

**Below are tributes sent in the days just after he died.**

***From Amy Pasquinelli, a postdoc when Gabe was a graduate student in the Ruvkun lab:***

*This is such sad and shocking news. It still hasn't sunk in that Gabe is no longer around. We were supposed to meet up during an upcoming west coast visit for a Cell meeting he was organizing in Nov. Gabe was one of the healthiest people I ever knew and I just can't understand how he could suddenly succumb to some mysterious infection in one of the best hospitals in the world. Thank you so much for keeping us apprised of the situation and the terribly sad final outcome. Some kind of memorial is definitely warranted for someone who touched so many lives in his utterly unique and angelic manner. Please let me know if I can help in any way. Here are some of my thoughts...*

*I considered Gabe a good friend and actually was one of the people I kept in touch with most frequently. I just reviewed our correspondence ever since I moved out here and realized that just about every year I would ask you or him directly about some scientific or reagent question and Gabe would always provide a prompt and hugely helpful response. He was one of the most reliable people I know and I had the pleasure of meeting up with him on almost every trip back to Boston. I remember especially one evening in Fall when it ended up just being me and Gabe one on one at some bar. He had recently graduated and was excited about post doc prospects but was also very determined to finish his papers in your lab - a quality I now really appreciate as people leave my lab often move on with half finished papers, expecting someone else to finish up. I saw that type of excitement doubled in Gabe last Aug when we were at the CSHL meeting, his first assignment as a new editor at Cell. He really was glowing when telling me about his new position at Cell and it was clear that this really was his calling and that he was going to be an amazing editor. His natural curiosity, intellect and ability to just listen and think deeply clearly made this an ideal career choice. I am glad my last live interaction with Gabe was with an exceptionally happy, satisfied and inspired friend.*

*One story that came up at CSHL and almost everytime we got together because it made us laugh involves probably my very first outing with Gabe. Now, I am not sure this story is appropriate for all but I think at least you will get a kick out of it and can decide to share it or not. It was the last evening of a worm meeting that had been held in Georgia, at Emory I think, and several of us Ruvkunites were there including the new rotator, Young Gabe, as Scott Kennedy had christened him. As the worm party was winding down some of us wanted to venture into Atlanta and check out the club scene. As I recall it, Ali Frand, Weiqing Li, me and Young Gabe as our only male representative ended up at some cheesy club in a popular area called Buckhead. As the ladies were trying to dance, random meathead jocks were coming up and trying to grind behind us. We expressed our displeasure and next thing I knew, I saw Young Gabe sidling up behind one of the meatheads and doing the exact same thing to him as he was trying to do to us. Now with anyone else this could have started a nasty fight but Gabe was so innocent and nonchalant in his method that the guy just laughed and moved on. Gabe proceeded to "protect" us several times throughout the night and we ended up having a really fun time until Weiqing fell asleep on one of the couches at the club and we got kicked out (we tried to explain that she really was just tired and not messed up but it was time to go anyway).*

*I have attached probably my favorite picture of Gabe, which was taken at the 7's, of course, actually on my last night before moving to SD. I will remember Gabe as always smiling, helpful, smart, peaceful and as someone I will truly miss.*

*Take care,*

*Amy*



***From Sean Curran, a postdoc when Gabe was a graduate student and a postdoc in the lab:***

*Dear Hayes family,*

*I am at a loss for words to say to you during this time. I overlapped with your son in the Ruvkun Lab. Gabe was one of the kindest and most generous people I have ever met. It was a pleasure to have had the opportunity to get to know him.*

*Although, I'm sure you know what an amazing man your son was as an individual, I hope you know that he was an important and loved member of a community that truly would not have been the same without him.*

*While I was in Boston, I organized a recurring poker game for the folks in Wellman and Simches to gather together and let off steam. Gabe stripped us of our \$5 buy-in for the evening, more times than I like to admit, but what I remember most was his grace when he lost and his humble nature when he won. Gabe was one of the few people where I honestly never knew if he was bluffing or not. I will always remember those evenings in the lab and Gabe is a major part of that memory.*

*Gabe also got me into running. Upon taking a job in California I ran my first half marathon. This was only possible from the training and example of Gabe during our run*

*around the Charles. Usually I only saw him running in the distance ahead of me, he was really fast, but his perseverance was an example to strive for. Since then I've run a dozen half marathons.*

*Thank you for raising such a wonderful man. He truly touched my life as well as so many others. If there is anything I can do, please don't hesitate to ask.*

