

Ruben Dries

Biomedical Scientist, System Biologist, Data Explorer

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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 aforementioned 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 and ChIA-PET data to unravel how the dynamics of chromatin reorganization can contribute to tumor plasticity and subsequently mediate tumor resistance. 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).

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).

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 **Co-mentor of PhD student Sam Tracy [Harvard, Statistics]**
"Imputing single-cell expression dropouts using an iterative 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, 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 & TTseq 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

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| 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

- 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

- 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

Published articles

“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, Bufo 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
Akabay EA, Koyama S, Liu Y, Dries R, Bufo 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, 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, 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, Kessar N, Vanderhaeghen P, van Ijcken W, Grosveld FG, Goossens S, Haigh JJ, Fishell G, Goffinet A, Aerts S, Huylebroeck D, Seuntjens E.

References

Postdoc period:

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Kwok-Kin Wong, MD, PhD

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Guo-Cheng Yuan, PhD

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Boston, USA
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Phd period:

Danny Huylebroeck, PhD

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Frank Grosveld, PhD

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