UNIVERSITY OF TORONTO

CSDB
Collaborative Specialization in Developmental Biology

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Season's Greetings everyone!

As we transition to 2024 (!), I'm very excited to update you on planned events for the next semester, culminating in our annual retreat in May. After a series of great talks this semester, our steering committee student reps have been very hard at work lining up our seminars for January to May:

- January 25th: Ahilya Sawh, one of our newest faculty members
- February 21st: Todd Blankenship
- March 27th: Melissa Mann
- May 1st: Jeff Farell
- May 29th: annual Old Mill Retreat (keynote speaker: Benoit Bruneau)

Please follow e-mails from CSDB (and out website) for upcoming talks. I highly encourage students to take advantage of the opportunity to interact with our visiting speakers at the trainee lunch or pub event scheduled with each seminar by our outstanding student members of the steering committee. Students - please also add to our suggested speaker list, and take an active role in hosting your suggested speaker! It is a great way to network and (perhaps) line up a future postdoc.

Speaking of which, our student reps (Charlotte Martin, Zaleena Akheralie, Marynelle Icmat and our newest member, Una McNally) all work hard behind the scenes to organize these events and provide invaluable feedback on how CSDB is run. Jeff Stulberg has stepped down after a long run on the committee, and I would like to thank him profusely for all the effort and great contributions he has added to CSDB. Outside the committee, trainees are encouraged to participate more generally by attending our seminars, suggesting speakers that they feel would add to our program, etc. Students – attendance at these events is a key part of your program!

We are planning to launch the second iteration of our trainee grant competition later this summer (details to follow). Please see an interview below from the winners of our first competition. I am very excited that we will be partnering with DSCB at SickKids to have a careers-focused event with DSCB and CSDB alumni **March 26th** (details to follow). Olena Zhulyn has been very hard at work finalizing what will be a fantastic array of speakers and round table attendees. This will expand greatly on the roundtables we had at the retreat last year, with a career-centric focus.

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.

I'm happy to highlight the following:

New CSDB Faculty:

Madeline Hayes

Ahilya Sawh

Olena Zhulyn

New CSDB Students (welcome)

Zi Qi Lin (MSc; Cox)

Claire Turke (PhD; Reinke)

Cherry Wan Ya Liu (MSc; Scott)

Marie Rachel (PhD; Ciruna)

Una Mcnally (MSc; Harris)

Maria Fahim (MSc; Scott)

Sifa Quibria (MSc; Bruce)

Donna Guan (MSc; Bruce/Harris)

Simon Monis (PhD; Wilson)

Tanner Zoche (PhD; Derry)

Jooyeong Kwak (MSc; Rosenblum)

Graduated Students (congrats!)

Nicole Lindsay-Mosher (PhD; Pearson)

Jonathan Palozzi (PhD; Hurd)

Gordana Scepanovic (PhD; Fernandez-Gonzalez)

Amanda Charlesworth (PhD; Claycomb)

Adrian Loe (PhD; Kim)

Mallory Wiggins (PhD; Pearson)

Michele Ly (MASc; Fernandez-Gonzalez)

Denise Rebello (PhD; Ciruna

As always, please feel free to pass on feedback and suggestions to me via e-mail or in person at a CSDB event.

Best for the end of 2023 and the start of 2024,

Ian

Follow us on Twitter: @DevBio_UofT.

And on our website: devbio.utoronto.ca

Interview with Esra Erkut and Matthew Chang on their 2022-23 winning CSDB Grant Proposal Competition

I interviewed **Esra Erkut** (3rd year PhD student in the Scott Lab) and **Matthew Chang** (3rd year PhD student in the Protze Lab) about their 2022-23 winning CSDB Grant Competition Proposal titled "Functional validation of non-coding variation in human heart development and disease". We will be hosting another grant competition this year. So, stay tuned for future announcements.

Charlotte: **Can you briefly summarize the work you outlined in the grant proposal?**

Esra: The broad idea was that we have a bottleneck in the field of human genetics where you have non-coding mutations that have been identified through genome-wide association studies and whole genome sequencing. However, it is incredibly difficult to validate non-coding genetic variation. So, we were proposing a framework where in the first part you would use our established Scott/Wilson Lab aCNE (accessible conserved non-coding elements) sets to prioritize non-coding regions that are more likely to be developmental cardiac enhancers. Then, through collaboration with the SickKids Cardiac Genome Clinic, we have identified patient mutations in some of these candidate enhancers and we will be using the zebrafish reporter assay, that we have established in the Scott lab, to validate whether these are indeed enhancers. As well as, whether patients' mutations are in fact changing the activity of these enhancers. Then any interesting hits would be carried on into Aim 2, which I will let Matt take on.

