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Biology Faculty Adds New CDM Researchers to Its Ranks

J. David Lambert, Assistant Professor

Walking into Hutchison Hall 338, the new laboratory of Assistant Professor David Lambert, one cannot help but notice a few seawater tanks filled with hundreds of snails. These are the mollusc *Ilyanassa obsoleta*, a fascinating subject of classical embryology for over a hundred years. Their early embryos have invariant "spiral" cleavage patterns. Resulting daughter cells are large and accessible to experimental manipulations. Daughter cells also differ in size and developmental fate. Using modern molecular tools, the Lambert lab is now studying the mechanisms of early embryonic patterning in *Ilyanassa.* Other spiralian embryos will also be studied to ask how patterning processes evolve.

Developmental cell fates are determined by two different mechanisms, by cell-cell interactions, or by asymmetric distribution of determinants to daughter cells. While a graduate student in Lisa Nagy's lab at the University of Arizona, Dave discovered a new mechanism to distribute patterning molecules to specific daughter cells in *Ilyanassa*. This involves the 'centrosome', a cytoplasmic organelle that functions as an organizer of microtubules and other cellular processes. The mRNAs of conserved developmental patterning genes such as *Dpp*, *Eve*, and *Tolloid* are localized to particular centrosomes before they are segregated to specific and different daughter cells. (See beautiful pictures at Dave's web site.) At

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Vera Gorbunova, Assistant Professor

Two of the newest additions to the faculty came as a team. Our new Assistant Professor, Vera Gorbunova, and her husband Andrei Seluanov, an Assistant Professor of Research, were both born in St. Petersburg (Leningrad at that time). They met at a college preparatory program for high school students at St. Petersburg State University. St. Petersburg State University is the second largest school in Russia so it is lucky that they met at all. Both subsequently entered a five-year program at the University to earn a Masters degree with a specialty in Genetics, and married in their first year of college. However, the dissolution of the USSR in 1991 made the political and

scientific situation in Russia increasingly unstable. Andrei and Vera made the decision to emigrate to Israel where they were accepted into the Masters program at the Weizman Institute of Science after interviewing with the Dean. For their Ph.D. research Vera and Andrei pursued separate paths at the Weizman Institute. Vera specialized in plant genetics, studying transposable elements in plants with Dr. Avi Levy. Working with corn is faster in Israel because the

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(Dave Lambert, *continued)*
Rochester, these exciting observations have now been expanded to include ~ 50 other mRNAs from early embryos (50% of mRNAs tested so far). Assisting Dave is his lab tech Evan Kingsley, UR class of 2004, a cell and developmental biology major. Centrosomal localization of molecules and subsequent segregation to specific cells could specify the developmental potential of tiers of cells as they are born in early snail embryos. The goal of the Lambert lab is to identify these mRNAs and their developmental roles, and to study the mechanism of centrosomal localization.

Dave's interests in developmental biology and evolution began at Yale. Though he entered as an anthropology major, a class in physical anthropology and evolution in the sophomore year convinced him to shift into biology and invertebrate zoology. Dave recalled fondly his undergraduate research experiences. For his senior thesis with Leo Buss he cloned *Hox* genes from *Bryozoan*, an encrusting marine organism. Also, before going to Arizona for graduate school he spent a year in the same lab observing feeding habits of hydroids. Significant findings (published here for the first time) are that hydroids wave their tentacles in response to glutathione but will only engulf sephadex G-50 beads if they are loaded with dCDP.

After six very successful years in Arizona Dave returned to Yale to work with Kevin White on the mechanisms of adaptation in *D. sechellia*; his postdoctoral research supported by a Helen Hay Whitney fellowship. Dave and family arrived in Rochester in July 2004. Dave's wife Emily is an MD doing a medical internship at Strong Memorial Hospital, Wendell is a very cute 24 months old boy, and another Baby Lambert is on the way. This fall Dave taught half of BIO 226 Developmental Biology introducing to students new aspects such as "evolution and development". He is now looking forward to spending more time in his new lab. Welcome Dave!

(Vera Gorbunova, *continued*)
climate allows researchers to grow corn all year round. Andrei's thesis work involved studying the biochemistry of membrane proteins in *E. coli* with Dr. Eitan Bibi.

Although they did not pursue aging research during their graduate careers both had become excited about the field after hearing a lecture on the topic in college (neither can remember who spoke). After receiving their doctoral degrees they decided to pursue aging research together. They went to McGill University in Montreal to work with Dr. Siegfried Hekimi on aging in *C. elegans*. They have been an extremely productive research team ever since. After two years at McGill, they decided that human cells were a more practical system for the study of aging and they left to continue their post-doctoral work with Olivia Pereira-Smith at Baylor College of Medicine. During this time they developed a strategy for sorting "old" and "young" cells by size using flow cytometry. This strategy works because the "old" cells are larger. Using this technique, they were able to demonstrate that the overexpression of telomerase induces senescence in primary human skin cells. When Dr. Pereira-Smith left Baylor for San Antonio, Vera and Andrei went to work with John Wilson for two years, where they pursued projects that combined their interests in DNA repair and aging.

Their research focuses on the mechanism of age-related genomic instability. Genomic rearrangements are a hallmark of aging cells leading to exponential increase in cancer incidence. The mechanism of age-related genomic instability is unknown. Vera and Andrei have found that DNA repair by nonhomologous end joining becomes less efficient and more error-prone in senescent cells. They are currently researching the molecular mechanisms that trigger age-related decline of DNA repair.

Vera and Andrei came to Rochester in August of 2004. They bring with them their 8-year-old son, Michael, a second grader at Webster's Plank South Elementary school and 2-year old Moshe. Welcome Vera, Andrei and family!

