



Hello everyone,

I'm not sure what happened to the end of 2022 (!), but in any event here is our first CSDB newsletter of 2022/23. This semester promises to be a busy and exciting one, with our graduate student steering committee members being hard at work organizing student-invited seminars. We had some great talks from our own **John Calarco** and **Rajan Jain** (U Penn) to close out 2022, with lively discussion at the post-seminar student pub events. We have upcoming talks from **Jeff Biernaskie** (February 23<sup>rd</sup>), **Lisa Julian** (March 29<sup>th</sup>) and **Armen Saghatelian** (April 27<sup>th</sup>) to look forward to, as well as a talk from **Sara Nunes de Vasconcelos** next week (February 8<sup>th</sup>). Watch for the flyers and announcements!

Our annual **Old Mill Retreat** is scheduled for May 30<sup>th</sup>, featuring a keynote address from **Janet Rossant**. On a related note, the **Great Lakes Developmental Biology** meeting will be held in Toronto June 28<sup>th</sup> -29<sup>th</sup>, with FREE registration. A big thanks to **Jonathan Palozzi**, **Zaleena Akheralie** and **Charlotte Martin** for all their work organizing the seminars, in particular for student invited talks. They will be polling students for a fresh list of faculty to invite for a seminar and visit – please respond with great suggestions!

A reminder that I am aiming to incorporate postdoctoral researchers into our program – please encourage postdocs in your lab to contact Cindy and join our e-mail list. I would like to develop events where postdocs take leadership roles AND get to bolster their “teaching” portfolio at the same time. This will add to a regular, monthly series of events we are developing for 2023/24.

In other news, a big thanks to **Jeffrey Stulberg** and **Rodrigo Fernandez Gonzalez** for running our first student grant competition. And congratulations to **Matthew Chang** (Protze lab) and **Esra Erkut** (Scott lab) for their winning proposal on modeling non-coding congenital heart disease mutations in a human gastruloid model. Hopefully, the prize will help support some exciting research! We will be evaluating this first iteration of the grant competition and hopefully will be trying for something bigger and better in the future.

In the past few months **Sally Kim** (PhD, Jurisicova lab) and **Mengyi Song** (PhD, Scott lab) have graduated from the program. Congratulations, and all the best on your next endeavours! A warm welcome to new members of CSDB: **Ran Xu** (MSc, Ciruna lab), **Brook Falk** (PhD, Brill lab), **Byrn Martin** (MSc, Ramalho-Santos lab), **Marynell Icmat** (PhD, Brill lab), **Jevithen Nehru** (MSc, Saltzman lab), **ZhuYi Wang** (PhD, Smibert lab), **Katerina Kiriakopoulos** (PhD, Maass lab) and **Maria Fahim** (MSc, Scott lab); and our newest faculty members - **Shinichiro Ogawa** (LMP), **Michael Wilson** (MoGen) and **Sara Nunes de Vasconcelos** (IBBME, LMP).

Best,

Ian

PS – a special thanks to **Charlotte Martin** for putting together this month's featured interview of our CSDB alum Mengyi Song and Xuefei Yuan.

## CSDB ALUMNI INTERVIEW with Dr. Mengyi Song and Dr. Xuefei Yuan

I interviewed Dr. Mengyi (Candy) Song, and Dr. Xuefei Yuan about the process of writing and publishing their recent article “*GATA4/5/6 family transcription factors are conserved determinants of cardiac versus pharyngeal mesoderm fate*” published in **Science Advances** in March 2022. They are both recent graduates from CSDB and were co-supervised by Dr. Ian Scott and Dr. Michael Wilson.



**Charlotte:** Can you briefly summarize the article?

*Mengyi (Candy):* Broadly speaking our paper is about transcription factors and cell fate. In particular, we are looking the GATA transcription factors in zebrafish. They are named GATA since their binding motifs are G-A-T-A. We are looking at these transcription factors and how they guide the mesendoderm cells to a cardiac fate.

**Charlotte:** Was there a result that you found most interesting or exciting when you were analyzing the data that you wanted to highlight in the article?