*Sincerely,  
Sean*

***Below is Gabe with Ali Frand***



***From Ying Liu, a postdoc who overlapped for about a year with Gabe when he was a postdoc in the lab:***

*This is so sad. I just can't believe it. When you sent us those updates, I always feel Gabe will get better and some time next month he'll stop by and talk to us. My overlap with Gabe is short. But the time is already long enough to make me feel he's one of the best and sweetest person in the world. I wish his parents will recover soon from the loss and want to tell them that they have a fabulous son.*

*On February this year, I saw a nice review article on Cell and noticed that the author is our Gabe. So I sent him a message to let him know that I really enjoy his writing, and that is a terrific reviewer article. Gabe replied me saying he's very happy to have his first Cell "paper". To my surprise, he then asked me if I'm back to my apartment, because I posted on Facebook several days ago that our apartment building had an electronic generator explosion. Yes, Gabe is always a considerate person and he helps us in many ways.*

*During my group meeting, I mentioned that I need to find a strain to look at mitochondrial morphology. Right after the meeting, Gabe dugged out several strains from his collection, gave them to me and wrote me a detailed note of their genotypes, before I asked him for*

*the strains. When I mentioned that I want to learn how to map a mutation during lunch, Gabe called me to his desk later in the day, opened his notebook and explained all the details to me using his own data. That is the first time when I looked at his notebook. It re-ensured my impression of him: He's a very organized and careful person. He wrote down all the details in his notebook, in a neat way.*

*I still remember the nights when Gabe and I worked in the lab. He sometimes took a break to water his Orchid. One night when he was watering the flowers again, I was chatting with him about his future job and suddenly I asked him why his Orchid looks so good but mine were not doing well. On the second day, when I stepped into the lab, I saw two 15ml falcon tubes on my desk, with Orchid food inside. Yes, they were from Gabe. On the tube, he wrote a detailed "protocol" of how to dilute the flower food and when to water the flowers. He saved my flowers. Tonight, when I get back home and see the flowers on the desk, I start thinking of Gabe and really miss him. I'm sure the flower will bloom again next spring, and I'm sure Gabe's life will keep blooming in heaven.*

*We are all very sad for the loss.*

*Best,  
Ying*

***From Dave Shore, who was a graduate student while Gabe was a postdoc in the lab:***

*This is terrible news.*

*My relationship with Gabe unfolded slowly. I will always remember him first as my bench mate, as this was, at first, the extent to which I knew him. With Gabe, learning how fascinating he was as a person occurs in layers, maybe for all of us who knew him. Just by working near him, I first noticed he surrounded himself with diverse reading materials, not just science, but also fields such as economics, plus of course a constant flow of music-- I believe classical, but one never knows for certain about another's ear buds. You'd also notice he had a... distinct... method of organizing his research paraphernalia. At some point it may come in handy that he speaks multiple language. And it might not take too long to find out he is quite athletic, between running and tennis. And of course, if you need help or advice, he is both insightful and generous. After a time, Gabe began to share with me about his personal life, his family, and Dane. I always felt those conversations were special. Gabe, to me, was always a person who spoke with care and these conversations seemed like a way of saying that he liked me, that he trusted me. My respect for Gabe is enormous, as a kind, caring, intelligent and, most of all, perhaps, a truly complex individual in the finest sense. It has been a great pleasure that we have remained in touch since my graduation from the lab. He has been a role model and a friend. Even now, his loss comes as a shock.*

*Dave*

***From Yan Qi, a postdoc during the time that Gabe was a postdoc in the lab:***

*So sad to hear Gabe's news:(( I didn't interact much with Gabe, but when I first joined lab, and had never touched a worm, or even a living non-bacterial organism in my life, I asked you who I should seek help from to learn the most basic worm handling skills. You suggested Gabe, and the first thing I asked Gabe for was a bunch of male worms and GFP worms and worms at different stages, so I could learn to tell them apart. How naive and strange my request was! I was indeed at absolutely ground zero as a worm researcher. Yet, Gabe gave me those worms--various different GFP strains indeed--immediately with no complaints, no strange look from his eyes. Years later,*

*coming out of your lab full of super ambitious and super busy postdocs, and looking back at those days that I crash-landed in your lab with wide eyes-open being totally green with worm genetics, I now understand why you suggested Gabe. He is just so **kind**, so knowledgeable, and so competent as a worm geneticist.*

