Curriculum vitae

Personal Information

Family name, First name: Marine Jean-Christophe

Date of birth: October 5th, 1968- *Nationality:* Belgian

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Education

1996	PhD (*cum laude*), University of Liège (ULG), Belgium
1991	Masters in Biochemistry (*Honours*), University of Liège (ULG), Belgium

Residencies & Research Fellowships

2000-2003	Postdoctoral Marie Curie Fellow (EU), European Institute of Oncology (IEO), Milan, Italy.
1996- 1999	Postdoctoral Fellow, Howard Hughes Medical Institute Fellowship (HHMI), St. Jude Children's Research Hospital, Memphis, TN, USA.
1995	Research Fellow, Georg August Universität, Zentrum Biochemie Göttingen, Germany.
1993	Research Fellow, Department of Genetics, Yale University, USA.
1991- 1995	Graduate Student, IRSIA-FRIA (PhD fellowship), Belgian Government

Previous Position

2003-2004	Research Associate FNRS, Free University of Brussels (ULB-IBMM), Belgium.

Current Positions

2017-*present*	Science Director, Centre for Cancer Biology, VIB, Belgium
2009-*present*	Professor KU Leuven, Belgium
2004-*present*	Group Leader, Laboratory of Molecular Cancer Biology, VIB, Belgium

Awards

2019	The Society of Melanoma Research Outstanding Research Award
2017	Price Dr. Karel-Lodewijk Verleysen-clinical medical research in the European Union
2014	Alexandre et Gaston Tytgat Prize (Oncology)
2013	Astra Zeneca Award (Oncology)
2007	European Association for Cancer Research, EACR Young Cancer Researcher Award
2007	KBS prize of the Yvonne and Jacques François de Meurs Foundation on 'fundamental research on malignant brain tumors'
2006	Fonds André Vander Stricht, King Baudouin Foundation: "Molecular mechanisms and role of signalling molecules in cancer"
2006	EMBO Young Investigator

Supervision of graduate students and postdoc fellows

Since 2004, the Marine lab hosted/trained 15 Postdocs, 21 PhD and 8 Master Students, the vast majority of whom obtained personal national (i.e. FWO) or international fellowships (i.e. Marie Curie).

Teaching activities

2014–*present*	Coordinator – Hot Topics in Oncology (30h/year), KULeuven
2014–*present*	Coordinator – Advances in Oncology, (30h/year), KULeuven

I dedicate 60 hours per year to share my knowledge of cancer biology and passion to research with young PhD students and trainees; this is something I enjoy doing and take very seriously.

Organisation of scientific meetings/events (selection)

2016	Cell Symposium: Hallmarks of Cancer, Co-organizer, Ghent, Belgium
2015	The non-coding genome, VIB Training course, Co-organizer, Leuven, Belgium
2014	International Mouse models skin cancer conference, Co-organizer, Montepellier, France
2009	MDM2 Workshop V, Co-organizer, Ghent, Belgium

Institutional responsabilities & Science meets society activities (selection)

2017–*present*	Director of the VIB Centre for Cancer Biology (11PIs and more than 200 researchers)
2017–*present*	Member of the Bureau of the Department of Oncology, KULeuven
2017–*present*	Member of the steering committee of TRACE (KULeuven PDX facility)
2017–*present*	Active member of LifeTime initiative (A visionary proposal for a EU-Flahship)
2017–*present*	Member of the VIB management and single-cell accelerator committees
2017–*present*	Responsible for the VIB/CCB Distinguished lecture series
2015–2017	Director of the cancer program of the Dpt. of human Genetics, KULeuven
2009–2012	Member of the VIB Group Leader committee
2008–2013	Coordinator EU-FP7 consortium (ONCOMIRs)
2010–*present*	EACR Board member (Belgium representative)
2007–*present*	Lecturer in "Master & PhD Program in Biomedical Sc", ULB, Belgium

Patents, Industrial collaborations & Consultant activities (selection)

2018–*present*	Research project with Astra Zeneca (Therapy resistance, single-cell sequencing, PDXs)
2014	Scientific Advisory Board, Aileron Therapeutics Inc.
2010–2016	Research projects with SANOFI and J&J Pharmaceutica (p53 Reactivation therapy)
2010–*present*	Scientific advisor for Roche, Novartis, SANOFI and J&J Pharmaceutica
2004–*present*	More than 10 patent applications in the field of Oncology