*Xuefei:* One of the things I found most interesting was when we first got the single-cell data and did some basic analysis to get an idea what happened when the embryos lost *gata5/6*. Previously, in zebrafish and even other vertebrates *gata5/6* were mainly linked to cardiac development within the mesoderm. However, we noticed there were so many other mesodermal lineages that were labelled by *gata5/6* expression early on. Also, when we compared cell composition between wildtype and *gata5* knockdown embryos they displayed a quite dramatic reduction of many mesodermal lineages. For example, blood, pharyngeal and kidney populations. Which was surprising to us.

**Charlotte:** Are there any results that you couldn't include that you wish people were able to hear about?

*Candy:* Xuefei kind of got into this question already when she mentioned the blood lineage. That is something we are working on right now and is going to be another paper. Previously, our plan was to combine all different lineages into one paper, but we discovered it was probably too much. So, we decided to split the paper into two.

**Charlotte:** Was this your first “first author” article? If you had previous publications with smaller contributions how was this process different?

*Candy:* It is a different scenario for both of us. This was my first “first author” paper but previously, I was also involved in a paper that was Xuefei's main project. When I came into the lab that project was almost ready to be published but there were still some experiments that needed to be done. Xuefei planned all the work and I mostly just followed along. Which is a bit different than this one. I got the opportunity to make part of the figures for her paper, but I didn't really go through the entire editorial process. For example, writing the rebuttal letter. However, for this one since we were co-first authors, I was involved in everything from the very beginning. Writing the paper, editing the paper with our PIs Ian and Mike and writing a rebuttal letter.

**Charlotte:** Anything you wanted to add Xuefei?

*Xuefei:* Just briefly, this is my second “first author” paper and I would say it feels really nice when you have a partner in crime, a real collaborator. Who you can share both the frustrations as well as the excitement and have discussions with. Candy did a lot of work for this paper, and it felt nice to have her, compared to my first paper which I finished mostly by myself.

*Candy:* I just wanted to add a little bit on that. As Xuefei mentioned it was really nice to have a collaborator. It was nice to have the feeling that you have someone that is doing the same thing as you and that you have each other's back. Because if you are working on your own sometimes there is stuff that you have to troubleshoot or you may have a really frustrating day and you don't have anyone to share it with. Though it's not nice to share these negative thoughts and energy, it's nice to have someone to talk things out with.

**Charlotte: How long was the process from initial writing to final publication?**

*Candy:* I would say probably two years. What do you think Xuefei?

*Xuefei:* Yes, I briefly checked the dates in our shared drop box, and I think our first version that we gave to our PIs was in May of 2020. Then our first submission was December 2020. We submitted to Nature Cell Biology, but we didn't pass the editors and then we immediately submitted it to Science Advances in December/January. Then we can talk about this later, but they gave us a very long list of revisions plus there was COVID. So, our resubmission was in October of 2021. Then final acceptance in 2022. Once it was accepted there was a lot of editorial stuff, which can be surprising if it is your first paper. I think Candy did most of that. Finally, it was published in March 2022.

**Charlotte: What is the editorial stuff? I've never heard of that. Is it formatting and such?**

*Candy:* Yes, mostly. The most painful thing was that the journal had a limit for the number of references you can cite, and we had to cut down a lot of references and make some tough choices.

**Charlotte: Since, you brought it up, what was the review process like? Did they ask for many changes or additional experiments?**

*Xuefei:* I would say it was a relatively long revision. The review document we got was quite long and we had four reviewers compared to three, which is more common. Each one of them gave us a list of comments and there was not much overlap. We had to add a lot of new data into our revision, including the ATAC-seq data which was not in the paper before. Although, we had done that experiment in parallel, we hadn't added it. Since, I had already left the lab at that time, Candy did most of the experiments they asked for to get the paper published.

**Charlotte: That is interesting because I liked the ATAC-seq data, that was something I found very interesting.**

*Candy:* There was also a second round of revisions, though it was shorter. I don't know if that is common since it was my first paper.

**Charlotte: Is there any other part of the process that surprised you or took longer than expected?**

*Candy:* The second review schedule was very tight. It came right before Christmas, and they asked for a 3-week turnaround. Of course, you can ask for an extension, but I thought the time was tight.