Matthew: What I am interested in general is a way to study human embryogenesis. Currently, we do that with stem cells and in the field, there has been a lot of recent stem cell derived embryo models. I am working with one called the gastruloid. We use human pluripotent stem cells to model human gastrulation. So, what we were hoping to achieve with the hits that Esra found (or will find) in Aim 1 is that I would use the gastruloids to validate and see how those hits effect human heart development. Basically, looking at how in our system they effect cardiac progenitor migration, survivability or proliferation etc. in the context of the embryo.

Esra: I think that the collaboration is the key part here. The zebrafish is an excellent model for studying vertebrate heart development because a lot of the core principles of cardiac development and core genes are conserved across vertebrates including zebrafish and humans. However, with all animal models, at a certain point it is not exactly a human, and I am really interested in human heart development and human patients. So, that's where I feel Matt's work really complements it.

Charlotte: **You started to answer this but why did you choose to collaborate with each other? Did you have an existing collaboration or was the grant competition a way to start something new?**

Matthew: We met in rotations during first year and kind of kept in touch with each other as we went through the program. So basically, she was doing heart related stuff with Ian Scott and I was doing heart related stuff with Stephanie Protze and it just felt pretty natural. She had some hits and I wanted to build this system and it would be a good tool to show that the system is valuable, at least from my part.

Esra: Exactly, it's a good way to functionally validate hits with [Matt's] really cool system. Actually, I think we had talked about collaborating before this grant competition. I think we met and sat down and really discussed it around the time of our first committee meetings.

Matthew: I think it was really easy for me to work with Esra. I think we divided the way we wrote the grant really well. So, we were each able to do our own part and then came together and decided what we wanted to keep, and we wanted to throw out.

Charlotte: **How is the project going? Have you had a chance to do some of the things you outlined or has anything changed?**

Esra: In terms of the first part where we are talking about prioritizing regions and then testing those in zebrafish, that is actively what I am doing for part of my PhD. I have found a really interesting hit where a patient mutation within a specific enhancer appear to weaken its cardiac enhancer activity and I am currently following this up with mutant models in zebrafish. This is something that I think would be a really key hit to then bring to the gastruloid model but from my understanding that still needs a bit of fine-tuning.

Matthew: I am also still actively working on the model. I have established/found a pretty good optimization to our protocol. Now I am doing a lot of characterization of the gastruloid system to see if we are accurately recapitulating the events and morphologies that are happening, that we know of, in my system. Then hopefully once I have understood a little bit about how cardiogenesis is happening in the system, we can start looking at examples of disease modelling with the hits that Esra has found.

Charlotte: **Your work seems to really complement each other's. How did you find the process working with someone else on the grant proposal?**

Matthew: I think it was really easy for me to work with Esra. I think we divided the way we wrote the grant really well. So, we were each able to do our own part and then came together and decided what we wanted to keep, and we wanted to throw out.

Esra: Also, I think because we had met before we started writing, we had established what the key ideas and the aims were going to be.

Charlotte: **We will be doing this grant competition again this year. Therefore, do you have any advice to anyone wanting to apply?**

Esra: I feel like one thing is having an internal deadline for yourself prior to real deadline. Especially if you are writing with someone else there will be a period of editing and revising to make it flow together. So, if you can, set a deadline before it is due to get your respective parts done and then fine tune it from there.

Matthew: I'd say for me it was to just take advantage of the other person's brain because sometimes I feel like I know what I am writing and it makes sense to me but to have someone else who kind of knows what I am doing but also doesn't, read it over and ask questions. It was really helpful to have another perspective.

Esra: I definitely agree, it helps keep it to a more general science audience because you have someone else helping you weed out all the little nitty gritty details. Allowing you to just get to the core basic idea of what you are trying to get across with your proposal.

**This interview was edited for length and clarity.*

Esra Erkut
Scott lab

Matthew Chang
Protze lab

Selected Publication

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