Research Around the Department Takes Off In Many Directions

Kelly Dyer, Postdoctoral Fellow, Jaenike lab

Biologists have only recently started to appreciate the enormous impact of parasites on host evolution. Parasites are ubiquitous—no organism can escape from them (including, of course, humans), and even parasites can have parasites. And their effects can be dramatic: parasites can regulate their host's population dynamics, alter behavior, contribute to the extinction and formation of new species, and perhaps even foster and maintain sexual reproduction. The relationship between a parasite and its host requires a delicate balance – although parasites harm hosts for

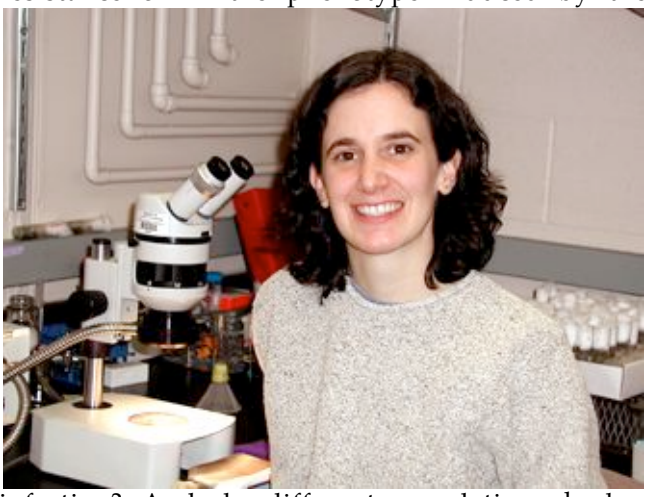
their own benefit, they also depend on healthy host populations for their own transmission.

Some parasites are transmitted primarily from a mother to her offspring through the egg cytoplasm. This method of propagation means that the more often these parasites are transmitted to female offspring, the faster they spread. As a result, these crafty microbes have evolved a variety of ways to ensure that every generation they infect a greater proportion of the females in a population. One common way microbes accomplish this is by selectively killing the male offspring of the host, leaving less competition for the remaining (and useful) females. Several groups of bacteria have independently evolved this 'male-killing' strategy, and include known parasites of flies, butterflies and beetles. The ecological and evolutionary consequences of harboring a male-killer are significant: initially, they can cause host populations to become female biased, and if males become sufficiently rare then the host—and the parasite—may go extinct.

A large portion of my graduate research focused on understanding the evolutionary dynamics of these male-killing parasites. In collaboration with my advisor, Dr. John Jaenike, and a technician in the lab, Miranda Minhas, I have been studying the interaction between a male-killing *Wolbachia* bacterium and its natural host, the fly *Drosophila innubila*. *D. innubila* inhabits the forested mountains, or so-called 'sky islands,' of Arizona, New Mexico, and the Mexican Sierra Madre, where it lives and breeds exclusively on fleshy mushrooms. The unlucky sons of female *D. innubila* infected with the male-killing *Wolbachia* die as embryos. We investigated the population dynamics and interactions between the *Wolbachia* and its host at three levels: within a single host, the host population, and the host species.

A three-year study of a large population of *D. innubila* in the Chiricahua Mountains of Arizona revealed that the population-level effects of this male-killer are important: about one-third of wild-caught females are infected, and because these females almost always produce only daughters, the population as a whole has become female-biased. Perhaps we caught this *Wolbachia* infection shortly after its invasion and this population of *D. innubila* is en route to extinction due to the effects of the male-killer? To address this question, we inferred the evolutionary history of the infection using patterns of DNA polymorphism in both the host and the parasite genomes. Surprisingly, these data showed that the male-killing *Wolbachia* infection in *D. innubila* is evolutionarily old. In spite of strong selection pressure on the host to evade the male-killer, we found no evidence for host resistance, and instead the spread of the infection appears to be limited by its own imperfect transmission from mother to daughter. This finding of a stable infection is in striking contrast to the other few characterized examples of male-killers in other species, all of which appear to be very recent infections, and also demonstrates the potential for long-term evolutionary impacts of male-killers on their hosts.

Host-parasite interactions can be dynamic both in space and time, and so next we utilized the highly fragmented geographic distribution of *D. innubila* to address the relationship between local and global dynamics of the male-killing infection. We studied whether different populations of *D. innubila* have evolved along different evolutionary paths: for example, do populations vary in their level of resistance or in the phenotype induced by the



infection? And do different populations harbor different levels of *Wolbachia* infection? We collected flies from eight geographically distinct sky island populations, and found that in all populations the *Wolbachia* infection is associated with virtually complete male killing. Thus, while some male-killers produce different phenotypes in other, closely related hosts, we found no such differences between populations of *D. innubila*. However, while the *Wolbachia* infection occurs in all of the main populations, among populations the infection prevalence and the resulting distortion in the population-level sex ratio of *D. innubila* varies significantly: populations with a higher infection prevalence are more female-biased. At the genetic level, the populations are much more differentiated at loci associated with *Wolbachia* (*i.e.*, the mtDNA) than at random "background" loci. We attribute this pattern to fluctuations in *Wolbachia* infection prevalence that occur within each isolated population rather than on a species-wide scale. Overall, then, these data suggest that evolutionary interactions between *D. innubila* and male-killing *Wolbachia* operate at the species rather than population level, but that the prevalence of infection is highly dynamic within local populations and largely independent among them.

The genetic data speak to long-term patterns, but even over short time scales we observe large fluctuations in the frequency of *Wolbachia* infection. For example, in the population of *D. innubila* from the Chiricahua mountains of Arizona, the frequency of *Wolbachia* in females decreased from 45% to 25% in just three years. Because we have found no evidence

