

# Ruben Dries

*Biomedical Scientist, System Biologist, Data Explorer*

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## 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 aforementioned 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

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|------------------|---|
| <i>2009-2015</i> | Catholic University of Leuven, Belgium and ErasmusMC, Rotterdam, The Netherlands<br><b>Joint-doctorate in Biomedical Sciences</b><br>- K.U.Leuven 21 December 2016<br>- Erasmus M.C. 4 January 2017 |
| <i>2003-2009</i> | Catholic University of Leuven, Belgium<br><b>Master in the Biomedical Sciences with great distinction.</b>  |

## Research Experience

- |                     |   |
|---------------------|---|
| <i>2018-present</i> | Dana Farber Cancer Institute, USA<br>Department Comp. Biology & Biostatistics<br><b>Joint Research Fellow in the groups of R. George &amp; G.C. Yuan</b>  |
| <i>2016-2018</i>    | Dana Farber Cancer Institute, USA<br>Department Comp. Biology & Biostatistics<br>Department of (Pediatric) oncology<br><b>Joint Research Fellow in the groups of R. George, K.K. Wong and G.C. Yuan</b> |

	2016-2017	Broad institute (Cancer programme)
	2013-2015	Erasmus MC, The Netherlands Department of Cell Biology <b>Scientific co-worker &amp; PhD student in the group of Danny Huylebroeck.</b>
	2009-2013	KULeuven, Belgium Department of Development and Regeneration, Celgen <b>PhD student in the group of Danny Huylebroeck.</b>
	2009	University of Ioannina, Greece Institute of Molecular Biology & Biotechnology <b>Summer internship in the group of Carol Murphy</b>
	2008-2009	Tsinghua University, China <b>Undergraduate thesis student in the group of Anming Meng</b> "Contribution to the functional analysis of RNF11 in the zebrafish embryo"
<b>Teaching Experience</b>	2017-2019	<b>Co-mentor of PhD student Sam Tracy [Harvard, Statistics]</b> "Imputing single-cell expression dropouts using an iterative bootstrap clustering approach"
	2016	<b>Supervisor for summer student Bennett H. Parsons [MIT, CS]</b> "Establishing a flexible high-throughput ChIPseq pipeline"
	2015	<b>Teaching Assistant for 'Hot Topics' journal club</b> "Role of Omics in Developmental Biology"
	2013	<b>Supervisor for Biomedical Sciences student, Kurt Buhler</b> Labrotation for 2nd year master students "Derivation of Epiblast and Neural Stem Cells from mESC."
	2012	<b>Supervisor for Biomedical Sciences student, Jasper Neggens</b> 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."
<b>Honors</b>	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**

	<b>Talks</b>
2018	<b>“Guided chromatin reorganization as a mechanism of cellular plasticity in cancer” [invited talk]</b> CReM (The Center for Regenerative Medicine) Boston University & Boston Medical Center, USA
2015	<b>“Transcriptional dynamics in a TGFbeta centric relational network during early neurogenesis” [selected talk]</b> Syboss (Systems Biology of Stem cells and Reprogramming) Double symposium, Oberstdorf, Germany
2014	<b>“Signaling Pathways as Transcriptional Systems”</b> IUAP (Interuniversity Attraction Poles Programme) ErasmusMC, Rotterdam, The Netherlands
2014	<b>“TGFbeta Signaling Pathway as a System” [selected talk]</b> BSCDB (Belgian Society for Cell and Developmental Biology) University of Antwerp, Antwerp, Belgium
2013	<b>“From Developmental to Systems Biology”</b> 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 (Interuniversity 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, Koulina 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 Crieckinge 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, Debruyne J, Dobrev MP, Dries R, Esguerra C, Francis A, Ibrahim 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"** *Stem Cells*

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"** *Nature Biotechnology*

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**

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