

## LSB speaker discusses the role of mobile DNA elements in nature

By Deepa Singh

Understanding the significance of mobile DNA elements is important, because half of human genome is derived from them, according to [Phoebe Rice, Ph.D.](#)

([http://bmb.uchospitals.edu/Faculty\\_and\\_Research/o2\\_Research\\_Interests/o5\\_Nucleic\\_Acid\\_Biochemistry.php?faculty\\_id=123](http://bmb.uchospitals.edu/Faculty_and_Research/o2_Research_Interests/o5_Nucleic_Acid_Biochemistry.php?faculty_id=123)) Rice presented her work on DNA transposition and site-specific recombination, both processes that involve movement of DNA from one location to another, in a seminar Dec. 12 sponsored by the NIEHS Laboratory of Structural Biology.

Mobile DNA elements, also known as the transposons or transposable elements, represent a potent force for change within both prokaryotic and eukaryotic genomes, and can be a major source of mutation. "In bacteria, it can facilitate evolution and antibiotic resistance, and often provide enzymes that make useful biotech tools," explained Rice, pointing to the translational potential of her research.

The host of Rice's seminar was [Matthew Schellenberg, Ph.D.](#), a visiting fellow in the Genome Stability Structural Biology Group headed by Scott Williams, Ph.D. Rice is a professor in the Department of Biochemistry and Molecular Biology at the University of Chicago. Her group combines biochemistry and X-ray crystallography to study different stages of protein-DNA interactions during transposition and recombination.

### Convergent and divergent evolution of bacteriophage Mu transposome

For DNA transposition, Rice used the example of bacteriophage Mu, a bacterial virus that propagates itself by repeated transposition and integration into its host genome. Cancer-causing retroviruses, such as HIV, use a similar mechanism to integrate into their host genomes. Therefore, understanding the mechanism of Mu transposition is important in efforts to prevent and cure retroviral diseases.

Structural studies of DNA transposase MuA, in complex with bacteriophage DNA ends and the target DNA, determined intertwined networks of protein-protein and protein-DNA contacts. MuA, in the absence of DNA, consists of a single subunit that has five domains and is usually represented or cartooned as beads on a string. But in the presence of DNA, four subunits of MuA assemble on the DNA, while the same domains on different subunits have different functions.

According to Rice, "The structure is quite compact, but is made up of a tangled mess of three DNA segments and four proteins."

Compared to other DNA transposases and retroviral integrases, the MuA complex has a different arrangement of the DNA-binding domains and regulatory domains, but the domain containing the catalytic site is quite similar. In her conclusion, Rice noted that all DNA transposases diverged a long time ago from a common catalytic domain, but have all converged back to transcatylation, since they all recognize one end of DNA and engage chemically on the other end.

### Proposed model for the site-specific recombination of serine recombinases

In the second part of her talk, Rice focused on site-specific recombination that moves mobile DNA elements between nonhomologous sites within a genome and produces genetic variants upon which evolution depends. The recombinases are often classified into serine-recombinase families and tyrosine-recombinase families, based on their active site nucleophile.

Many serine recombinases function as resolvases. "The resolvases are required to clean up after some DNA transposases and also after replication," explained Rice. They resolve the original host DNA that is still fused to the target DNA with a transposon at the junction, and convert large DNA molecules into smaller ones.

The structure of the several recombinases in complex with DNA is known, but there is still confusion about how they exploit DNA topology to regulate recombination. After comparing several different recombinases, Rice's lab proposed a divergent-convergent evolution, since they all have similar sequence, structure, and topology, but the details of how they exploit that topology are very different.



Rice, left, joined Williams and host Schellenberg, right, following her talk. (Photo courtesy of Steve McCaw)



Rice played with a handmade stuffed DNA prop she used during her talk to illustrate the structure of recombinases in complex with DNA. (Photo courtesy of Steve McCaw)

Concluding her talk, Rice described her latest work on a different pair of serine recombinases that are encoded by the mobile genetic element that turns garden-variety *Staphylococcus aureus* into the methicillin-resistant form of the bacterium, MRSA. Infection is increasingly common in crowded settings, such as hospitals, posing a significant public health challenge, due to the difficulty of treating new strains, as they evolve, with currently available medications.

(Deepa Singh, Ph.D., is a visiting fellow in the NIEHS Mechanisms of Mutation Group.)

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