*May Gabe rest in heaven!*

*Best,*

*Yan*

***From John Kim who was a postdoc when Gabe was a beginning graduate student, and collaborated with Gabe:***

*I want to remember Gabe. He was a remarkable fellow and played a critical role in introducing me to the world of C. elegans genetics and small RNAs. We published several papers together because it was so much fun to collaborate with Gabe. But he was also much more than a scientific colleague as we shared a bond through our common love of classical music and our regular runs along the Charles. Who else could recommend and discuss at length Jascha Horenstein's Mahler symphony recordings over morning coffee, or patiently explain all the arrows and which way they point in the heterochronic pathway, or leave you in his dust running the 5.6-mile loop around the Charles River in the late afternoon, and then go out for late night Chinese food? Who else studies the scores of the Wagner operas before taking the train down to New York to see them? And who else would spend hours carefully editing your manuscripts and provide gentle, thoughtful comments devoid of ego or self-promotion? He was a great friend and respected colleague and I will remember him throughout my career.*

*John*

***From Siu Sylvia Lee who was a postdoc during the time Gabe was a graduate student in the lab:***

*It's very sad to hear about Gabe's passing. Despite the seriousness of Gabe's illness, I had always thought he'd pull through – I know all of us had the same hope.*

*I cannot imagine the suffering that Gabe's parents are going through, but it's comforting to know you and so many others are there offering support. It's also comforting to know Gabe had a little bit of time when he was conscious and knew that he was surrounded by family and friends.*

*I actually saw Gabe earlier this summer (June), when he came to Cornell for a reunion activity and also to talk to faculty and students & postdocs in his role as a Cell editor. He was the same old Gabe, soft-spoken and kind, and it was very clear he was really thrilled about his new position at Cell. His talk to the students & postdocs about his experience as an editor and how he got to be an editor was overwhelmingly well-received. I remember sitting in the audience feeling proud that I got to work with Gabe and we share the common bond as Ruvkun alumni. I am really glad I got to see him in June. In a way, that made his passing even more unimaginable. But I am glad my memory of Gabe was a very happy and confident Gabe who was clearly looking forward to the many adventures that lie ahead.*

*Take care,*

*Sylvia*

***From Chris Carr, a postdoc during the time Gabe was a graduate student and postdoc:***

*This is terrible news. I took the train to Nice-Ville this morning to rent a car and found the office closed for a bit -- so I walked the beach, picking up pebbles in reflection. ....*

*A few thoughts on Gabe: I didn't know Gabe well, and yet, he impacted my time in the lab and probably had a bigger influence on me than I ever suspected. Looking back at all my emails, I realize just how essential and positive he was in addressing issues that mattered to many people and the lab as a whole. He was a master of the gentle reminder. A couple times I was late preparing snack for the kitchen and Gabe emailed a gentle "growing restlessness down here." A couple years ago he sent us (you and I) a video of a shuttle launch (subject: "Atlantis blastoff and dancing") writing "I'm sure NASA has better video, but I'll bet it won't include the dancing kids." Always acting with humility (same email): "I'm completely thrown by G&D being eager to have my revision, but I could get used to it." Gabe chose his words carefully. When he spoke, he was understated, spoke carefully, and presented some essential thought that apparently no one had managed to notice.*

*I lost my best friend when I was 22 and saw how hard it was (and still is sometimes) for his parents. Some things you never get over, you just learn to live with them. I don't know Gabe's family although I did meet Dane from time to time in the tea room. As a parent and husband, I can only imagine their grief. Below is my email to Gabe during his illness in case you want to share it.*

Chris

**From:** "Christopher Carr" <[christopher.e.carr@gmail.com](mailto:christopher.e.carr@gmail.com)>

**Subject:** **Welcome back**

**Date:** October 9, 2013 3:12:18 PM GMT+02:00

**To:** "Gabe Hayes" <[gabriel\\_hayes@yahoo.com](mailto:gabriel_hayes@yahoo.com)>

Hi Gabe--

Hopefully you are emerging from your trials and tribulations and on your way to a full recovery.

*I have experienced nothing like what you have undergone, except a minor pneumonia and plenty of air hunger at high altitude. It can be quite scary and I can only begin to imagine your own experience.*

*I am writing to say thanks for your kindness these many years since I joined Gary's lab in 2005. You are respected in the lab as technically competent, thoughtful, and kind. I always appreciated our interactions and I remember so many times entering the kitchen to find you there with a cup of tea in your hands. I hope you will be back to enjoying a cup soon.*

With my warm regards and best wishes for a speedy recovery,  
Chris

**From Justine Melo, a postdoc when Gabe was a graduate student and postdoc:**

*After reading your email of two days ago I was feeling so upbeat about Gabe. Getting your note yesterday was like a leaden punch to chest. I read it no more than 10 minutes before I had to go give a class and I remember shaking my head furiously in my office to try and clear my mind to go in there. It was a terrible hour, and a terrible day.*