Reviewing & Consultant activities (selection)

2018–*present*	Life Science Alliance Editorial Board member
2016	Review panel member, ANR (RNA metabolism), France
2008–2016	Review panel member, FNRS (Biological Sciences), Belgium
2008–*present*	Cell Death and Differentiation Editorial Board member
2004–*present*	Grant Review for AICR (UK), ARC & ANR (France), Welcome Trust (UK), ERC (EU), …etc
2004–*present*	Reviewer for journals such as Cell, Nature, Cancer Cell, Nature Medicine, Nature Cell Biology, Nat Rev Cancer, EMBO J, ...

Original discoveries & Main contributions

As a young HHMI postdoc, I joined Prof J. Ihle at St. Jude Children Research Hospital, Memphis, Tennessee, where I gained expertise in mouse genetics. I ***established key roles for SOCS1 and SOCS3 as negative regulators of cytokine signaling***, leading to two back-to-back breakthrough publications in Cell in 1999 (as a first author). These studies paved the way to numerous studies by other investigators addressing the roles of SOCS proteins in inflammatory disease and cancer. This work has become textbook knowledge in molecular biology and immunology. Since then, I have entertained the idea that cancer is (also) a signal transduction disease. I then joined the laboratory of Prof. P.G. Pelicci at the European Institute of Oncology, Milan, Italy on a EU Marie Curie fellowship. I was key in establishing the functional mouse core facility at the institute and developed my first own independent research line dedicated to unraveling new signaling pathways that act upstream and downstream of the p53 tumor suppressor gene. Among other discoveries, I was one of the first to ***show the importance of MDM4 in the regulation of p53*** *in vivo*, to dissect its mechanisms of action and highlight its importance in cancer development (Migliorini *et al*., 2002; Danovi *et al*., 2004). I moved back to Belgium where I established my own independent research group first at ULB and then at VIB-UGent. Since then my lab has focused on the mechanisms by which cancer-specific **non-mutational (i.e. epigenetic and (post-)transcriptional) events** modulate tumor initiation, progression and therapy outcome. We continued studying the regulation of p53 stability and transcriptional activity by MDM2 and MDM4; We ***identified the MDM4-p53 axis as an attractive therapeutic target*** for the treatment of p53 wild-type tumors, such as melanoma (Gembarska *et al*., 2012; Dewaele *et al*., 2016) and introduced the concept of ***cancer cell-specific p53 reactivation therapy***, which keeps on attracting a lot of attention from the pharma industry. My lab finally moved to VIB-KULeuven, where we developed the concept of aberrant RNA biology in cancer and the ***targeting of cancer cell-specific malignant RNAs***, which I believe is a promising therapeutic concept. During this period, my laboratory also developed a growing interest in various aspects of **melanoma biology**. Genetically engineered mouse and PDX models of melanoma have been developed and are currently being extensively characterized and improved. We, for instance, developed a lineage tracing mouse

model of melanoma which allowed us to visualize and characterize the very first molecular and cellular events associated with melanoma initiation in living mice (Köhler *et al*. 2017). This study, which highlighted the nongenetic plasticity of differentiated melanocytes and their ability to serve as tumor initiating cells, provided ***in vivo evidence that mature, differentiated somatic cells can be at the origin of cancer***. The PDX melanoma models were used to dissect various mechanisms of therapy resistance and test novel combinatorial treatment options (Rambow *et al*., 2018; Rapino *et al*., 2018, Talebi *et al*., 2018). Our recent work highlighted ***drug-tolerance and MRD cellular heterogeneity,*** an observation that raises important therapeutic challenges which we propose to tackle in the future. Our lab has recently developed new tools and a wide range of expertise in single-cell multi-OMICs and in vivo modeling of therapy resistance.

10 YEARS TRACK-RECORD

Publication output of the last 10 years:

>90 publications (out of a total of >130) of which >30 as senior author.
>10.000 citations (out of a total of >12k); >80 citations per article (current h-index >50).

Patent Applications (selection):

2018 RXR antagonists for use in melanoma treatment
2018 CD36 antagonists for use in melanoma treatment
2018 Melanoma disease stratification

The above applications are based on our recent work on drug tolerance and MRD biology and form the basis for the enclosed AXA proposal.