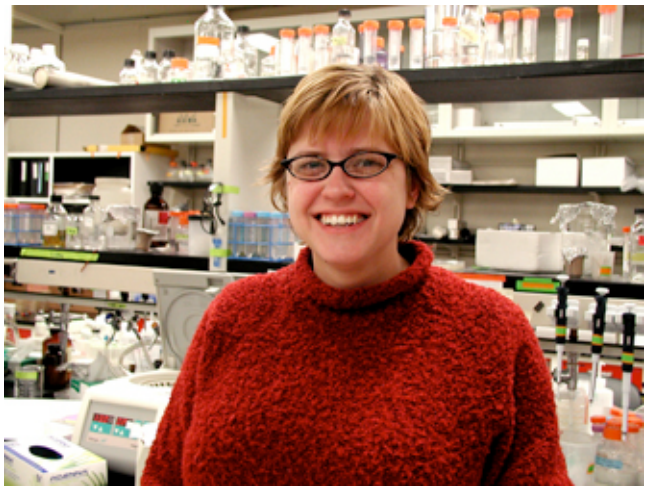
for genetic suppression of *Wolbachia*, we surveyed a few environmental variables known to affect similar bacteria. Our results from experiments with antibiotics were especially interesting: we found that even very small amounts of antibiotics almost immediately restore a normal 1:1 offspring sex ratio. By varying the amount of antibiotics that we fed to infected female flies, we found that we could control the density of the *Wolbachia* infection within each female fly. Consequently, we could also manipulate the female-bias of her offspring: females with low bacterial densities produced more sons. We further showed that bacterial density is an epigenetic, heritable trait. Importantly, not only is the bacterial load heritable, but as we showed using flies that naturally vary in their bacterial load, so is the offspring sex ratio itself.

The parasite density within the host affects both the rate of transmission of *Wolbachia* from an infected female to her offspring as well as the level of male-killing, thus directly linking processes that control *Wolbachia* dynamics within the host to the larger scale population-level dynamics. Since these flies live in mushrooms, some of which naturally produce antibiotics, it is a tantalizing possibility that the antibiotics the flies may encounter in their natural environment have a large effect on population-level *Wolbachia* dynamics, possibly explaining locally fluctuating infection frequencies. Other factors that may affect intra-host *Wolbachia* density include stochastic changes in density at the level of the host primordial germ cell and selection acting directly on *Wolbachia*'s growth rate and carrying capacity within the host.

In sum, these and other studies I have completed during my time in Rochester provide a window into the largely unappreciated realm of the ecological, evolutionary, and genomic effects of sex-ratio distorters. With the accelerating rate of discovery of such elements, it is becoming clear that their total impact on the evolutionary biology of insects and other organisms must be substantial. Furthermore, a broad understanding of these and other host-parasite interactions will have significant implications for our own medical and agricultural practices and will also guide our interpretation of what creates or diminishes biological diversity.

Kelly was the recipient of a 2003 Edward Peck Curtis Award for Excellence in Teaching by Graduate Students.

Leah Jablonski, Graduate Student, Sia lab



In the summer of 2000 the Graduate Education in the Biomedical Sciences (GEBS) summer research program placed me in the lab of Dr. Elaine Sia, a new faculty member in the Biology department. In order to complete my summer project to my satisfaction, I continued to work with Dr. Sia while I finished my B.S. Degree in Biotechnology at RIT and joined the lab as a technician after graduating in the summer of 2001. Because the project that I started as a GEBS student continues to raise new questions, I am still working on it as a third year graduate student in Dr. Sia's lab.

In the Sia lab, we use *Saccharomyces cerevisiae* as a model organism to study mitochondrial genome stability. My project focuses on the physical arrangement and packaging of DNA in the mitochondria. Mitochondrial DNA (mtDNA) is packaged into a histone-like nucleoprotein structure called nucleoids. The nucleoid is the unit of inheritance of mtDNA. It is also the site of replication of and transcription from mtDNA. Many proteins associated with this structure are known, but the functions are as yet undetermined. This is true for my main protein of interest known as Mgm101p, which stands for **M**itochondrial **G**enome **M**aintenance defect. A deletion of *MGM101* quickly causes a complete loss of mtDNA. This dramatic phenotype suggests that Mgm101p is crucial for maintenance of the mtDNA, and the rapidity of the loss may suggest a structural role in the packaging or inheritance of mtDNA.

We have some evidence that Mgm101p is modified by the small ubiquitin like modifying protein SUMO. SUMOylation of proteins has been implicated in a wide variety of protein functions including, protein-protein interactions, protein localization, and the stabilization of its modified proteins. I am constructing strains in which Mgm101p cannot be SUMOylated to determine whether SUMO modification affects Mgm101p function. These strains will be used to look at the localization, function and stability of Mgm101p when the interaction with SUMO is abolished. I am also supervising Lidza Kalifa, an undergraduate in our lab, to examine the effects of Mgm101p protein-protein interactions. Like

many mitochondrial proteins, Mgm101p is encoded in the nucleus and transported into the mitochondria. We can therefore use many standard yeast genetic techniques to analyze the function of Mgm101p. By looking at the protein modifications, protein-protein interactions, localization and DNA binding of Mgm101p we can ascertain how Mgm101p stabilizes mtDNA.

Jonathan Millen, Graduate Student, Goldfarb lab

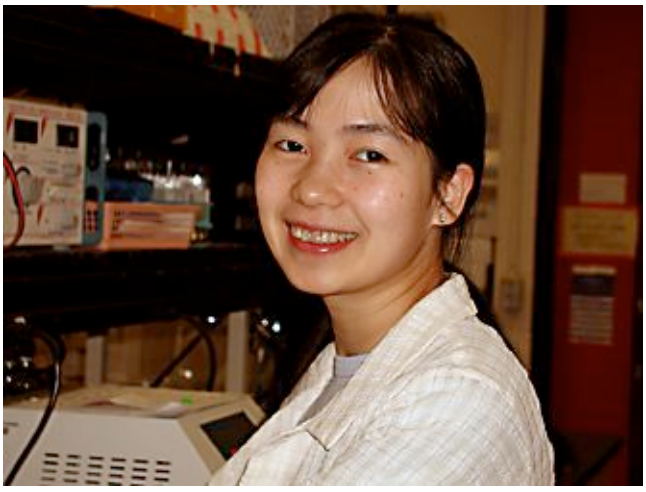
With future designs on graduate school, I spent much of my undergraduate career in the lab. Through Pennsylvania State's co-operative education program, I was able to gain valuable practical lab experience at both the Walter Reed Army Institute of Research and the pharmaceutical company GlaxoSmithKline. In 2002, I graduated with a BS in Biology and a minor in Astrobiology; then I was off to study at the University of Rochester.

