



Graduate Research Highlights • Publication Update

Nature Structural & Molecular Biology Volume 13 Number 9 September 2006

Argonaute-1 directs siRNA-mediated transcriptional gene silencing in human cells

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Argonaute proteins are the core components of effector complexes that facilitate RNA interference (RNAi). Small interfering RNAs (siRNAs) targeted to promoter regions mediate transcriptional gene silencing (TGS) in human cells through heterochromatin formation. RNAi effector complexes have yet to be implicated in the mechanism of mammalian TGS. Here we describe the role of the human Argonaute-1 homolog (AGO1) in directing TGS at the promoters for human immunodeficiency virus-1 coreceptor CCR5 and tumor suppressor RASSF1A. AGO1 associates with RNA polymerase II (RNAPII) and is required for histone H3 Lys9 dimethylation and TGS. AGO1, TAR RNA-binding protein-2 (TRBP2) and Polycomb protein EZH2 colocalize to the siRNA-targeted RASSF1A promoter, implicating Polycomb silencing in the mechanism of mammalian TGS. These results establish a connection between RNAi components AGO1 and TRBP2, RNAPII transcription and Polycomb-regulated control of gene expression.



First author, Daniel Kim, studies transcriptional gene silencing in the Rossi lab.

The Helix asked Daniel Kim a few questions about his paper.

How did you get involved with the research that led to the publication?

My interest in the area of mammalian transcriptional gene silencing (TGS) began after I read a 2004 Science paper by a former post-doc in the Rossi Lab, Dr. Kevin Morris, who is now an assistant professor at the Scripps Research Institute. Although Kevin left our lab a few months after I joined, we had some very interesting conversations regarding the mechanism of TGS, and I began working with him on testing whether siRNAs directed against the HIV-1 coreceptor CCR5 promoter could induce TGS. Kevin and Louisa Villeneuve, who did a rotation through the Rossi lab just before I joined, had begun screening these CCR5-targeting siRNAs, and after Kevin left the lab, I took over the project, which at that time was still in its infancy.

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Mission Statement:

The Helix newsletter seeks to inform, empower, and connect our student body in order to focus and promote our graduate school's growth and accomplishments.

Through The Helix, we intend to inform City of Hope and its faculty that our graduate program remains accomplished in research, ultimately reflecting the caliber of our students and our program.

The Helix also seeks to empower. To inspire, motivate, and give confidence to our graduate students as they explore and accomplish their goals.

Furthermore, by connecting our students, we can nurture an academic environment, establish collaborations, and initiate scientific progress.

THE CAREER CORNER

Network Your Way to Success!

Jonie Watanabe Tsuji,
Career Counselor

What do you think is the most successful method in finding a job?

- A) Posting your resume online at job sites like Career Builder or Monster.com
- B) Looking in the Sunday Los Angeles Times Classified section
- C) Talking to people and spreading the word that you are available, and what your skills are.

Although choices A & B are probably the easiest to do, they are the most passive and not as successful. C is the most successful method in finding a job – in case you didn't know it, the method I just described is called networking.

What is networking?

Networking is about making connections— it is a community of people. From the not so obvious, like your neighbor, your garbage man, your dentist, your child's friend's parent, to the obvious like your lab mate, advisor, and former professor. You name it, anyone you come into contact with is part of your network. Networking is not - playing a game, "kissing up," or "brown-nosing." So how do you network? First, know yourself. (What is important to you? What are your goals in life?). Secondly, know what you want in a job and what you have to offer. (What are

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Artists' rendition of the completed CITI building.

The modern CITI Building will serve as the new location of our graduate school.

by Chen Wu

Where will our new graduate school be located?

Do you have an answer? True, we currently have offices in the Miller building, but will there ever be more? More classrooms, more laboratories, and, inevitably, more graduate students?

A resounding “yes!” lies in the Cancer Immunotherapeutics and Tumor Immunology (CITI) Research Building (a.k.a the Arnold and Mabel Beckman Center). Construction of this five-floor clinical research building, located just east of Miller, is now underway and, with much anticipation, we are awaiting the dedication of the entire first floor to the City of Hope Graduate School of Biological Sciences.

The idea of having a central, self-sufficient location for our graduate school was formed as early as 1999, according to Dr. John Rossi, dean of the graduate school. A cost-effective strategy was met by reserving the first floor of the Beckman Center for our graduate school, a generous offer made by Drs. Michael Jensen and Andrew Raubitschek, whose efforts have helped propel progress of the CITI department.

Artists' renditions of the completed building illustrate a modern, fluid design with a glass and steel façade. Facilities will require electronic access for students and graduate school officials. They include a conference room and modern classrooms, all with overhead projection systems, available for our lectures. We'll no longer have to painstakingly search for rooms in which to conduct our journal clubs and meetings! Best of all, a teaching lab located at the southwest corner of our floor will be equipped with funding from a \$750,000 Parsons Foundation grant. All these new developments ensure that first-year courses will consist of more than the expected powerpoint slides and handouts. The largest room on the floor will be a lecture hall that will serve as the perfect location for our Leading Edge Lecture (LEL) symposia. A lounge, lunchroom, and library will also be built, rounding off our new home as the quintessential place for student social events, study groups, and Graduate Student Organization (GSO) meetings.

