updated on 07/01/2019

Ruben Dries

Biomedical Scientist, System Biologist, Data Explorer

www.rubendries.com I LinkedIn I rubendries *(Skype)*

Summary

During my PhD studies I acquired a broad background in early and late developmental processes, with a specific focus on neural specification and terminal differentiation. My research in the lab of Dr. Danny Huylebroeck included the generation of a systems biology based screening approach to study the gradual loss of embryonic stem cell pluripotency and subsequent acquisition of more committed neural cell fates. In addition, I also contributed to more detailed studies where I examined the role of specific transcription factors (TFs) or signaling pathways using high-throughput genomic methods such as RNA-seq, ChIP-seq and reduced representation bisulphite sequencing (RRBS).

As a postdoctoral research fellow and team member in the group of Dr. Rani George I continued to study aformentioned TFs and pathways, which are often key regulators in tumor formation, especially in pediatric tumors such as Neuroblastoma (NB) that originate through the aberrant control of developmental gene regulatory networks. As such, I focused on the multifunctional role of MYCN and ALK in tumor oncogenicity and development of drug resistance. More specifically I integrated scRNA-seq, ChIP-seq, Exome-seq, ChIA-PET and HiChIP data to unravel the role of tumor plasticity in mediating tumor resistance and more specifically the crucial role of induced changes in chromatin reorganization. In addition, I also studied the complexities of transcription using a highly selective CDK12/13 inhibitor in combination with an immediate response read-out of the transient-transcriptome (TT-seq) and polyadenylation landscape (polyA-seq).
Concurrently I have contributed in understanding the role of our immune system in the control or treatment of cancer progression in the lab of Dr. Kwok-Kin Wong. Using a (sc)RNA-seq approach I was able to stratify patients based on their immuno-phenotype, identify unique immune populations, or highlight genes and processes that can be targeted to drive immune (re-)activation during cancer treatment. In follow-up work I've also examined the contribution and variability of the epigenetic super-enhancer landscape during tumor formation and resistance development using a large set of patient-derived xenograft (PDX) samples.
In my role as a fellow in the group of Dr. Guo-Cheng Yuan I have developed an algorithm to impute dropout values which improves single-cell expression data and worked on novel tools and pipelines to analyze and interpret state-of-the-art spatial single-cell transcriptomic data (seqFISH+), which allows to study single cells in its native (tumor) microenvironment, specialized niche or supporting neighborhood.

Education

2009-2015 Catholic University of Leuven, Belgium and ErasmusMC, Rotterdam, The Netherlands
Joint-doctorate in Biomedical Sciences
- K.U.Leuven 21 December 2016
- Erasmus M.C. 4 January 2017

2003-2009 Catholic University of Leuven, Belgium
Master in the Biomedical Sciences with great distinction.

Research Experience

2018-present Dana Farber Cancer Institute, USA
Department Comp. Biology & Biostatistics
Joint Research Fellow in the groups of R. George & G.C. Yuan

2016-2018 Dana Farber Cancer Institute, USA
Department Comp. Biology & Biostatistics
Department of (Pediatric) oncology
Joint Research Fellow in the groups of R. George, K.K. Wong and G.C. Yuan

2016-2017 Broad institute (Cancer programme)

2013-2015 Erasmus MC, The Netherlands
Department of Cell Biology
Scientific co-worker & PhD student in the group of Danny Huylebroeck.

2009-2013 KULeuven, Belgium
Department of Development and Regeneration, Celgen
PhD student in the group of Danny Huylebroeck.

2009 University of Ioannina, Greece
Institute of Molecular Biology & Biotechnology
Summer internship in the group of Carol Murphy

2008-2009 Tsinghua University, China
Undergraduate thesis student in the group of Anming Meng
"Contribution to the functional analysis of RNF11 in the zebrafish embryo"

Teaching Experience

2017-2019 **Co-mentor of PhD student Sam Tracy [Harvard, Statistics]**
"Imputing single-cell expression dropouts using an interative bootstrap clustering approach"

2016 **Supervisor for summer student Bennett H. Parsons [MIT, CS]**
"Establishing a flexible high-throughput ChIPseq pipeline"

2015 **Teaching Assistant for 'Hot Topics' journal club**
"Role of Omics in Developmental Biology"

2013 **Supervisor for Biomedical Sciences student, Kurt Buhler**
Labrotation for 2nd year master students
"Derivation of Epiblast and Neural Stem Cells from mESC."