Xiaoyuan Song, Graduate Student, Gorovsky lab

I had no idea about which lab to choose for my first research rotation. At the time, I was taking Marty Gorovsky's Advanced Cell Biology course. I chose his lab because I was very impressed with his kindness and patience. I chose a small rotation project, the cloning of the *Tetrahymena thermophila* metallothionein gene, *MTT1*, and then construction of an inducible promoter from its 5' flanking sequences. Work on this was started by one of Marty's former graduate students, but the project was suspended before *MTT1* was cloned. I had successfully cloned the gene by the end of the rotation period. Yuhua Shang, another

Two thousand four has been quite the busy year! My fiancée (Melissa) and I adopted two cute little kittens that we named Nola and Boone; they are littermates and have just recently turned one. We bought a house in Chili about the same time I passed my qualifying examination. As of August 7th, Melissa became my wife. We honeymooned in Key West and missed all the hurricanes. But, enough about the man. How about the mission?

After rotating through three wonderful labs I settled in the Goldfarb lab. It is here that a wide range of topics in cell biology are studied. Currently, we have projects uncovering the secrets of nuclear transport, autophagy, apoptosis, aging, and oxidative stress resistance in *S. cerevisiae* (the last two being within my sphere of influence). Originally, I was attracted to the lab by the proposed lifespan experiments. Lifespan and aging have been studied in yeast for several years now due to their naturally short lifespan, its sequenced genome, the ease of genetic manipulation, and the availability of knockout collections of its nonessential genome. Lifespan in yeast is often measured by the number of times a cell divides before senescence; this is known as replicative lifespan. Since this is true for most eukaryotic cells, it stands to reason that if all of the cells in the human body have an increased replicative lifespan, then the human (overall) should live a longer and perhaps better life. Normally observing replicative lifespan is an arduous and time consuming task involving the removal of each new bud as it completes cytokinesis. We have gotten around this problem with a strain of yeast that reproduces normally in glucose, but produces replicatively dead daughter cells. A simple growth curve in glucose can show the difference between strains with different replicative lifespans. In the immediate future, experiments with chemical libraries will be screened for compounds that extend replicative lifespan.



graduate student has used *MTT1* as the basis for an inducible expression cassette, which is now widely utilized by *Tetrahymena* labs.

Upon joining the lab, I chose to study histone H1 for my thesis project. Function of linker histones (H1s) on transcription has been shown to be gene specific in several species including *T. thermophila*. Knockout and mutagenesis experiments suggested that *T. thermophila* macronuclear H1 specifically regulates gene transcription through its phosphorylation, yet there is no direct demonstration of the gene specific association of H1 phosphorylation state and transcription at the level of individual genes. I wanted to demonstrate this association. At that time, only two candidate genes, *ngoA* and *Cyp1*, were known. Since *Cyp1* is a member of a multi-gene family, Marty suggested that initially I focused on *ngoA*. The *ngoA* gene is not expressed in wild-type *T. thermophila* log growing cells. However, in log growing mutant cells that lack histone H1 (ΔH1), the basal transcription of the *ngoA* gene (but not global gene transcription) was increased to detectable levels. This suggests that H1 can specifically repress basal expression of the *ngoA* gene. In a mutant strain of *T.thermophila* (E5), in which the five phosphorylation sites (S or T) of H1 were replaced by glutamic acid (E) to mimic the fully phosphorylated H1 state, the basal transcription of the *ngoA* gene is also activated, as in H1 knockout cells. Based on these observations, we hypothesize that dephosphorylated H1 must be present on the promoter of the *ngoA* gene in order to keep it repressed in wild-type growing cells.

Cloning of *ngoA* proved to be much more difficult than *MTT1*. I had a great deal of trouble with inverse PCR amplification of *ngoA*. It turned out that the cDNA sequence of *ngoA* that was sent to us by the lab that sub-cloned its cDNA was actually that of the wrong strand, so my initial primer sets could not anneal and the inverse PCR failed repeatedly. I am indebted to Yuhua, who suggested that I design primers to the other strand. Using this new primer set, I was quickly able to amplify and clone the *ngoA* gene. Mapping the promoter for the *ngoA* gene by serial 5′ deletions also took me quite a long time but it was still successful. However, the central hypothesis of my thesis project, namely that histone H1 is specifically de-phosphorylated when it is associated with *ngoA* in growing cells was disproved. I could never see *ngoA* specific H1 dephosphorylation by the chromatin immunoprecipitation (ChIP) assay. It seemed that all the time and effort that I spent cloning and mapping the *ngoA* promoter was wasted! To add insult to injury, I could not determine the function of *ngoA*, since I could not discern any phenotypic abnormalities in *ngoA* knockout cells. What a disappointment!

At this trying time, Yali Dou, a former postdoc in our lab who worked on histone H1, suggested that I try ChIP on the *T. thermophila CDC2* kinase gene, and monitor the phosphorylation status of the histone H1 on the *CDC2* promoter when it's inactive during cell starvation. *CDC2*, the main cell-cycle kinase gene, was cloned by Yali via subtractive hybridization of RNAs from starved E5-A5 cells. It is expressed in long starved E5 (the E5 mutation mimics H1 constitutive phosphorylation) cells, but not in A5 cells (the A5 mutation mimics H1 dephosphorylation). In wild type growing cells where most H1 is phosphorylated, *CDC2* is highly expressed. However, the *CDC2* gene is only weakly expressed when H1 is extensively dephosphorylated after long term starvation of wild type cells. When H1 dephosphorylation during starvation is inhibited by the phosphatase inhibitor okadiac acid (OA), *CDC2* expression increases in response to OA dosage. Yali also had evidence that H1 is the *in vivo* substrate for CDC2 kinase in *T. thermorphila*. These results suggest that there is a positive feedback between H1 phosphorylation and *CDC2* expression, and we expect that H1 associated with the promoter of the *CDC2* gene is dephosphorylated in starved cells when the gene is inactive. My ChIP experiments were indeed fruitful—they show that dephosphorylated H1 is enriched on the *CDC2* promoter, and these data comprise a substantial part of my current thesis project. I'm really grateful to Yali for her initial suggestion, since one ChIP positively influenced the direction of my work. One of Marty's favorite aphorisms fits this situation well: the amount of work in research doesn't always equal the amount of results in research!

