hearts with Long QT 2. T.LIU, B.R. CHOI, M.D. DRICI, G.SALAMA. J Cardiovasc Electrophysiol. 2005 May; 16(5):525-7.
12. Mice display gender differences in halothane-induced polymorphic ventricular tachycardia. M.D. DRICI, L.BAKER, P.PLAN, J.BARHANIN, G. ROMÉY, G. SALAMA. Circulation 2002, 106 : 497-503.
13. Influence of gender on drug-acquired long QT syndrome. M.D. DRICI. Eur. Heart. J. 2001, 3 : K41-K47.
14. Is gender a risk factor for adverse drug reactions? The example of drug-induced long QT syndrome. M.D. DRICI, N. CLEMENT. Drug. Saf. 2001, 24 : 575-585.
15. Novel mutations in KvLQT1 that affect IKs activation through interactions with IsK. C. CHOUABE, N. NEYROUD, P. RICHARD, I. DENJOY, B. HAINQUE, G. ROMÉY, M.D. DRICI, P. GUICHENEY, J. BARHANIN. Cardiovasc. Res. 2000, 45 : 971-980.
16. The bee venom peptide tertiapin underlines the role of IKACH in acetylcholine-induced atrioventricular blocks. M.D. DRICI, S. DIOCHOT, C. TERRENOIRE, G. ROMÉY, M. LAZDUNSKI. Br. J. Pharmacol. 2000, 131 : 569-577.
17. Studies on the mechanism of a fatal clarithromycin-pimozide interaction in a patient with Tourette syndrome. D.A. FLOCKHART, M.D. DRICI, T. KERBUSCH, N. SOUKHOVA, E. RICHARD, P.L. PEARLE, S.K. MAHAL, V.J. BABB. J. Clin. Psychopharmacol. 2000, 20 (3): 317-24.
18. Comparison of tegaserod (HTF 919) and its main human metabolite with cisapride and erythromycin on cardiac repolarization in the isolated rabbit heart. M.D. DRICI, S.N. EBERT, W.X. WANG, I. RODRIGUEZ, X-K LIU, B.H. WHITFIELD, R.L. WOOSLEY. J. Cardiovasc. Pharmacol. 1999 ; 34 : 82-88.
19. Effects of phrixotoxins on the Kv4 family of potassium channels and implications for the role of Ito1 in cardiac electrogenesis. S. DIOCHOT, M.D. DRICI, D. MOINIER, M. FINK, M. LAZDUNSKI. Br. J. Pharmacol. 1999 ; 126(1) : 251-263.
20. Cardiac actions of erythromycin: influence of gender. M.D. DRICI, B. KNOLLMANN, W-X WANG, R.L. WOOSLEY. JAMA 1998 ; 280 : 1774-1776.
21. HERG and KvLQT1/IsK, the cardiac K<sup>+</sup> channels involved in long QT Syndrome, are targets for calcium channel blockers. C. CHOUABE, M.D. DRICI, G. ROMÉY, J. BARHANIN, M. LAZDUNSKI. Mol. Pharmacol. 1998 ; 54 (4) : 695-703.
22. Prolongation of QT interval in isolated feline hearts by antipsychotic drugs. M.D. DRICI, W-X. WANG, X-K. LIU, R.L. WOOSLEY, D.A. FLOCKHART. J. Clin. Psychopharmacol. 1998 ; 18 (6) : 477-481.
23. Conventional antihistamines slow cardiac repolarization in isolated perfused (Langendorff) feline hearts. W-X. WANG, S.N. EBERT, X-K. LIU, Y.W. CHEN, M.D. DRICI, R.L. WOOSLEY; J. Cardiovasc. Pharmacol. 1998 ; 32 (1) : 123-128.
24. Involvement of IsK-associated K<sup>+</sup> channel in heart rate control of repolarization in a murine engineered model of Jervell and Lange Nielsen syndrome. M.D. DRICI, I. ARRIGHI, C. CHOUABE, J.R. MANN, M. LAZDUNSKI, G. ROMÉY, J. BARHANIN. Circ. Res. 1998 ; 83 (1) : 95-102.
25. Gender differences in the cycle length-dependent QT and potassium currents in rabbits. X-K LIU, A. KATCHMAN, M.D. DRICI, S.N. EBERT, I. DUCIC, M. MORAD, R.L. WOOSLEY. J. Pharm. Exp.

Ther. 1998 ; 285 (2) : 672-679.

26. Regulation of potassium channel expression and cardiac repolarization in the rabbit heart by sex steroid hormones. M.D. DRICI, T.R. BURKLOW, V. HARIDASSE, R.I. GLAZER, R.L. WOOSLEY. Circulation 1996 ; 94 :1471-1474.

Selected Chapters in books in the field of sudden death

1. Drug-induced sudden death. D. RODEN AND M.D. DRICI.

In : Sudden Cardiac Death. 2006. Eds : Priori S.G., Zipes, D.P. Blackwell Publishing. Oxford U.K and Malden, MS, USA . pp 177-189.

2. Molecular pathophysiology of cardiomyopathies. D. ESCANDE, M.D. DRICI and J. BARHANIN. In : Heart Physiology and Pathophysiology, 4th edition. 2000. Eds : Sperelakis N., Kurachi Y., Terzic A., Cohen M.V. San Diego, CA-USA; Academic Press. pp 1097-1105.

3. Cardiac K<sup>+</sup> channels and inherited long QT syndrome. M.D. DRICI and J. BARHANIN. Chapter 14. In : Handbook of Experimental Pharmacology, Vol 147. Pharmacology of ionic channel function. 2000. Eds : Endo M., Mishina M., Kurachi Y. Heidelberg, Germany; Springer-Verlag GmbH & Co. KG. pp 347-362.

4. Drug and metabolic factors in sudden death. M.D. DRICI, D.A. FLOCKHART, R.L. WOOSLEY. In : Sudden Cardiac Death : Past, Present, and Future. 1997. Eds : Dunbar S.B., Ellenbogen K.A. Armonk, N.Y; Futura Publishing Company Inc. pp 75-84.

#### Projects

1989-1993: Chief of the clinical Pharmacology Unit with conception of and supervision and investigator or principal investigator of multiple clinical trial of Phase 1 (ocular, cardiac electrophysiology), Phase 2 (venous pressure, systemic hypertension, heart failure), phase 3 (hypertension, heart failure, angina)

1994-1997 : Georgetown University and FDA : investigator of phase I clinical trials (gender differences) , experimental and basic pharmacology in the domain of cardiac repolarisation (rabbit, rat and mice models in repolarisation, patch clamp technique

1997-2003 : University of Nice CNRS : Fundamental and Experimental pharmacology : patch clamp, murine electrophysiology, cell transfection in the domain of ionic channels (potassium, sodium, calcium)

2003-present Professor of Medicine and Clinical Pharmacology: pharmacovigilance, data safety monitoring boards, clinical trials of pharmacovigilance.

#### Memberships

Fellow of the European Society of Cardiology

Member of the Cardiac Electrophysiology Society

Member of the French Society of cardiology

Member of the French Society Hypertension

Member of the French Society of Pharmacology and Therapeutics

Member of British Society of Pharmacology,

Member of IUPHAR and head of its Subcommittee on Pharmacoevidence / Pharmacovigilance

#### Other Relevant Information

Trained in Clinical Pharmacology at Georgetown University (Washington DC, USA), and at the Food and Drugs Administration

Full professor since 2003 at the University of Nice

Served on the French National Board of Pharmacology and Board of Hypertension.

Expert in Cardiology (preclinical and clinical) and clinical trial methodology to the french drug agency (ANSM)