2014 A lncRNA as a key therapeutic target for anti-melanoma therapy
2014 The lncRNA NEAT1 is a key oncogenic driver and therapeutic target
2014 Targeting exon 6 inclusion as a cancer cell-specific therapeutic approach

The above applications propose the targeting of cancer cell-specific malignant RNAs as an attractive therapeutic avenue, a concept that emerged from our pioneering work on the role of lineage-specific lncRNAs in cancer. These IPs form the basis for a new company that will aim at bringing this concept into the clinic. The company, of which I am the scientific founder, will be officially created in Dec. 2018.

2011 Targeting MDM4 in cutaneous Melanoma
2010 MicroRNA-based cancer therapy by specific targeting of p53-deficient tumors
2006 Method for treating ocular cancer

Invited lectures: In total I gave >70 invited lectures in the past 10 years, of which several Keynote or Plenary lectures at international meetings and workshops including CSH meetings, Annual International Meeting of mouse models of cancer, Keystone Meetings, Cell symposium ("Hallmarks of cancer"), Bi-annual p53 International workshop, Bi-annual MDM2 International workshop, Lorne Cancer Conference, Annual International Melanoma Meetings (SMR), etc...

Contribution to the early careers of junior scientists: I dedicate substantial energy, time and effort to mentor and prepare PhD students and postdocs optimally for their future career. I offer the postdocs the possibility to micro-manage their own mini-group by supervising other PhD students and technicians. I help them prepare presentations for job interviews... In total, 13 postdocs completed their training of which 12 have an independent position: 65% in academia, 15% in industry, 20% in other sectors (clinic & patent office). Former postdocs *E. Leucci*, *P. Froment*, *A. Martoriati, D Nittner, V Depaepe, M Dewaele* are now independent group leaders, assistant professors and/or staff scientists. *A Rogiers* is now a clinical oncologist.

Major collaborations relevant to our current work: We have ongoing collaborations with the labs headed by Stein Aerts (VIB/KULeuven) for his expertise in "enhancer logic" and machine learning and with whom we have developed tools such as i-Regulon or SCENIC; Thierry Voet (KULeuven) for his role as an early developer of single-cell multi-OMIC methods and with whom we have developed a protocol for combined single-cell ATAC and RNA-seq (A&T-seq); Cédric Blanpain (ULB, Belgium) for his expertise in CSC biology and lineage tracing and with whom we have a long-standing collaboration on various aspects of cancer biology (EMT, ...) that led to publications in Nature, Nat Med, Cell Stem Cell or Nat Cell Biol; Manfred Claassen (ETHZurich, Switzerland) for the machine learning approach applied to spatial data; Ben Simons (University of Cambridge, UK) for his help with mathematical modeling of clonal evolution; Oliver Bechter (UZLeuven), Sabine Tejbar (UZLeuven), Frederic Amant (UZLeuven), Johan Vansteenkiste (UZLeuven), Keith Flaherty (MGH, Boston, USA) and Mitchel Levesque (ETHZurich, Switzerland) for access to clinical samples.