At first, the *CDC2* project progressed smoothly. The last small step, a functional study of the dephosphorylated H1 enriched region on the *CDC2* gene, took almost an entire year to finish. If nothing else, during my five plus years of graduate study, I have learned that the cycle of happiness followed by disappointment, followed by happiness, is very common in research. I have realized that doing research is difficult, but it is also extremely rewarding.

I'm grateful for all of the mentorship that I have received here in the Gorovsky lab, especially for Marty's advice on "the big scientific picture", and for all of Jody's help with the details of science. Finally, I deeply appreciate all the input that I have received from the Gorovsky lab members—especially insights provided by Yuhua Shang and Yali Dou.

Qun Yu, Graduate Student, Bi lab

I began my graduate study at China Agricultural University in 1998. I participated in the development of safe and effective methods to prevent plants from pest attacks using microorganisms as biopesticide. My research experience in China reinforced my interest in microbiology and molecular biology and motivated me to pursue advanced studies in the US. I started my Ph.D. study in Dr. Xin Bi's lab after obtaining my M.S. degree in 2001. Dr. Bi's lab is interested in gene silencing and its related questions. Gene silencing was first identified in the mating-type loci of yeast, but it has been recognized to be a general phenomenon in eukaryotic cells, as exemplified by X-chromosome inactivation in female mammals. The region in which genes are silenced is called heterochromatin, and the region in which genes are expressed is called euchromatin. Based on recent studies, a model that heterochromatin can promote its own propagation has been proposed. This model for silencing poses an intriguing question of how the propagation of silent chromatin is stopped. Studies in *Drosophila* and vertebrate genomes suggest that euchromatin and heterochromatin are often demarcated by specialized DNA sequences referred to as boundary or insulator elements. Similar sequences that could block the spread of heterochromatin have also been identified in yeast recently and were referred to as barrier elements. My projects focus on identifying novel chromatin barrier elements and examining the mechanism of their function.

So far, I have demonstrated that the upstream activating sequences (UAS) of many highly expressed genes exhibit barrier activity. Analyses of these barriers indicate that binding sites for transcriptional regulators may participate in barrier function. These UASs are dispersed across the genome and might play a role in defining functional chromosomal domains. Moreover, I found that tethering the transcriptional activation domains of some transcription activators to DNA was sufficient to recapitulate barrier activity. These transcription activators have been implicated in recruiting histone acetyltransferase (HAT) complexes to promoter sequences. Interestingly, I found directly targeting HAT complexes could also counteract transcriptional silencing in yeast. I am currently examining the molecular details of how a targeted HAT may disrupt silent chromatin and de-repress the gene embedded in it. I am especially interested in determining whether or not histone acetylation causes complete disruption of silent chromatin. Moreover, I have demonstrated that sequences devoid of histones can also serve as barriers to the spread of silencing. Therefore, different boundary elements may use different strategies to oppose encroaching silent chromatin. Currently, I am examining the mechanisms that underlie the boundary functions of the transcriptionally silent loci in yeast. In higher eukaryotic organisms including humans, transcriptional silencing is similar to yeast at the molecular level. Mechanisms for barrier function may be well conserved from yeast to humans. Therefore, I would like to test yeast boundary elements function in higher cells and vice versa.

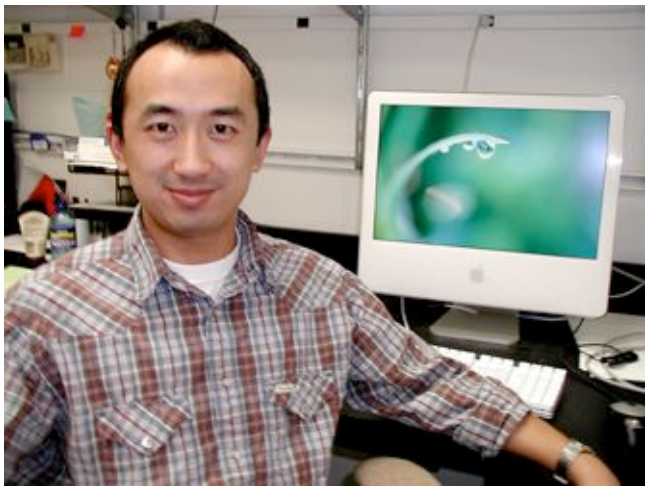
Besides my intelligent advisor, I am fortunate to have Joe Sandmeier, Yanfei Zou, Susan Elizondo and Hengpei Xu as my colleagues. I really enjoy the relationships I have established with these individuals. I want to thank Joe and Yanfei, especially, for all their help in the lab.

Another thing I want to mention is that it is so great having Yanfei as my roommate. What can be better than having a nice and considerate roommate? In Lincoln, Nebraska, I suffered a noisy roommate for a whole year; it was a terrible experience. Yanfei and I are interested in traditional Chinese food cooking; however, we haven't had time to take advantage of our cookbooks yet. Since we moved from Lincoln with Dr. Bi, we have spent most of our time working in the lab; therefore, I haven't formulated any strong impression of Rochester yet, besides the weather. The summer here is so nice that we get along well without an air-conditioner. Although I wish we could explore the city of Rochester and its surrounding further, we would prefer to spend more time cooking some real traditional Chinese food together. I am sure this will be possible after Yanfei passes her qualifying exam. I know she will do well.

Xian Zhang, Graduate Student, Eickbush lab

One of the important findings from the human genome sequencing project is that more than 30% of the human genome is comprised of repetitive DNA sequence. These "parasite DNA" or "selfish DNA" are mostly transposable elements which propagate themselves and trigger mutations by insertions and ectopic exchanges in all eukaryote genomes. The Eickbush lab uses the R2 element as a model system to study the biology of transposable elements and their impact on the host genome. R2 is a non-LTR retrotransposable element and exists in all arthropod orders as well as other phyla. R2 elements insert specifically into the 28S genes of the ribosomal DNA (rDNA) locus and interrupt the formation of the large ribosomal subunit.