Justine

***From Harrison Gabel, a graduate student when Gabe was also a graduate student:***

*I was deeply saddened to hear that Gabe had passed away. I had been keeping him in my thoughts and hoping with each new e-mail update from you, that good news was on the way.*

*I admired Gabe for his kindness and his thoughtful curiosity about life and science. Please relate my condolences to the Hayes family and to his partner if you see them again soon.*

*Best,  
Harrison*

***From Duo Wang, a fellow PhD student in Gabe's class and a lab mate from 2000 through 2005***

*Gabe will always be in my memory whenever I look back at my graduate school years and my life as a young scientist in Gary's lab. I first met Gabe in the summer of 2000 when I started my rotation with Gary. We both fell in love with the science, the lab and decided to join the lab at about the same time. Over the next five years, we were in the trench together and burned through many crazy projects, until we each found our call. For me, it was small interfering RNA (siRNA); For Gabe, it was micro RNA (miRNA).*

*Just like the two molecules that shaped our PhD research, we shared so much in common, from the lab social life to everyday work routines, but couldn't be more different. Gabe was always calm, sweet and social. In comparison, I was impatient and prone to mood swings. I remember a late night when I managed to waste another Northern, I went to bury myself with all the junk food I could gather in the break room. There I found Gabe, eating his perfectly packed dinner. So I started venting my frustration. I ranted for a good half an hour. I might have even got tearful at some point. Gabe just listened and listened, occasionally chimed in with his sweet, soft voice. Not even once, he expressed the slightest hint of disinterest or showed any attempt to interrupt me. At some point, his calmness started to spread over and I magically found peace with the Science God again. Similar events happened a couple of times until I had my breakthrough with the eri genes and the Rb pathway mutants. I gave Gary and Scott Kennedy all the credit for guiding me scientifically. However, I wouldn't get there without the emotional support from Gabe. In my mind, he will remain that warm, shy but incredibly strong figure who brought calmness and resilience to a world full of anxiety and uncertainty. I miss him dearly. May he rest in peace.*

***From Meng Wang, a postdoc when Gabe was a graduate student in the lab:***

*Gabe has been a wonderful colleague and friend. He has helped me a lot on my project. I have written two little points to share.*

*Gabe is a bright colleague who every scientist wants to work with. He is so smart, sharp and knowledgeable, who always gives others valuable advices and shares his inspiring ideas. Because we worked in different topics, he often saw what I didn't see. I still remembered when I struggled with the problem that some of my candidates from the sqt-3 screen couldn't give the same phenotype in wild type background, it was Gabe who suggested me to test whether sqt-3 is RNAi sensitive and to examine the phenotype in the RNAi sensitive background. This work will not move forward to the next step investigation without his wonderful advice. Gabe is also a friend who can be counted on anytime when I need help. He is so patient, kind and warmhearted. I couldn't remember how many times Gabe helped me read my fellowship application and*

*manuscript. Unlike many people only sending their changes, Gabe went through all his suggestions and comments every time with me. In a way, he was old fashioned; he marked the changes and wrote down his suggestions on printed pages with pen, and then explained to me one by one why he thought it would be better in his way. But I have learned so much from him this way. Even now, when I am writing my grants and papers, I can some time still hear Gabe's soft and gentle voice in my mind "It would be better to use 'suggest' than 'indicate' here. It is common not to use 'the' here. ...". I will miss Gabe and he will live in my heart for ever.*

*Meng*

*From Ho Yi Mak, a postdoc when Gabe was a graduate student in the lab:*

Gabe's passing was all too sudden and tragic. I have tried to jog my memory about Gabe since receiving your email. Gabe joined the Ruvkun lab a few months before my arrival and therefore our time in the lab completely overlapped. There are no particular stories to tell but Gabe and I interacted almost daily when I was in your lab because his bench was in the neighboring bay when we were in the Wellman building. Gabe cared deeply about fair-play in science. He was vigorous about his own work and generous in offering his ideas and opinions. I will remember fondly the frequent take-out dinners from the 'King and I', afternoon runs around the Charles River, discussions about German operas, and a holiday dinner that Gabe graciously hosted. Gabe will forever be associated with what's good about Boston in my mind.

