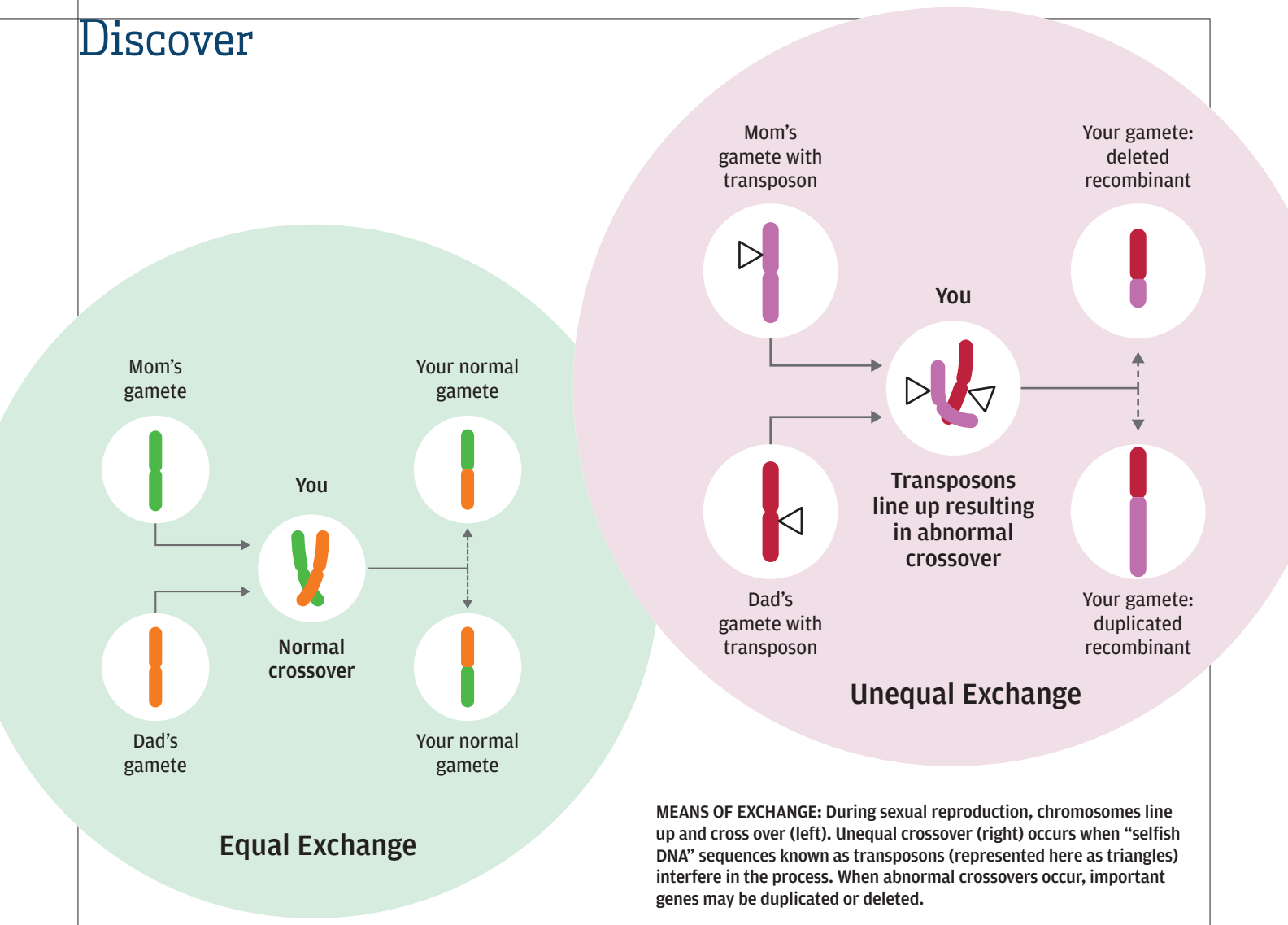

MEANS OF EXCHANGE: During sexual reproduction, chromosomes line up and cross over (left). Unequal crossover (right) occurs when "selfish DNA" sequences known as transposons (represented here as triangles) interfere in the process. When abnormal crossovers occur, important genes may be duplicated or deleted.

The Genes of Genetic Recombination

Scientists have long recognized that the exchange of genetic material in a process known as genetic recombination is vital to natural selection. During recombination, chromosomes from each parent "cross over," mostly lining up properly, but occasionally so-called "selfish DNA" intervenes to cause deletions or insertions of chromosomes that manifest as birth defects. Some species display far more crossover than others, leading scientists to hypothesize that crossover rates have evolved to balance the benefits of crossing over with its risks.

Dean's Professor of Biology Daven Presgraves and PhD candidate Cara Brand have accomplished a milestone in learning about such evolutionary dynamics. By studying two species of fruit flies, they discovered a gene, *MEI-218*, that controls the rate of recombination. In a paper published in *Current Biology*, they explain how *MEI-218* controls differences in the rate of crossing over between species and the evolutionary forces at play.

Selfish DNA sequences known as transposons—repetitive genetic elements that do not seem to have benefits to their hosts—are distributed throughout the genome. Transposons are akin to viruses, but instead of injecting themselves in cells, they invade genetic material. If abnormal crossovers occur between transposons in different locations on the chromosomes, the chromosomes do not line up properly and important genes may be duplicated or deleted.