"Nothing in biology makes sense except in the light of evolution", as said by T. Dobzhansky. My research in the lab focuses on the evolution of R2 elements and the rDNA locus. In empirical experiments, I followed the R2 insertion patterns in a



number of *Drosophila simulans* lines and found that in some fly lines one can score R2 retrotransposition events within one generation by comparing R2 elements in parents and offspring. This is surprising because transposable elements are normally believed to be dormant with occasional activity due to their deleterious effect on the host. This high R2 activity has been monitored for more than two years until now; R2 elements in these lines seem to be "out of control". Two projects have been started since the discovery of these R2-active *D. simulans* lines. One project is to study the patterns of R2 retrotransposition. I am screening R2 elements in parents and offspring of different families to identify new R2 insertions. The data suggested that some retrotransposition events must have happened early on in the development of the female germ line cells because about one third of her sons shared the same R2 new insertion. Another interesting finding was that accompanying the frequent R2 retrotransposition, deletions of existing R2 elements occurred as well. Every deletion event always involved multiple elements which suggested that intra-chromatid recombination could be the mechanism. The other project is to compare R2-active lines and R2-inactive lines to locate the "control locus" for R2 activity. Dr. Danna Eickbush in our lab has found that active lines had much higher R2 RNA transcripts than inactive lines. Studying crosses between active and inactive lines she showed that the activity was linked to the X chromosome. I am trying to do a detailed mapping of the X chromosome with genetic markers.

Another approach to understanding the evolution of R2 insertions and the ribosomal DNA locus is to do computer simulations. The rDNA locus is comprised of a tandem array of hundreds of rDNA units. The sequences of different units stay highly homogenized within a species. This phenomenon, termed concerted evolution, is important to study the evolution of gene families but still poorly understood. The simulation model I have developed incorporates evolutionary forces such as recombination, natural selection and R2 retrotransposition. Different parameters of the model are being tested to address questions like what are the rates and effects of these forces, how can the rDNA locus and R2 insertions be stably maintained and what is the distribution of R2 insertions along the rDNA locus as a result of concerted evolution. Our lab is also gathering information from different *Drosophila* populations about their rDNA loci and R2 elements. The simulation with the right set of parameters should give rise to results similar to what one sees in nature. Combining the simulation model and empirical data, we will have a good understanding of the turnover of R2 elements, the dynamics of the rDNA locus and the evolutionary forces in play.

Undergraduate Summer Research Fellows Present Poster Symposium

The twenty-second annual Undergraduate Program in Biology and Medicine (UPBM) Poster Symposium was held in Hutchison Lounge on Friday, October 8, 2004, along with posters presented by Chemistry Department undergrads and grads as part of Meliora Weekend. The UPBM session featured the summer research of the eight 2004 de Kiewiet Summer Fellows as well as posters by four other UPBM majors.

Presenters were kept busy explaining their projects to fellow undergraduates, faculty, lab personnel, alumni and parents.

de Kiewiet Fellows

Max Banko, BMG
Analysis of the inner mitochondrial membrane protein Yhm2p
Mentor: Elaine Sia, Biology

Steven Chan, BBC
Multiple translocation pathways through the yeast nuclear pore complex
Mentor: David Goldfarb, Biology

Patrick Corey, BEB
Ethanol induced responses of *Drosophila* species
Mentor: James Fry, Biology

Brandi Davis, BBC
Creation of a cDNA library of *Physarum polycephalum* and the cloning of H1
Mentor: Jeff Hayes, Biochemistry and Biophysics

Vanessa Franco, BNS
Mistakes in communication between brain and muscles
Mentor: Marc Schieber, Neurobiology and Anatomy

Andrew Hart, BNS
Dopamine receptor activation mediates CaMKII activation in the avian basal ganglia
Mentor: Kathy Nordeen, Brain and Cognitive Science

Jason Moore, BNS
Cross-spectral channel gap detection in the aging CBA mouse and humans
Mentor: Jim Ison, Brain and Cognitive Science

Julie Sullivan, BEB
Male mate choice in *Drosophila innubila*
Mentor: John Jaenike, Biology

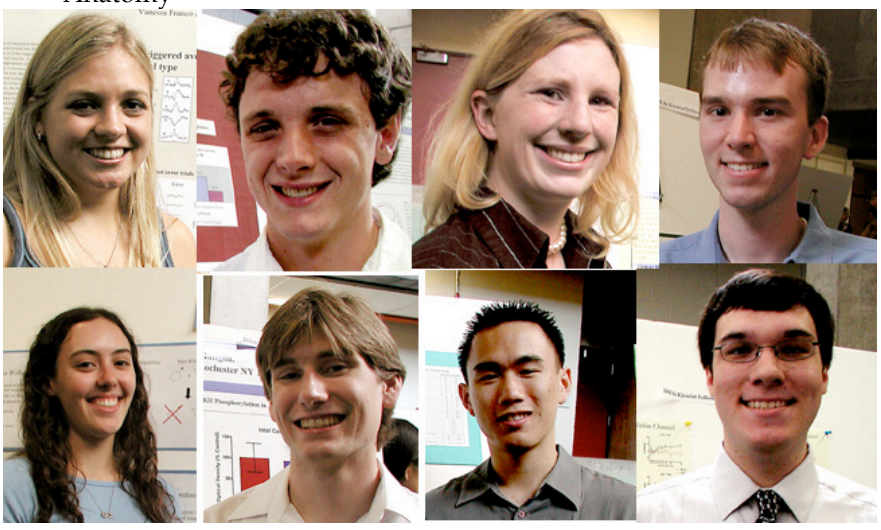
UPBM Majors

Varun Chowdhry, BBC
Interaction between M-2 subunit and the thyrotropin releasing hormone receptor
Mentor: Patricia Hinkle, Pharmacology and Physiology

Lidza Kalifa, BMG
The mitochondrial genome maintenance protein Mgm101p
Mentor: Elaine Sia, Biology

Erika Logan, BEB
Calculating copulations
Mentor: John Werren, Biology

Stephanie McGarry, BIO
Maternal wellbeing and parenting satisfaction in the context of social supports
Mentor: Cheryl Kodjo, Pediatric Adolescent Medicine



Pictured left to right from top: Vanessa Franco, Patrick Corey, Brandi Davis, Max Banko, Julie Sullivan, Andrew Hart, Steven Chan, Jason Moore.