Once completed, the building will “provide a focal point of the school, and greatly help in fundraising,” said Dr. Rossi, and it will also provide students “a home of their own” for social activities.

Network

Continued from front page 1

your skills? Do you have your resume or CV done?) Identify people who can help you. (Your advisor would be a good place to start as well as other grad students and postdocs.) Finally, contact the person (referring the person who connected you), keep track of your progress, and ALWAYS, thank people and follow-up!

Remember, anyone can be a potential networking contact. Keep in mind that networking can also be serendipitous. You never know who you might bump into at your child's school play, the gym, or even out taking your dog to the local dog park. Have a 30-second personal advertisement ready in which you can articulate an answer to the question “Tell me about yourself.”

I know that everyone is not an extrovert, possibly, it is quite the opposite. If you want to check out a great networking website, look at Linkedin.com. Once you register, you invite your friends to sign up and be a part of your network. Within a short amount of time, you'll find that you can quickly be connected to many people. It even has a dial next to a potential contact's name which tells you how many connections away you are from that person. Talk about easy!

However, don't just do the online route, talk to people. Break out of your shell and get to know people.

Communication skills are essential in securing a job anyway, so practice!

Do you want to hear more success stories? Need help in composing that 30-second personal advertisement? Come see me. I'm here the second and fourth Fridays every month. Email me at jtsuji@coh.org and we'll set up an appointment. I look forward to meeting you!



Graduate Research Highlights

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What is the significance of the research and what specifically does your paper show?

When I began this work, very little was known regarding the mechanism of how TGS occurred in mammalian cells. Previous work from our lab and Steve Baylin's lab at Johns Hopkins had shown that repressive histone methylation marks were found at siRNA-targeted promoters, but it was unclear how this silent or heterochromatin formation was occurring. My hypothesis was that an Argonaute family protein was most likely involved in some sort of nuclear effector complex, and to make a long story short, I was able to demonstrate that Argonaute-1 directs TGS in mammalian cells.

What was the publication process like with NSMB?

The publication process with NSMB was very smooth and timely. The senior editor handling our manuscript was very supportive and helpful, and they accepted our paper 11 days after we submitted it, on August 8, 2006. What I

do have to mention though, is that we had initially submitted our work to Nature on January 17, 2006. After three rounds of peer-review that lasted six months, the senior editor at Nature decided to reject our manuscript and recommended forwarding it on to NSMB. The NSMB editor read the reviewers' comments from Nature and decided to accept our work.

Did you have to make many revisions?

The manuscript went through two extensive revisions to address the long lists of comments that we received after each round of peer-review at Nature, but we didn't have to make any revisions for NSMB.

Did you encounter any surprises that served as lessons?

Yes. One Nature reviewer in particular was very difficult to deal with, but in the end, I learned a valuable lesson in perseverance. I also learned just how high the bar is set at top journals such as Nature or Science, and the experience of going through such a rigorous peer-review process helped me to grow as an aspiring scientist.

2007 RSO Highlights

Each Spring, graduate students are given the opportunity to attend the Research Staff Organization (RSO) Advance held in Lake Arrowhead, CA. The advance is fun, informative, and thought-provoking. Students are encouraged to present their research and share ideas with their colleagues in a relaxed environment that fosters learning and companionship.

Below are some of the highlights from this year's trip!



First-year students Michael Hedvat, Lin Wang, Yuelong Ma, and Jason Chen (l to r) refresh themselves after attending a long day of presentations.

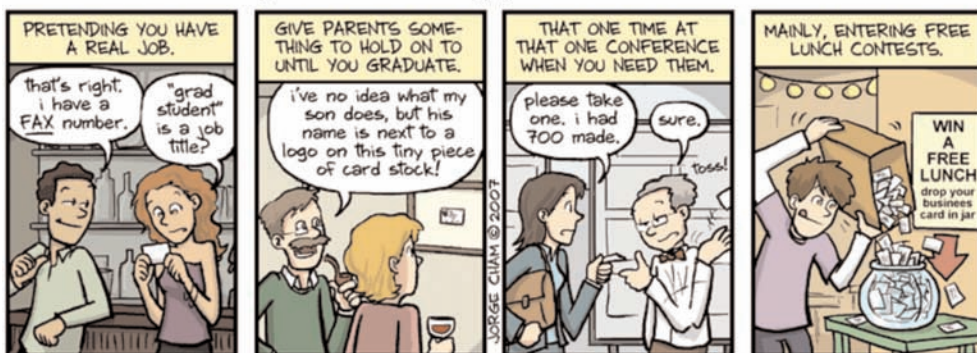


Third-year student, Kumi Sakurai, explains the details of her work to professor Yuan Chen during an RSO Advance poster session.



Third-year student, Selma Masri, gave an award-winning talk at the 2007 RSO Advance Retreat held at UCLA's conference center in Lake Arrowhead, CA.

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Check out our calendar for upcoming events! (Use your gmail account)

<http://www.google.com/calendar/render?cid=thehelixnewsletter%40gmail.com>

Questions? Comments? Contributions? Please contact us at: thehelixnewsletter@gmail.com

Welcome to our new students

Jerlissa Arizala
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April Ochoa
Rongze Lu
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