2012 **Supervisor for Biomedical Sciences student, Jasper Neggers**
Labrotation for 2nd year master
"Characterization and evaluation of an in vitro neural differentiation protocol for mESCs optimized for an esiRNA mediated perturbation and qPCR analysis."

Honors

2018 Abstract selected for oral talk at the Keystone meeting (international)

2015 Abstract selected for oral talk at the Syboss meeting (international)

2014 Abstract selected for oral talk at the BSCDB meeting (national)

2009-2012 IWT Fellowship: Strategic Basic Research Fund (2 x 2 years)

2009-2009 Full time paid summer internship (2 weeks)
Ioannina University, Greece

2008-2009 Travel and study grant for undergraduate thesis at
Tsinghua University, China

Technical lab skills

General

- DNA / RNA / miRNA isolation
- PCR, cloning, qRT-PCR
- Western blot
- Sequencing
- Immunofluorescence staining

Specialized

- Experimental and statistical design
- RNAi (esiRNA, siRNA, shRNA, miRNA)
- esiRNA design, construction and application
- optimization of semi/high throughput applications/screens
- mouse stem cell cultures (embryonic, epiblast, neural)
- ChIP-seq
- Single-cell qRT-PCR (custom workflow and analysis)
- Fluidigm hands on experience: C1 + Biomark HD platform

Master thesis

- Zebrafish handling
- Injection and ISH of zebrafish embryos

Computational skills

Programming languages & libraries

- R, Git, Bash (daily use)
- Python, SQL, AWK (conversant)

Software & Operating systems

- Macintosh, Unix/Linux, Windows (OS)
- Rstudio, Git/Github, ImageJ, Inkscape, Gimp (free)
- Office, IPA, GeneVestigator (proprietary)

Genomic datasets

- Bulk & single-cell RNAseq and qPCR
- Spatial transcriptomics (seqFish+)
- Histone and TF ChIP binding
- Reduced representation bisulfite sequencing (RRBS)
- ChIA-PET & HiChIP data analysis
- Start-seq, polyA-seq & TT-seq data analysis
- Regulatory network analysis

Certificates & Training

Wet lab

- Animal handling
- Stem Cell Summer School, Hydra, Greece
- Gene Regulatory Network Summer School, MBL, Woods Hole, USA

Bioinformatics

- LFS101x Introduction to Linux (edX)
- Introduction to Linux for bioinformatics (VIB)
- Getting and Cleaning Data with R (Coursera)
- R Graphics course (FLAMES)
- Advanced Programming in R (FLAMES)
- Data Visualization with J. Aerts & A. Vande Moere (FLAMES)
- NGS data analysis (MGC Leiden)
- Version Control with GIT (MGC Leiden)
- Python Programming Course (MGC Leiden)

Languages

Dutch: Mother tongue
English: Fluent, spoken and written
French: Basic, spoken and written
German: Notions, spoken and written

Conferences

2018 **Keystone** (Joint symposia: Chromatin architecture and chromosome organization & Gene control in development and disease) Whistler, Canada)

2015 **Syboss** (Systems Biology of Stem Cells and Reprogramming) Double symposium, Oberstdorf, Germany

2015 **Winter School of the Collaborative Research Centre TRR81** "Chromatin Changes in Differentiation and Malignancies" Marburg-Giessen-Bad Nauheim-Rotterdam, Kleinwalsertal, Austria

2014 **IUAP** (Interuniversity Attraction Poles Programme) ErasmusMC, Rotterdam, The Netherlands

2014 **From Functional Genomics to Systems Biology** EMBL, Heidelberg, Germany

2014 **BSCDB** (Belgian Society for Cell and Developmental Biology) University of Antwerp, Antwerp, Belgium

2013 **IUAP** (Interuniversity Attraction Poles Programme) University of Liege, Liege, Belgium

2013 **IUAP** (Interuniversity Attraction Poles Programme) Research Park Zwijnaarde, Gent, Belgium

2013 **Syboss** (Systems Biology of Stem Cells and Reprogramming) Kirchberg in Tirol, Austria

Presentations

Talks

2018
"Guided chromatin reorganization as a mechanism of cellular plasticity in cancer" [invited talk]
CReM (The Center for Regenerative Medicine)
Boston University & Boston Medical Center, USA