**Charlotte: You already mentioned this briefly but how did you choose which journal submit to?**

*Candy:* Our first choice was Nature Cell Biology but because we didn't pass the editors, we switched to Science Advances. In terms of which journal to submit to, we had both read a lot of relevant papers in these journals. Also, we discussed it with our supervisors, since they have a better idea of which one to target.

*Xuefei:* We were also inspired that the journal had previously published similar work. For example, Nature Cell Biology published our collaborators work, the single-cell lineage comparison from Lionel Christiaen's lab. We also considered the audience of the potential journals. It's better if your work is published by a journal that can help your paper reach the right people, who will be really interested in your work. Also, the reputation of the journal and that kind of stuff.

**Charlotte: Final question, is there anything you which you had known at the beginning before starting to write/publish? Or any advice to your past self or people in the process right now?**

*Candy:* That is hard question. I kind of wish that I had known everything, but I guess it is really a process that you have experience for yourself. So, that you can really know how it works.

*Xuefei:* If I could give any advice, it's that the process will always take longer than you expect. So, just try not to be frustrated by this prospect.

*Candy:* You actually reminded me of those days. I feel like if I were to say something I would say, "just hang in there". You always feel that there is no end, but you just have to do things step by step and eventually you will get there. You just have to believe that.

*\*This interview was edited for length and clarity. Charlotte Martin*

## Selected Publications

**Anderson MK**, da Rocha JDB (2022) *Direct regulation of TCR rearrangement and expression by E proteins during early T cell development* **WIREs Mech Dis** Jul 18:e1578.

**Angers S** (2022) *Frizzled does not get bent out of shape by Wnt* **Sci Signal** Aug 23;15(748):eadd3535.

Cook DP, **Wrana JL** (2022) *A specialist-generalist framework for epithelial-mesenchymal plasticity in cancer* **Trends Cancer** May;8(5):358-368.

Endo Y, Groom L, Celik A, Kraeva N, Lee CS, Jung SY, Gardner L, Shaw MA, Hamilton SL, Hopkins PM, Dirksen RT, Riazi S, **Dowling JJ** (2022) *Variants in ASPH cause exertional heat illness and are associated with malignant hyperthermia susceptibility* **Nat Commun** Jun 13;13(1):3403.

Goodwin K, Jaslove JM, Tao H, Zhu M, **Hopyan S**, Nelson CM (2022) *Patterning the embryonic pulmonary mesenchyme* **iScience** Jan 29;25(3):103838.

Hanna J, David LA, Touahri Y, Fleming T, Sreaton RA, **Schuurmans C** (2022) *Beyond Genetics: The Role of Metabolism in Photoreceptor Survival, Development and Repair* **Front Cell Dev Biol** May 18;10:887764.

Harrington S, Knox JJ, Burns AR, Choo KL, Au A, Kitner M, Haeberli C, Pyche J, D'Amata C, Kim YH, Volpatti JR, Guiliani M, Snider J, Wong V, Palmeira BM, Redman EM, Vaidya AS, Gilleard JS, Stagljar I, Cutler SR, Kulke D, **Dowling JJ**, Yip CM, Keiser J, Zasada I, Lautens M, **Roy PJ** (2022) *Egg-laying and locomotory screens with C. elegans yield a nematode-selective small molecule stimulator of neurotransmitter release* **Commun Biol** Aug 24;5(1):865.

Jussila M, **Boswell CW**, **Griffiths NW**, **Pumputis PG**, **Ciruna B** (2022) *Live imaging and conditional disruption of native PCP activity using endogenously tagged zebrafish sfGFP-Vangl2* **Nat Commun** Sep 23;13(1):5598.

Langille E, Al-Zahrani KN, Ma Z, Liang M, Uuskula-Reimand L, Espin R, Teng K, Malik A, Bergholtz H, El Ghamrasni S, Afiumi-Zadeh S, Tsai R, Alvi S, Elia A, Lu Y, Oh RH, Kozma KJ, Treka D, Narimatsu M, Liu JC, Nguyen T, Barutcu S, Loganathan SK, Bremner R, Bader GD, **Egan SE**, Cescon DW, Sorlie T, **Wrana JL**, Jackson HW, **Wilson MD**, Witkiewicz AK, Knudsen ES, Pujana MA, Wahl GM, **Schramek D** (2022) *Loss of epigenetic regulation disrupts lineage integrity, induces aberrant alveogenesis and promotes breast cancer* **Cancer Discov** Sep 15:CD-21-0865.