Brand and Presgraves hypothesize that the change in recombination rates between two species of fruit flies may reflect an adaptation to their different amounts of transposons. One species, *D. melanogaster*, has more transposons in its genome than *D. mauritiana*, so *D. melanogaster* may have evolved a lower rate of crossing over in order to avoid the higher risk of harmful crossovers between transposons.

If that's the case, *MEI-218* is constantly evolving to an ever-changing optimum. The evolution of MEI-218 is similar to genes involved in immunity, Presgraves says. "That should make some intuitive sense because genes involved in immunity are constantly adapting to the changing community pathogens that are challenging us all the time."

The gene has so far only been investigated in fruit flies, but the research into recombination has applications for humans. "During meiosis at least one crossover per chromosome, in general, is required to make sure the chromosomes separate properly," Brand says. "Either a lack of crossing over or crossing over in the wrong regions of the genome is what leads to many birth defects." —Lindsey Valich

MICHAEL OSADCIW

Fracking Chemicals Linked to Immune Imbalance

A study led by Paige Lawrence, chair of environmental medicine, links chemicals associated with fracking to damage to the developing immune system in mice.

"This discovery opens up new avenues of research to identify, and someday prevent, possible adverse health effects in people living near fracking sites," she says.

Fracking (shorthand for hydraulic fracturing) involves pumping millions of gallons of chemical-laden water deep underground to fracture rock and release oil and gas. About 200 chemicals have been measured in wastewater and in surface water or groundwater in fracking-dense regions. Of the chemicals found in groundwater, several have been classified as endocrine disrupters, meaning they can interfere with hormones and derail hormone-controlled systems.

For the study, published in *Toxicological Sciences*, Lawrence and her team tested the impact of fracking chemicals on the immune system because it's greatly influenced by hormones.

The team added the chemicals to the drinking water of pregnant mice at levels similar to those found in groundwater near fracking sites. She and her colleagues found that mouse pups—particularly females—who were exposed to a mixture of 23 fracking chemicals in the womb had abnormal immune responses to several types of diseases later on, including an allergic disease and a type of flu.

Moreover, the mice were especially susceptible to a disease that mimics multiple sclerosis.

Lawrence and her colleagues believe the chemicals derail cellular pathways that control which immune cells are spurred to action. The group plans to continue to investigate how fracking chemicals interact with the developing immune system in ways that will inform biomedical scientists, health care professionals, policy makers, and the public.

—Susanne Pallo

Protecting Horses—and Humans—from Deadly Flu

Flu vaccines for horses haven't been updated in more than 25 years, but Rochester researchers have developed a new live equine influenza vaccine that is safe and more protective than existing vaccines. That's important not only to horses and their owners, but also to humans, since animals such as horses, pigs, and dogs are the most likely source of future human pandemics.

Although it hasn't happened yet, it's possible that animals could be infected with multiple influenza viruses and have the potential to act as "mixing vessels," generating new flu strains that could infect people. The strains would be particularly dangerous because people wouldn't have pre-existing immunity.

In the journal *Virology*, Luis Martinez-Sobrido, an associate professor of microbiology and immunology at the Medical Center, and lead author Laura Rodriguez, a research assistant professor in Martinez-Sobrido's lab, describe a new "live-attenuated" vaccine that's given as a spray through the nose. Created using a genetic engineering technique called reserve genetics, the new vaccine is designed to replicate and generate an immune response in the nose, where the flu first enters a horse's body, but not in the lungs, where replication of the virus can cause disease.

HORSE SENSE: Rochester work to develop a new vaccine to protect horses from multiple strains of flu virus may have important implications for protecting humans from viruses as well.

The use of reverse genetic approaches to create the live-attenuated equine vaccine confers an additional major advantage not available until now: the vaccine can be updated quickly and easily to protect against newly emerging equine influenza strains.

Traditional equine vaccines, which are made in eggs, take months to produce and do not allow the flexibility to update against newly emerging viruses.

—Emily Boynton

Bugs in the Gut Could Make You Weak in the Knees

Bacteria in the gut, known as the gut microbiome, could be the culprit behind arthritis and joint pain that plagues people who are obese, according to a study by Rochester researchers published in *JCI Insight*.

Osteoarthritis is the greatest cause of disability in the United States, affecting 31 million people. Sometimes called "wear-and-tear" arthritis, osteoarthritis in people who are obese was long assumed to be a consequence of stress on joints. But a team led by Michael Zuscik, an associate professor of orthopaedics, Robert Mooney, a professor of pathology and laboratory medicine, and Steven Gill, an associate professor of microbiology and immunology, provides the first evidence that bacteria in the gut—governed by diet—could be the driving force behind the condition.

The researchers fed mice a high-fat "cheeseburger and milkshake" diet. Just 12 weeks of the diet made mice obese and diabetic, nearly doubling their body-fat percentage compared to mice fed a low-fat, healthy diet. They had more harmful bacteria in their guts compared to lean mice, which caused inflammation throughout their bodies, leading to rapid joint deterioration.

Surprisingly, the harmful gut bacteria, inflammation, and osteoarthritis were completely prevented when the high-fat diet of obese mice was supplemented with a prebiotic. While their weight was unaffected, the knee cartilage of obese mice who consumed an oligofructose supplement was indistinguishable from that of the lean mice.

"Cartilage is both a cushion and lubricant, supporting friction-free joint movements," says Zuscik. "When you lose that, you have to replace the whole joint. Preventing that from happening is what we, as osteoarthritis researchers, strive to do."

—Susanne Pallo

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