Ruben Dries

Biomedical Scientist, System Biologist, Data Explorer

www.rubendries.com | LinkedIn | rubendries (Skype)

Summary

During my PhD 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 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 the 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 and key role of MYCN 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 dynamic and induced 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 from single-cell expression data, worked on inferring the spatial position of single-cells based on derived interaction information and contributed to the analysis and interpretation of spatial single-cell transcriptomic data (seqFish).

-a	u	^	2	tı	0	n
Lu	u	v	а	ч	v	

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

Broad institute (Cancer programme) 2016-2017 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. University of Ioannina, Greece 2009 Institute of Molecular Biology & Biotechnology Summer internship in the group of Carol Murphy Tsinghua University, China 2008-2009 Undergraduate thesis student in the group of Anming Meng "Contribution to the functional analysis of RNF11 in the zebrafish embryo" **Teaching** 2017 Co-mentor of PhD student Sam Tracy [Harvard, Statistics] "Imputing single-cell expression dropouts using an interative bootstrap **Experience** clustering approach" 2016 Supervisor for summer student Bennett H. Parsons [MIT, CS] "Establishing a flexible high-throughput ChIPseq pipeline" Teaching Assistant for 'Hot Topics' journal club 2015 "Role of Omics in Developmental Biology" Supervisor for Biomedical Sciences student, Kurt Buhler 2013 Labrotation for 2nd year master students "Derivation of Epiblast and Neural Stem Cells from mESC." Supervisor for Biomedical Sciences student, Jasper Neggers 2012 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** Abstract selected for oral talk at the Keystone meeting (international) 2018 Abstract selected for oral talk at the Syboss meeting (international) 2015 Abstract selected for oral talk at the BSCDB meeting (national) 2014 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, Rmarkdown, Bioconductor, Bash (daily use)
 Python, SQL, Git, 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
- Histone and TF ChIP binding
- Reduced representation bisulfite sequencing (RRBS)
- ChIA-PET 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 Mo	pere (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

	Talks
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

Presentations

Posters

2015

2018 "The CTCF paralog BORIS promotes novel chromatin regulatory interactions in cancer cells"

<u>Dries R</u>, 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

"Transcriptional dynamics in a TGFbeta centric relational network during early neurogenesis"

<u>Ruben Dries</u>, 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"

<u>Ruben Dries</u>, 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"

<u>Ruben Dries</u>, Kathleen Coddens, Tineke Notelaers, Catherine Verfaillie, Stein Aerts, Danny Huylebroeck EAB (External Advisory Board) KUL, Leuven, Belgium

Published articles

"Decomposing spatially dependent and cell type specific contributions to cellular heterogeneity" Nature Biotech 2018 Accepted 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, <u>Dries R</u>, 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, <u>Dries R</u>, 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,

"CDK4/6 Inhibition Augments Antitumor Immunity by Enhancing T-cell Activation." Cancer Discovery 2017 November

Thomas RK, Farago AF

Deng J*, Wang ES*, Jenkins RW, Li S, <u>Dries R</u>, 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, <u>Dries R</u>, 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, <u>Dries R</u>, 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

<u>Dries R</u>*, 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." ICI. 2016 September

Lizotte PH*, Ivanova EV*, Awad MM, Jones RE, Keogh L, Liu H, <u>Dries R</u>, 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, <u>Dries R</u>, 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, <u>Dries R</u>, 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.

Articles in revision

Not available for public

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