2015
"Transcriptional dynamics in a TGFbeta centric relational network during early neurogenesis" [selected talk]
Syboss (Systems Biology of Stem cells and Reprogramming)
Double symposium, Oberstdorf, Germany

2014
"Signaling Pathways as Transcriptional Systems"
IUAP (Interuniversity Attraction Poles Programme)
ErasmusMC, Rotterdam, The Netherlands

2014
"TGFbeta Signaling Pathway as a System" [selected talk]
BSCDB (Belgian Society for Cell and Developmental Biology)
University of Antwerp, Antwerp, Belgium

2013
"From Developmental to Systems Biology"
IUAP (Interuniversity Attraction Poles Programme)
Research Park Zwijnaarde, Gent, Belgium

Posters

2018 **"The CTCF paralog BORIS promotes novel chromatin regulatory interactions in cancer cells"**
Dries R, Debruyne DN, Sengupta S, Day DS, Gao Y, Gray NS, Wong KK, Yuan GC, Young RA, George RE
Keystone (Chromatin architecture and chromosome organization), Whistler, Canada

2015 **"Transcriptional dynamics in a TGFbeta centric relational network during early neurogenesis"**
Ruben Dries, Tineke Notelaers, Agata Stryjewska, Enrico Glaab, Kathleen Coddens, Stein Aerts, Frank Grosveld, Catherine Verfaillie, Danny huylebroeck
Syboss (Systems Biology of Stem cells and Reprogramming) Double symposium, Oberstdorf, Germany

2014 **"Transcriptional dynamics in a TGFbeta centric network during early neurogenesis"**
Ruben Dries, Tineke Notelaers, Agata Stryjewska, Enrico Glaab, Kathleen Coddens, Stein Aerts, Catherine Verfaillie, Danny huylebroeck
From Functional Genomics to Systems Biology, EMBL, Heidelberg, Germany

2013 **"Integration of TGFbeata family signaling in the dynamic transcriptional regulatory network of early neurogenesis"**
Ruben Dries, Kathleen Coddens, Agata Stryjewska, Tineke Notelaers, Enrico Glaab, Catherine Verfaillie, Stein Aerts, Danny Huylebroeck
IUAP (Interunivesity Attraction Poles Programme), University of Liege, Liege, Belgium

2013 **"Integration of TGFbeata family signaling in the dynamic transcriptional regulatory network of early neurogenesis"**
Ruben Dries, Kathleen Coddens, Agata Stryjewska, Tineke Notelaers, Catherine Verfaillie, Stein Aerts, Danny Huylebroeck
Syboss (Systems Biology of Stem cells and Reprogramming) Double symposium, Oberstdorf, Germany

2012 **"An esiRNA mediated perturbation screen to identify TGFbeta cross-talk in mESC at different stages of early neural commitment"**
Ruben Dries, Kathleen Coddens, Tineke Notelaers, Catherine Verfaillie, Stein Aerts, Danny Huylebroeck
EAB (External Advisory Board)
KUL, Leuven, Belgium

Articles

Published

"The CTCF paralog BORIS promotes novel chromatin regulatory interactions in cancer cells" Nature 2019 August
Dries R*, Debruyne D*, Sengupta S, Seruggia D, Gao Y, Sharma B, Huang H, Moreau L, McLane M, Day DS, Marco E, Chen T, Gray NS, Wong KK, Orkin SH, Yuan GC, Young RA, George RE

"RESCUE: imputing dropout events in single-cell RNA-sequencing data" BMC Bioinformatics 2019,
Tracy S, Yuan GC, Dries R#

"CDK12 loss in cancer cells affects DNA damage response genes through premature cleavage and polyadenylation" Nature Communications 2019
Dries R* , Krajewska M*, , Grassetti AV, Dust S, Gao Y, Huang H, Sharma B, Day DS, Kwiatkowski N, Pomaville M, Dodd O, Chipumuro E, Zhang T, Greenleaf AL, Yuan GC, Gray NS, Young RA, Geyer M, Gerber SA, George RE

"Transcriptome-scale super-resolved imaging in tissues by RNA seqFISH+" Nature 2019
Eng CHL, Lawson M, Zhu Q, Dries R, Koulena N, Takei Y, Yun J, Cronin C, Karp C, Yuan GC, Cai L