Best,  
Ho Yi

***From Xiaoyun Wu, a postdoc when Gabe was a graduate student and postdoc:***

*The news of Gabe's passing stayed heavy. My heart would ache every time I saw his picture. To this day, a warm candle light sits center on my desktop and deep in my heart. Its soft orange glow resembles the gentle and yet steadfast personality of Gabe that brings peace and warmth to my heart.*

*It was a true honor to have known Gabe, to be touched by his sincerity and humbleness, and be inspired by his steadfast attitude towards research. To me, Gabe equals resourceful and reliable. Being the one who has seen a dozen years of the Ruvkun lab, he practically became the encyclopedia of all the research projects as well as many random lab matters. From worm knowledge, to protocols, to reagents, to random matters tracing back to an ancient time in the lab history, Gabe was never tired of answering my questions or never neglected my requests. Despite being the most senior, Gabe never stopped being a caring and considerate lab citizen. He would always only take what he needs (rather than what he can). One little example was the shabby low end microscope that he "stuck with". Over the many years, he declined numerous opportunities to claim a better scope – all I heard was a simple "this is sufficient for what I do".*

*I was also extremely inspired by Gabe's "nothing can stop me" attitude towards experiments. In his plain words, any laborious screen or tedious mapping became so trivial and joyful, and any tricky IP or unusual biochemical assay became so easy and achievable. Often times, before you know, he would already have done a screen,*

*mapped the candidates, made tagged transgenic lines and observed interesting phenotypes.*

*My memories of Gabe include his elegant orchids. Many late nights when I was tired of working, I would go to his desk and admire his elegant orchids. Long lasting large white flowers blossomed on carefully arched stems -- breathtakingly beautiful.*

*With both of our post-Ruvkun jobs near Kendall Square, I had the pleasure of running into Gabe on my way to work. These short run-ins had become my news source for friends and former colleagues. Gabe traveled a lot. Each place he visited, he would always try to connect with former colleagues and friends and bring back all the updates and news. The last piece of news he shared with me was the arrival of Buck's baby daughter. For his humble and caring nature, Gabe had become the ambassador among his friends and colleagues.*

*I often have the illusion that Gabe is still with us. I would still run into him on the Red Line. I can still see him walking next to me, listening attentively and giving his thoughtful comments. The thought of Gabe's passing brings heartache. A candle lit for our dearest Gabe. Miss him.*

*Xiaoyun*

***From Zhen Shi, a graduate student from the period when Gabe was a postdoc in the lab:***

*I'm terribly sorry and shocked. It's crazy to think about our dearest labmate has left....don't know what to say...but I will try to come up with some narrative by next week. Gabe has helped me tremendously and was my in-lab mentor, especially at the time I was a young graduate student. It also reminds me that tedious lin-14 experiment we did together: it wouldn't have been possible without Gabe's effort and patience. His extreme care to science and everything is contagious.*

*Really really sad. But may Gabe's calmness and endurance pass on.*

*Take care,  
Zhen*

More from Zhen Shi  
Story of lin-14 and lin-4 and Gabe

We all know how indispensable lin-14 and lin-4 are for a growing worm; same as Gabe for my graduate career.

I could never image that our lin-14 paper published in PLoS ONE (a journal I was always laughing at...), turned out to be my most precious gift in memory of Gabe. All the recollections about this work are still so clear, and the sorrow for the loss of Gabe is such intense, as I dugged out our manuscript and correspondence and lab notes. The work was initially triggered by Bartel's paper suggesting that miRNAs predominantly act to decrease target mRNA levels. Gary had been pushing us to re-visit this old controversy, but it was a tough question and no one was willing to take this 'assignment'. In the end, Gary decided that I - a young student at the time - should take the lead as part of my Ph.D. training... Fortunately, super nice sweet Gabe volunteered

to help me out.

We were doing a very refined time-course experiment to study the dynamics of lin-4 miRNA in regulation of lin-14 mRNA, and had to collect worms every 3 hours for 24 hours. We were extremely careful in synchronizing the animals and even fixed some animals for inspection of their stages under the microscope. This turned out to be a huge pain in the ass as it took more than 2 hours for each sample collection, which left us only a couple of minutes to take a break... I can hardly imagine how it can be accomplished without Gabe's extreme patience and endurance. I'd always be proud and inspired by this feat.

Interestingly, the paper even includes an experiment done by Gary. It was a mixed funny and sacred feeling to hold those gigantic films of Northern Blot that Gary did more than 20 years ago, actually, at the year when I was born...and to make it a figure on our paper. Our modern real-time quantitative PCR gets the same results as Gary's old school northern blot.

My last round of correspondence with Gabe was during the final revision of the manuscript, when Gabe came to rescue when I was crazily busy at a summer course and wasn't able to take care of the manuscript at the time.