Leigh ND, **Currie JD** (2022) *Rebuilding limbs, one cell at a time* **Dev Dyn** Sep;251(9):1389-1403.

Liu J, Sahin C, Ahmad S, Magomedova L, Zhang M, Jia Z, Metherel AH, Orellana A, Poda G, Bazinet RP, Attisano L, Cummins CL, Peng H, **Krause HM** (2022) *The omega-3 hydroxy fatty acid 7(S)-HDHA is a high-affinity PPAR $\alpha$  ligand that regulates brain neuronal morphology* **Sci Signal** Jul 5;15(741):eabo1857.

Matute JD, Finander B, Pepin D, Ai X, Smith NP, Li JZ, Edlow AG, Villani AC, Lerou PH, **Kalish BT** (2022) *Single-cell immunophenotyping of the fetal immune response to maternal SARS-CoV-2 infection in late gestation* **Pediatr Res** Apr;91(5):1090-1098.

**Martin CJ**, **Calarco JA** (2022) *Approaches for CRISPR/Cas9 Genome Editing in C. elegans* **Methods Mol Biol** 2468:215-237.

**Meyer-Miner A**, **Van Gennip JLM**, Henke K, Harris MP, **Ciruna B** (2022) *Resolving primary pathomechanisms driving idiopathic-like spinal curvature using a new *katnb1* scoliosis model* **iScience** Aug 28;25(9):105028.

**Nunes SS**, de Oliveira Silva J, Fernandes RS, Miranda SEM, Leite EA, de Farias MA, Portugal RV, Cassali GD, Townsend DM, Oliveira MC, de Barros ALB (2022) *PEGylated versus Non-PEGylated pH-Sensitive Liposomes: New Insights from a Comparative Antitumor Activity Study* **Pharmaceutics** Jan 24;14(2):272.

Pieters VM, Rjaibi ST, Singh K, Li NT, Khan ST, Nunes SS, Dal Cin A, **Gilbert PM**, **McGuigan AP** (2022) *A three-dimensional human adipocyte model of fatty acid-induced obesity* 2022 **Biofabrication** Aug 19;14(4).

Qashqari H, McNiven V, Gonorazky H, Mendoza-Londono R, Hassan A, Kulkarni T, Amburgey K, **Dowling JJ** (2022) *PURA syndrome: neuromuscular junction manifestations with potential therapeutic implications* **Neuromuscul Disord** Oct;32(10):842-844.

Seroussi U, Li C, Sundby AE, **Lee TL**, **Claycomb JM**, **Saltzman AL** (2022) *Mechanisms of epigenetic regulation by C. elegans nuclear RNA interference pathways* **Semin Cell Dev Biol** Jul;127:142-154.

Simões S, Lerchbaumer G, Pellikka M, Giannatou P, Lam T, Kim D, Yu J, **Ter Stal D**, **Al Kakouni K**, **Fernandez-Gonzalez R**, **Tepass U** (2022) *Crumbs complex-directed apical membrane dynamics in epithelial cell ingression* **J Cell Biol** Jul 4;221(7):e202108076.

**Stulberg J**, **Tropepe V** (2022) *In Situ Quantification and Isolation of Müller Glial Cells by Fluorescence-Activated Cell Sorting from the Regenerating Larval Zebrafish Retina* **Methods Mol Biol** ;2429:345-356.

**Stutt N**, **Song M**, **Wilson MD**, **Scott IC** (2022) *Cardiac specification during gastrulation - The Yellow Brick Road leading to Tinman* **Semin Cell Dev Biol** Jul;127:46-58. Review.

**Thompson PK**, **Chen ELY**, de Pooter RF, Frelin C, Vogel WK, Lee CR, Venables T, Shah DK, Iscove NN, Leid M, **Anderson MK**, **Zúñiga-Pflücker JC** (2022) *Realization of the T Lineage Program Involves GATA-3 Induction of *Bcl11b* and Repression of *Cdkn2b* Expression* **J Immunol** Jul 1;209(1):77-92.