"**Identification of spatially associated subpopulations by combining scRNAseq and sequential fluorescence in situ hybridization data"** Nature Biotech 2018 December
Zhu Q, Shah S, Dries R, Cai L*, Yuan GC*

"Co-clinical trial of olaparib and temozolomide in SCLC PDX models uncovers new biomarkers of sensitivity." Cancer Research 2018 May
Drapkin BJ, George J, Stanzione M, Yeap BY, Mino-Kenudson M, Christensen CL, Dries R, Phat S, Zhong J, Myers DT, Licausi JA, Sundaresan T, Kem M, Abedpour N, Sequist LV, Shaw AT, Hata AN, Toner M, Maheswaran S, Haber DA, Peifer M, Thomas RK, Farago AF, Dyson NJ

"NK cells mediate synergistic antitumor effects of combined inhibition of HDAC6 and BET in a SCLC preclinical model." Cancer Research 2018 April
Liu Y, Li Y, Liu S, Adeegbe DO, Christensen CL, Quinn MM, Dries R, Han S, Buczkowski K, Wang X, Chen T, Gao P, Zhang H, Li F, Hammerman PS, Bradner JE, Quayle SN, Wong KK

"Genomic and functional fidelity of small cell lung cancer patient-derived xenografts." Cancer Discovery 2018 March
Drapkin* BJ, George J*, Christensen CL, Mino-Kenudson M, Dries R, Sundaresan T, Phat S, Myers DT, Zhong J, Igo P, Hazar-Rethinam MH, Licausi JA, Gomez-Caraballo M, Kem M, Jani KN, Azimi R, Abedpour N, Menon R, Lakis S, Heist RS, Büttner R, Haas S, Sequist LV, Shaw AT, Wong KK, Hata AH, Toner M, Maheswaran S, Haber DA, Peifer M, Dyson N, Thomas RK, Farago AF

"CDK4/6 Inhibition Augments Antitumor Immunity by Enhancing T-cell Activation." Cancer Discovery 2017 November
Deng J*, Wang ES*, Jenkins RW, Li S, Dries R, Yates K, Chhabra S, Huang W, Liu H, Aref AR, Ivanova E, Paweletz CP, Bowden M, Zhou CW, Herter-Sprie GS, Sorrentino JA, Bisi JE, Lizotte PH, Merlino AA, Quinn MM, Bufe LE, Yang A, Zhang Y, Zhang H, Gao P, Chen T, Cavanaugh ME, Rode AJ, Haines E, Roberts PJ, Strum JC, Richards WG, Lorch JH, Parangi S, Gunda V, Boland GM, Bueno R, Palakurthi S, Freeman GJ, Ritz J, Haining WN, Sharpless NE, Arthanari H, Shapiro GI, Barbie DA, Gray N, Wong KK.

"Interleukin-17A Promotes Lung Tumor Progression through Neutrophil Attraction to Tumor Sites and Mediating Resistance to PD-1 Blockade." J Thorac Oncol 2017 August
Akbay EA, Koyama S, Liu Y, Dries R, Bufe LE, Silkes M, Alam MM, Magee DM, Jones R, Jinushi M, Kulkarni M, Carretero J, Wang X, Warner-Hatten T, Cavanaugh JD, Osa A, Kumanogoh A, Freeman GJ, Awad MM, Christiani DC, Bueno R, Hammerman PS, Dranoff G, Wong KK.

"Synergistic Immunostimulatory Effects and Therapeutic Benefit of Combined Histone Deacetylase and Bromodomain Inhibition in Non-Small Cell Lung Cancer." Cancer Discovery 2017 August
Adeegbe DO, Liu Y, Lizotte PH, Kamihara Y, Aref AR, Almonte C, Dries R, Li Y, Liu S, Wang X, Warner-Hatten T, Castrillon J, Yuan GC, Poudel-Neupane N1, Zhang H, Guerriero JL, Han S, Awad MM, Barbie DA, Ritz J, Jones SS, Hammerman PS, Bradner J, Quayle SN, Wong KK.