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July 4<sup>th</sup>:  
Hi Gabe,  
need your help.....

our manuscript needs a few final polish (see below)... I am currently doing the physiology course at woods hole.. we are working like 24/7 and I really don't have any time to do it.....could you help just change several wordings according to reviewer 1's comments? I have attached the revision ms and figures.

please take your time. I think we're good if we can send it back in a few weeks.

thanks,  
zhen

Gabe again came to rescue:  
August 8<sup>th</sup>:  
Hi Zhen,

I've read through the whole manuscript and made the requested changes along with a few of my own. There are just a couple things I had questions about (see below).

Overall, I think it's clear. There are some interesting points for thought, and I enjoyed reading it. I'm also attaching a response to the reviewers' comments, although it seems superfluous. The only point I haven't responded to is on how much RNA was reverse transcribed.

Thanks again for doing the lions' share of the work on this!

Cheers,

Gabe

-pg 3, line 14: "100 <mu>g total RNA" to "100 ng total RNA"

*Hmm, was it actually 100 ng? 100 µg doesn't seem outlandish to me, but I have been away from the bench for a year... I didn't change this.*

Top of p. 2:

it should be noted that many of the studies were *in vitro* assays or experiments using synthetic reporters and/or via manipulating miRNA abundance.

*I changed "synthesis" to "synthetic". Is this what you meant?*

*On the Northern blots:*

"Phosphor screens exposed to the Northern blot were scanned on a PhosphorImager."

*Is this true? I'd have thought it was film, which was developed with an X-OMAT and scanned years later with just a regular optical scanner.*

*I changed "indirect" to "changes in" in the following sentence.*

*More importantly, the misexpression of LIN-14 protein is decoupled from the mis-specification of L1 stage cell fates, so that molecular phenotypes can be interpreted without the complication of changes in developmental fate phenotypes.*

*In the middle of the Discussion there's a reference to lin-4 miRNA levels increasing more than 500 fold, but earlier we said 5000 fold. Which is it?*

Thinking back, I wouldn't say it was my most exciting result, nor was it a fun experiment. But it is through this experience that I become to be respectful to every paper and every piece of work, no matter how big or small. This was a priceless lesson I learned from, Gabe.

***From George Church, a professor who collaborated with Gabe on a couple of papers"***

*It slowly sank in that Gabe, you and I co-authored two papers together a decade ago.*

*We live in a strange and sad time -- one foot in the 21st century and the other stuck in "medieval" times, as you say.*

*Parents and Pls should not see their offspring die. Indeed "Rage, rage against the dying of the light" ... for everyone.*

*--Geo*

***From Iva Greenwald, a professor at Columbia University, with whom Gabe did a small set of collaborative experiments:***

*I just saw the announcement of Gabe Hayes' passing on the Cell website. I was so sorry (and shocked) to see this terrible news. It must be difficult for you and your lab members. I just felt I had to write...*

*With sympathy,*

*Iva*

**From Oliver Hobert, also at Columbia**

To: Gary Ruvkun <ruvkun@molbio.mgh.harvard.edu>

oh god

.... just the Cell website. That's horrible, horrible, horrible. So sorry.

**Gary Ruvkun memories**

Gabe came to graduate school at Harvard Medical School in 1999, doing coursework for a year and joining the Ruvkun lab in 2000. Gabe did both his PhD thesis in my lab as well as a full postdoc there. Gabe's projects explored how microRNAs regulate their target mRNAs.

Gabe began in my lab with a rotation where he tried extracts of Chinese herbal medicines seeking to modulate insulin signaling defects of *C. elegans*. His background in botanical studies made him aware of rich history of medicinals from plants and we wanted to see if any of these possible drugs would influence universal signaling pathways, one of which is insulin signaling. The idea was that even if herbal medicine is 99% as untrue as astrology, there is 1% that is real pharmacology discerned by astute observers of plant-animal interactions---we wanted to find the 1% that is real. Gabe went down to an herbalist in Chinatown with Weiqing Li and with his \$15 budget limit that I set, purchased a set of 30 different remedies. He prepared a number of teas from the herbs and he tried to cure the dauer arrest of a *daf-2* insulin signaling mutant with these extracts. It was a fun rotation project, which failed, but it was evidence of his broad interests and openness to unorthodox ideas.

After he joined the lab, we were in the throws of the miRNA revolution, as dozens of new miRNAs emerged from genome analysis. Gabe immediately joined this research endeavor, first working closely with the informatics team from George Church's lab, and with postdoc John Kim on our efforts to discover new conserved miRNAs in *C. elegans*. Gabe did a lot of the Northern analysis attempting to verify these miRNA genes, some informatic analyses assessing the quality of the predicted stem loops, and shared first-authorship on this study in *Molecular Cell*. It was excellent training for him. Importantly, this project immersed Gabe in the electricity of the tiny RNA field.