Pictured left to right from top: Stephanie McGarry, Varun Chowdhry, Lidza Kalifa, Erika Logan.

Congratulations

Thesis Defenses

On June 15, 2004, **Jeffrey Bush** defended his thesis "Understanding craniofacial malformation in the *Dancer* mutant mouse." Jeff did his research with Rulang Jiang in the Department of Biomedical Genetics, Center for Oral Biology and Department of Biology. He is currently a postdoctoral fellow in the Department of Biomedical Genetics at the University of Rochester Medical Center.

Shian-Jang Yan, whose advisors were Bob Fleming, Department of Biology, and Willis Li, Department of Biomedical Genetics, defended his thesis "Multiple cell signaling pathways and a selector protein in *Drosophila melanogaster* wing development" on August 12, 2004. He is also currently a postdoctoral fellow in the Department of Biomedical Genetics at the University of Rochester Medical Center.

Junqiang Ye defended his thesis "Effects of chromatin structure on the transcription and retrotransposition of R2 retrotransposable elements" on August 18, 2004. Junqiang did his graduate studies in Thomas Eickbush's lab and is now a postdoctoral fellow at Harvard University in the Department of Molecular and Cellular Biology.

On September 20, 2004, **Kelly Dyer** defended her thesis "Population genetics of sex ratio distortion systems in *Drosophila*." Her research was conducted under the supervision of John Jaenike. Kelly remained at the University of Rochester as a postdoctoral fellow in the Jaenike lab for a few months. Having received a Royal Society postdoctoral fellowship, she will be moving to the University of Edinburgh to work with Brian Charlesworth.

Jonathan Bollback, whose research advisor was John Huelsenbeck, defended his thesis "Experimental bacteriophage evolution and theoretical systematics" on October 29, 2004. Jonathan has moved on to a postdoctoral fellowship at the University of Coppenhagen's Institute of Zoology Bioinformatics Centre.

Awards and Grants

David Goldfarb received a NIH Pilot project grant of $50,000 direct for September 1, 2004 - August 31, 2005 for his research "Molecular screen for lifespan extension in yeast." Additionally, NIH funded a $100,000, RO3 grant for his proposal on "High Through-Put Genomics Approach To Lifespan in Yeast" for 2 years, beginning January 15, 2005.

Robert Minckley has been appointed to the National Science Foundation, Ecology panel, covering the topic: "The Contribution of Specialist Pollinators to Generalist Plants: When do Specialists Matter?" His appointment runs July 2004-June 2007.

Rita K. Miller received a grant of $360,000 for September 2004 - August 2007 from the National Science Foundation for her research "The role of Bik1p in positioning the mitotic spindle in yeast."

Tip Benyajati was invited to honorary membership in the Golden Key International Honour Society, an academic honour society "which recognizes and encourages scholastic achievement and excellence among college and university students from all academic disciplines." The University of Rochester chapter held the induction ceremony on November 9, 2004. Tip was pleased to see several of her Biology advisees also inducted since the Golden Key membership is extended only to the top 15% of juniors and seniors.

Marriages and Births

Xiaoyuan Song and **Qingyuan Zhu** proudly announced the birth of their son, Albert, who was born on June 23, 2004. Albert entered the world weighing 6 pounds, 2 ounces, and was 21.6 inches in length.

Bonnie Baxter, welcomed her son Evan, who was born to her partner **Sally Norton** on December 28, 2004. Evan measured-in at 22.5 inches, and was 9 pounds, 12 ounces.

Albert

Bonnie & Evan

Arrivals & Departures

Professor Terry Platt has moved his primary appointment from the Department of Biochemistry and Biophysics in the Medical Center, to join us as Professor of Biology (effective retroactive to July 1, 2004). His office is located in Hutchison Hall 444, and he will be teaching Bio 113 in the spring semester of 2005. Particular interests include furthering the development and implementation of workshops in undergraduate science courses at the U. of R.

Professor Harold Hoops joined the Miller laboratory in June 2004 for a year long sabbatical as a Visiting Scientist . While in the Miller laboratory, he will be investigating the role of post-translational modification of Kar9p in positioning the mitotic spindle. Dr. Hoops teaches cell biology at SUNY-Geneseo.

The position of Biology Department Secretary went through several transformations this past year. **Lynn Stull** left the department at the end of August, to become the Secretary of the Dean's Office. **Cary McIver**, who filled in after Lynn, also moved on; she left mid-November and will be working at Nixon Peabody. **Sandra Stahlman** took over the position at the end of November 2004. A graduate of the U. of R., Sandy has just moved back to the area after living in the San Francisco Bay Area for over a decade.

Facilities Manager **Howard Bryant** died suddenly on August 25, 2004. He will be missed by all who worked with him. **Mary Bissell** stepped up to the plate and immediately filled the hole left by Howard; she was officially promoted to the job of Facilities Manager on November 1st, 2004.

Rose Covello moved from her position as bookkeeper to become the Assistant to the Facilities Manager, Mary Bissell, in September, 2004. Her duties now include ordering and receiving.

Jeanne Statt permanently took on the role of Biology Business Office Accounting/Bookkeeper in December, 2004, after starting in the position as a temp. in September. She works with Kathy Giardina and Louise Vanni to help maintain the Business Records. Jeanne works part-time at the U. of R. and full-time at home with her husband and 3 boys. She was previously employed at Weyth Lederle-Praxis Biologicals.