"**Zeb2 regulates cell fate at the exit from epiblast state in mouse embryonic stem cells."** Stem Cells 2016 September
Dries R*, Stryjewska A*, Pieters T, Verstappen G, Conidi A, Coddens K, Francis A, Umans L, van IJcken WFJ, Berx G, van Grunsven LA, Grosveld F, Goossens S, Haigh JJ, Huylebroeck D

"**Multi-parametric profiling of non-small cell lung cancers reveals distinct immunophenotypes."** JCI. 2016 September
Lizotte PH*, Ivanova EV*, Awad MM, Jones RE, Keogh L, Liu H, Dries R, Almonte C, Herter-Sprie GS, Santos A, Feeney NB, Paweletz C, Kulkarni M, Bass AJ, Rustgi AK, Yuan GC, Kufe D, Jänne PA, Hammerman PS, Sholl LM, Hodi FS, Richards WG, Bueno R, English JM, Bittinger M, Wong KK

"BMP-SMAD signaling regulates lineage priming, but is dispensable for self-renewal in mouse embryonic stem cells." Stem Cell Reports 2016 January

Fernandes MG, Dries R, Roost MS, Semrau S, Bernardo AdM, Davis RP, Ramakrishnan R, Szuha K, Maas E, Umans L, Escalona VA, Salvatoria D, Deforce D, 7 Criekinge WV, Huylebroeck D, Mummery C, Zwijsen A, Chuva de Sousa Lopes SM

"Few Smad proteins and many Smad-interacting proteins yield multiple functions and action modes in TGF/BMP signaling in vivo." Cytokine & Growth Factor *Reviews* **22**(5): 287-300.
Conidi A , Cazzola S, Beets K, Coddens K, Collart C, Cornelis F, Cox L, Debruyn J, Dobreva MP, Dries R, Esguerra C, Francis A, Ibrahimi A, Kroes R, Lesage F, Maas E, Moya I, Pereira PNG, Stappers E, Stryjewska A, van den Berghe V, Vermeire L, Verstappen G, Seuntjens E, Umans L, Zwijsen A, Huylebroeck D.

"**Directed migration of cortical interneurons depends on the cell-autonomous action of Sip1.**" Neuron. 2013 Jan 9;77(1):70-82.
van den Berghe V, Stappers E, Vandesande B, Dimidschstein J, Kroes R, Francis A, Conidi A, Lesage F, Dries R, Cazzola S, Berx G, Kessaris N, Vanderhaeghen P, van Ijcken W, Grosveld FG, Goossens S, Haigh JJ, Fishell G, Goffinet A, Aerts S, Huylebroeck D, Seuntjens E.

In revision

"Integrative analysis of the transcriptional dynamics of the TGFβ/BMP signaling pathway in transition from embryonic stem cells to neural progenitors"
Dries R, Stryjewska A, Coddens K, Notelaers T, Birkhoff J, Dekker M, Verfaillie CM, Eskeatnaf Mulugeta EM, Conidi A, Grosveld FG, Huylebroeck D

"Giotto, a pipeline for integrative analysis and visualization of single-cell spatial transcriptomic data"
Ruben Dries, Qian Zhu, Chee-Huat Linus Eng, Arpan Sarkar, Feng Bao, Rani E George, Nico Pierson, Long Cai, Guo-Cheng Yuan

* *shared first authorship*
\# *last author*

References

Postdoc period:

Rani George, MD, PhD
Department of Pediatric Oncology
Dana-Farber Cancer Institute
Boston, USA
Email: Rani_George@dfci.harvard.edu

Kwok-Kin Wong, MD, PhD
Director, Division of Hematology and Medical Oncology
Department of Medicine
NYU Langone
New York, USA
Email: Kwok-Kin.Wong@nyumc.org

Guo-Cheng Yuan, PhD
Department of Biostatistics
Dana-Farber Cancer Institute
Boston, USA
Email: gcyuan@jimmy.harvard.edu

Phd period:

Danny Huylebroeck, PhD
Director of Cell Biology
Department of Cell Biology
Erasmus MC
Wytemaweg 80, 3015CN Rotterdam
The Netherlands
Email: d.huylebroeck@erasmusmc.nl

Frank Grosveld, PhD
Laboratory of Regulation of transcription
Department of Cell Biology
Erasmus MC
Wytemaweg 80, 3015CN Rotterdam
The Netherlands
Email: f.grosveld@erasmusmc.nl

S.M. Chuva de Sousa Lopes, PhD
Dept. Anatomy and Embryology
Leiden University Medical center
The Netherlands
Email: S.M.Chuva_de_Sousa_Lopes@lumc.nl