I did not simply feed Gabe a project for his thesis. Gabe evolved the project himself, choosing to work within the *C. elegans* heterochronic pathway rather than on a random newly identified miRNA function in some other pathway. His reasoning was leverage: we could explore issues of how multiple miRNAs target mRNAs redundantly and non-redundantly. He focused on the *let-7* paralog *mir-84* and his work took him into the field of molting control, which allowed him to intersect another postdoc, Alison Frand, who had identified many molting factors using RNAi. It was very satisfying to me to see these two very different strands of work in the lab meet in productive ways. Gabe devised the approaches and wrote a wonderful, careful, complete paper that was published in *Development*.

But in addition to his study of *mir-84*, Gabe also did a bold project trying to use other miRNA promoters to drive particular miRNA expression at the wrong time or in the wrong tissue. In this study, he used the *lin-4* miRNA promoter to drive *let-7* miRNA expression two stages early and discerned the heterochronic defects on that misexpression. This work was written up for the Cold Spring Harbor Symposium where I presented it in the auditorium presided over by a painting of James Watson as well as

by the man himself.

Finally during his postdoc, Gabe did genetic screens for suppression of his high *mir-84* gene dosage phenotype, and identified the *somi-1* Zn finger factor that is the focus of the 2011 *Genes and Development* paper. Every aspect of this paper was driven by Gabe's choices, from the decision to use genetics to suppress high gene dosage of the *mir-84* gene to identify miRNA function cofactors, to the decision to study *somi-1* in great detail, to the decision to ramp up proteomics of protein interactors with SOMI-1, to the chromatin IP experiments with SOMI-1, to the RNAi screen of the candidates from proteomics. The paper evinced Gabe's fully developed scientific tastes in the tiny RNA field as well as in the modern approaches to dissecting problems like this. The scholarly research he did for this paper was in the chromatin remodeling factor field, a huge literature, that he dove into and distilled beautifully for his own work.

He published three major first author papers as a student or postdoc in my lab and an equal number of minor authorship papers:

Grad, Y\*, Aach, J\*, Hayes, G.D\*, Reinhart, B. , Church, G. M. , Ruvkun, G., and J. Kim. 2003. Computational and experimental identification of *C. elegans* microRNAs. *Molecular Cell*, 11:1253-63. (this was a shared first authorship between the first three authors).

Kim, J, Krichevsky, A, Grad, Y, Hayes, GD, Kosik, KS , Church, GM , and G Ruvkun. 2004. Identification of many mammalian neuron-expressed microRNAs that co-purify with polysomes, *Proc. Natl. Acad. Sci.* 101: 360-5.

Hayes, GD, AR Frand, and G Ruvkun. 2006. The *mir-84* and *let-7* paralogous microRNA genes of *Caenorhabditis elegans* direct the cessation of molting via the conserved nuclear hormone receptors NHR-23 and NHR-25. *Development* 133: 4631-4641. (shown below is a picture of Ali Frand and Gabe).

Hayes, GD and G. Ruvkun. 2006. Misexpression of the *C. elegans* miRNA *let-7* is sufficient to drive developmental programs. *Cold Spring Harbor Symp Quant Biol.* 71: 21-7. Regulatory RNAs.

Hayes, GD, C. Riedel, and G. Ruvkun. 2011 *Caenorhabditis elegans somi-1* encodes a zinc-finger protein that mediates microRNA activity of the *let-7* paralog *mir-84*. *Genes Dev.* 2011 Oct 1;25(19):2079-92.

Tabach, Y, A Billi, G Hayes, O Zuk, H Gabel, R Kamath, M. Newman, K Yacoby, B Chapman, M Borowsky, J Kim, G Ruvkun. 2013. Identification of new small RNA pathway genes from correlated patterns of phylogenetic retention and loss. *Nature* 493(7434):694-8. In this paper, Gabe worked very closely with Yuval Tabach, who as a bioinformatics specialist knew almost nothing about *C. elegans* functional genomics, to teach him worm biology and do some candidate gene screens based on Yuval's informatics and John Kim and Allison Billi's full genome RNAi screens.

Shi, Z., G Hayes, G Ruvkun. 2013. Dual regulation of the *lin-14* target mRNA by the *lin-4* miRNA. *PLoS One*, 8(9):e75475.