Publications

1. Bellefroid EJ, Ried T, Rivière M, **Marine J-C**, Levan G, Szpirer J, Szpirer C, Ward DC, Martial JA. Localization of the human KRAB finger gene ZNF117 (HPF9) to Chromosome 7qll.2. **Genomics** 14:780-781, 1992.
2. Bellefroid EJ, **Marine J-C**, Ried T, Lecocq PJ, Rivière M, Amemiya C, Poncelet DA, Coulie PJ, de Jong P, Szpirer C, Ward DC, Martial JA. Clustered organization of homologous KRAB zinc finger genes with enhanced expression in human T lymphoid cells. **EMBO J.** 12:1363-1374, 1993.
3. **Marine J-C**, Bellefroid EJ, Rivière M, Bourguignon C, Martial JA. Assignment of the human ZNF83 (HPF1) zinc finger gene to chromosome l9ql3.3-ql3.4. **Genomics** 21: 285-286, 1994.
4. Bellefroid EJ, **Marine J-C,** Matera AG, Bourguignon C, Desai T, Healey K, Bray-Ward P, Martial JA, Ihle JN, Ward DC. Emergence of the ZNF91 KRAB zinc finger gene family after the divergence between the anthropoid and prosimian primate lineages. **Proc. Natl. Acad. Sci.** USA 92:10757-10761, 1995
5. **Marine J-C**, Gilbert DJ, Bellefroid EJ, Martial JA, Ihle JN, Copeland NG, Jenkins NA. Chromosomal location of fifteen unique mouse KRAB-containing zinc finger loci. **Mamm. Genome** 7:413-416, 1996.
6. **Marine J-C**, Bellefroid EJ, Pendeville H, Martial JA, Pieler T. A role for Xenopus Gli-type zinc finger proteins in the early embryonic patterning of mesoderm and neuroectoderm. **Mech. Dev**. 63:211-225, 1997.
7. Ogawa T, Poncelet D, Kinshita Y, Noce T, Takeda M, Kawamoto K, Udagawa K, Lecoq P, **Marine J-C,** Martial JA, and Hosaka M. Enhanced expression seminoma of human zinc finger genes located on chromosome 19. **Cancer Genet. Cytogenet** 100:36-42, 1998.
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10. **Marine J-C**, Topham JD, McKay C, Wang D, Parganas E, Stravopodis D, Yoshimura A, and Ihle JN. SOCS-1 deficiency causes a lymphocyte dependent perinatal lethality. **Cell** 98:609-616, 1999.
11. **Marine J-C**, McKay C, Wang D, Topham JD, Parganas E, Nakajima H, Pendeville H, Yasukawa H, Sasaki A, Yoshimura A, and Ihle JN. SOCS-3 is essential in the regulation of fetal liver erythropoiesis. **Cell** 98:617-627, 1999.
12. Morrigl R, **Marine J-C**, Topham DJ, Teglund S, Sexl V, McKay C, Piekorz R, Wang D, Parganas E, Yoshimura A, and Ihle JN. Differential roles of cytokine signaling during T-cell development. **Cold Spring Harb Symp Quant Biol.** 64:389-95, 1999 (Review).
13. Kieslinger M, Woldman I, Moriggl R, Hofmann J, **Marine J-C**, Ihle JN, Beug H, and Decker T. Antiapoptotic activity of STAT5 required during terminal stages of myeloid differentiation. **Genes Dev** 14:232-244, 2000.
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15. Wang D, Feng J, Wen R, **Marine JC**, Sangster MY, Parganas E, Hoffmeyer A, Jackson CW, Cleveland JL, Murray PJ and Ihle JN. Phospholipase Cgamma2 is essential in the functions of B cell and several Fc receptors. **Immunity**. 13(1):25-35, 2000.
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17. Pendeville H., Carpino N., **Marine JC**., Takahashi Y., Muller M., Martial J.A., and Cleveland J.L. The ornithine decarboxylase gene is essential for cell survival during early murine development. **Mol Cell Biol** 21(19):6549-58, 2001.
18. Migliorini,D., Danovi,D., Colombo, E., Carbone, R., Pelicci, P.G., and **Marine J-C**. Hdmx recruitment into the nucleus by Hdm2 is essential for its ability to regulate p53 stability and transactivation. **J Biol Chem.** 277(9):7318-23, 2002.
19. Colombo, E., **Marine, J-C.,** Danovi, D., Falini, B., and Pelicci, P.G. Nucleophosmin regulates the stability and transcriptional activity of p53. **Nature Cell Biol**., 4(7):529-33, 2002.
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23. **Marine J-C**. and Jochemsen A. Mdmx and Mdm2: brothers in arms ? **Cell Cycle**, 3(7):105-109, 2004 (Review)
24. Pirot P., Van Grunsven L.A., **Marine J-C**., Huylebroek D. and Bellefroid E. Direct Regulation of the mouse Nrarp gene promoter by the Notch Signaling Pathway. **BBRC**, 322:526-34, 2004.
25. Viatour P., Dejardin E., Warnier M., Lair F., Claudio E., Bureau F., **Marine J-C**.,Merville M.P., Maurer U., Green D.R., Piette J., Siebenlist U., Bours V. and Chariot A. GSK3-mediated bcl3 phosphorylation modulates its degradation and its oncogenicity. **Molecular Cell**, 16: 35-45, 2004.
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