Bob and Lynne Angerer have made the move to the National Institutes of Health. Bob is now the Scientific Director of the Division of Intramural Research at NIDCR, and Lynne currently holds the

post of Senior Scientist in the Developmental Mechanisms Unit at NIDCR. Lynne reports that **Zheng Wei**, a former graduate student and post-doc in their lab at UR, has joined them as a staff scientist.

The Biology Department Welcomes Six Graduate Students During Fall 2004

Jianquan Chen graduated with a Bachelor of Science in Biotechnology from Northeast Normal University in 2000, and obtained his M.S. in Genetics in 2003, from the Institute of Genetics at the Chinese Academy of Sciences. Jianquan has come to UR to study Biology. In his spare time, he enjoys watching movies. Jianquan and his wife, Yinghui Yu, are expecting a daughter in April of 2005.

Zhiyong Mao obtained both a B.S. in Biology (2002) and a M.S. in Plant Biology (2004) from Nanjing University. He joins the Cell, Developmental, and Molecular Biology program here at UR. His hobbies include chatting with friends and co-workers, watching movies, and playing computer games.

In 2004, **Jeremy Rabinowitz** earned a B.S. in Biology from Cornell University, where he concentrated his studies on Genetics and Development. He'll be continuing his work in Developmental Biology with us here. Jeremy likes to camp, swim, and play basketball.

Rosemary Ryan comes to the UofR after completing a B.S. in Psychology, and a B.A. in German at Binghamton University in 2004. She'll be studying Biology at the graduate level. Rosemary enjoys camping, reading, hiking, sports, and watching movies (and confesses to have a special love for bad action movies).

Xi Shi joins us as a Biology graduate student, after obtaining her B.S. in Biology in 2001 from Nanjing Normal University. Her hobbies include reading and traveling.

Samantha England earned a Bachelor of Arts degree in Biology from Lake Forest College in 2004. Here at the U. of R., she'll be focusing on Developmental Biology. Samantha likes to play sports.

Off & On Campus

David Goldfarb was an invited speaker at the 3rd International Meeting on Yeast Apoptosis, in Salzburg, Austria, 8/18-22/04.

Goldfarb also functioned as a Guest Editor for the November 2004 Thematic issue of FEMS Yeast Research on "Apoptosis-like Cell Death Programs in Yeasts"

John Jaenike acted as a Study section member for the 2004 Grand Challenges in Global Health, an NIH/Gates Foundation.

Allen Orr gave the following talks over the last semester:

Keynote Speaker, University of Groningen, Jubilee Celebration for the Centre for Ecological and Evolutionary Studies, "Is a theory of adaptation possible?", September, 2004.

University of Amsterdam, Institute for Biodiversity and Ecosystem Dynamics, "The genetics of speciation in *Drosophila*," September, 2004.

Cornell University, Department of Ecology and Evolution, "The population genetics of adaptation," November, 2004.

University of Wisconsin, Madison, Department of Genetics, "The search for speciation genes in *Drosophila*," November, 2004.

National Academy of Sciences Colloquium: Systematics and the Origin of Species. On Ernst Mayr's 100th Anniversary, Beckman Center of the National Academies at Irvine, California. "The Genetic Basis of Reproductive Isolation and of Species Differences," given December, 2004.

Xin Bi delivered a short talk at the 2004 Chromatin Structure and Function Gordon Conference, Hilton, NH, in July. He covered the topic "Blocking the propagation of regulatory signals along the chromosome by nucleosome-excluding structures."

James Fry participated in the NSF Living Stock Collections study section on 12/9/04, and was invited to lecture at the Gordon Conference on Plant-Herbivore Interactions in Ventura, California ("Towards an evolutionary-genetic understanding of

host specialization in phytophagous insects," 3/04) and at the Society for Integrative and Comparative Biology in New Orleans ("Ethanol tolerance in *Drosophila*: evolutionary and ecological genetics," 1/04).

Robert Minckley was an invited speaker at the Entomological Society of America in November. He spoke on "Is bee diversity unusually high in Mediterranean deserts: if so, why?"

Marty Gorovsky presented the talk "Role of RNAi in DNA elimination in *Tetrahymena*." on the following occasions: the Chromatin Gordon Conference, Tilton, NH, July 4-9; for the symposium Bioscience 2004, Meeting of the British Biochemical Society, Glasgow, Scotland, July 19-24; at the University of California, Berkeley, Department of Molecular Biology and Biochemistry, October 13-15; at the University of California, Santa Barbara, Department of Biology, October 18-19; and at the Jane Coffin Child Annual Retreat, Interlaken, CT, October 22-24.

Recent Publications

Angerer

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Bi

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Fry

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Fry, J.D., C.M. Bahnck, M. Mikucki, N. Phadnis and W.C. Slattery. 2004. Dietary ethanol mediates selection on aldehyde dehydrogenase activity in *Drosophila melanogaster*. Integrative and Comparative Biology 44:275-283.

Fry, J.D. 2004. How common are overdominant mutations? Genetics 167:1031-1032.

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Goldfarb

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Goldfarb, D.S., A.H. Corbett, D.A. Mason, M.T. Harreman and S.A. Adam. 2004. Importin : a multipurpose nuclear transport receptor. Trends Cell Biol. 14:505-514.

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Kvam, E., K. Gable, T. Dunn and D.S. Goldfarb. Nvj1p sequesters the enoyl reductase Tsc13p into nucleus-vacuole junctions and affects cellular membrane dynamics. Molec. Biol. Cell., under revision.

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Mochizuki, K. and M.A. Gorovsky. 2004. Conjugation-specific small RNAs in *Tetrahymena* have predicted properties of scan (sen) RNAs involved in genome rearrangement. Genes Dev. 18:2068-2073.

Thazhath, R.M. Jerka-Dziadosz, J. Duan, D. Wloga, M.A. Gorovsky, J. Frankel and J. Gaertig. 2004. Cell context-specific effects of the beta-tubulin glycylation domain on assembly and size of microtubular organelles. Mol. Biol. Cell. 15:4136.

Hattman

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Jaenike

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Platt

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Sia

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