The last paper by Zhen and Gabe was a gift to me from the two of them: The paper addressed the 20-year debate about how miRNAs regulate target mRNAs. The analysis of whether miRNAs cause mRNA degradation or translational control had been dominated by a few labs, most obviously David Bartel's, using genome scale observations of mRNA abundance after chronic knockdown or chronic high gene dosage of a single miRNA, to ascribe biological response to the tiny changes in mRNA levels. Astonishingly, even twenty years after miRNAs were discovered, we still have very few validated miRNA target mRNAs to study. The *lin-4* miRNA and the *lin-14* mRNA represent such a validated pair of genes. Gabe determined the detailed sequence changes that cause a strong gain of function phenotype in the *lin-14(n355)* gain of function mutation and how it deletes *lin-4* complementary regions. He and Zhen then took detailed time points and quantitative reverse transcription PCR assays and immunoassays to monitor the abundance of *lin-14* mRNA and protein in finely staged wild type or *lin-14(n355)* animals. He and Zhen found complex regulation of *lin-14*, with an initial decline in both *lin-14* mRNA and protein abundance, followed by stabilization of *lin-14* mRNA levels accompanied by further decline in LIN-14 protein abundance dependent on binding of the *lin-4* miRNA to target sites in the *lin-14* 3' UTR. The paper was also a vehicle for publishing some of my Northern blots done when Gabe and Zhen were in diapers. These results pointed to the importance of translational inhibition in maintaining the decline in the level of LIN-14 protein.

Gabe was also the nicest person one could imagine. People in the lab just loved him. In fact, his long time baymate Weiqing Li flew in from Seattle to be here for his PhD defense. Gabe was more quiet than average, but it was an almost transcendent kind of quiet. And when he did speak up in group meetings, so fluent in developmental genetics and genomics, his advice was always listened to. As a postdoc he was the senior member of the lab in many ways and many people went to him for advice. Beginning graduate students were not afraid of him; they knew that he could be approached and would take the time to explain how to do experiments, especially genetics, in a methodical efficient way. When testimonials for Gabe flew into my inbox in the days after he died, literally a dozen people from my lab commented on how often they turned to Gabe for advice on their projects and how fond of Gabe they were. How they kept in touch and were so elated when Gabe had found his perfect calling managing the publication of papers and the exchange of ideas for *Cell*. I like to think that my lab ecosystem contributed to Gabe's wide palette of interests, but Gabe contributed to the evolution of this palette in the lab. If you add up the number of person years of scientific culture my lab represents, it sums to about 500 person years. Gabe was 1/40<sup>th</sup> of that total. I am 1/20<sup>th</sup> of that total. Gabe ties for second in contributions to the lab culture in such a numerical accounting, but in the tactical advising of projects day to day, a good case could be made that Gabe advised more graduate students and postdocs on how to do science day to day and may rank first in contributions to the culture of my lab. That he was such a non-seeker of the spotlight makes this all the more impressive.

When Gabe was deciding on a post-postdoc trajectory, we discussed the possibility of him becoming a journal editor. Gabe was exposed to much more than just small RNAs in my lab: he saw up close and personal a decade of work in longevity genetics, insulin signaling genetics, genetic analysis of regulation of metabolism, and full genome screens for lifespan, molting, fat storage, miRNA function, RNAi, enhanced RNAi, reproductive longevity, comparative genomics, and metagenomics of extreme environments. This gave him a more polychromatic view of science than he might have

had if he had worked in a lab just focused on tiny RNAs, which I think qualified him to judge work in many fields.

But I was concerned that he might not have the thick skin needed to say no to 90% of the submissions---Gabe did not have a mean bone in his body. I was concerned that he might be too shy to deal with the very entitled installed base of so-called important scientists, and the larger set of scientists desperate for a big name journal acceptance. He would have to face the extremes in ire or the extremes in desperation and sadness of the 90% rejection rate. But as he and I discussed what he would bring to this career, he convinced me that he might be a perfect journal editor. His combination of a highly evolved personal good taste in science and ability to not get into shoving matches over unimportant conflicts was a perfect combination for working at *Cell*. Gabe's calm demeanor and the respectful, no nonsense way that he deals with others undoubtedly worked well for him as an editor. What I could not envision was how he would blossom in the other roles that *Cell* editors play: in the cultivation of scientists at meetings to publish with *Cell*, in becoming a trusted ally in the process of bringing papers to publication.

So beyond the loss of a treasured former student and postdoc, Gabe's death is a tragic loss for the larger scientific enterprise. Gabe had found an important niche as a journal editor; he was serving an essential role for science there. Journals are the social equivalent of what the ribosome is to the cell, the printing press. Each of the editors at a major journal impacts the lives of 1000 science teams and probably 5000 scientists per year who submit papers. And this only counts the authors. If one counts the readers, it is far more. So in the loss of Gabe, the loss to science is a loss of a hub connected by thousands of spokes.

It is tragic in so many dimensions.

Gary Ruvkun