Brewing yeasts reveal secrets of chromosomal warfare and dysfunction

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Using two yeasts that have been used to brew tea and beer for centuries, researchers at Fred Hutchinson Cancer Research Center have revealed how reproductive barriers might rapidly arise to create species boundaries. *Schizosaccharomyces pombe* has been used to brew beer in Africa, whereas its close relative *S. kombucha* is a component of kombucha tea commonly found in health-food stores.

A team of researchers led by Dr. Sarah Zanders of the Basic Sciences Division at Fred Hutch, has uncovered why hybrids between these yeasts (commonly referred to as fission yeasts) are almost completely sterile despite being 99.5 percent identical at the DNA level.

The study, published this month in the open-access journal *eLife*, found that the surprisingly rapid onset of infertility has two major causes. First, the study revealed that genome rearrangements limit the ability of the hybrids to produce offspring that contain a full set of genes. Second, the study found that three meiotic drive genes severely decrease fertility in the hybrids. Meiotic drive genes are "selfish genes"' that persist and spread in populations by cheating the process of sexual reproduction to increase their own transmission. Zanders and colleagues found evidence of three independently acting meiotic drivers, which appear to somehow kill cells that do not inherit them. Their combined action is sufficient to almost completely debilitate hybrid fertility.

"Both changes in genome structure and meiotic drivers are commonly observed in other organisms, including in human populations," Zanders

said, "but our ability to discover and fully understand their biology is greatly improved in genetic model organisms like fission yeast."

The researchers also found that the two species and hybrids between them greatly differ in their propensity to experience aneuploidy, or aberrant chromosomal configurations. Such aneuploidy is commonly observed in human cancers and is also the underlying cause of birth defects such as Down syndrome. "The model we have developed provides an exciting means to uncover the causes underlying genetic predisposition to aneuploidy," Zanders said.

The work also exemplifies the uniquely collaborative scientific atmosphere at Fred Hutch. Zanders was co-advised by Dr. Gerald Smith, whose lab at Fred Hutch studies recombination and meiosis in fission yeast, and Dr. Harmit Malik, also of the Basic Sciences Division at Fred Hutch, whose lab studies evolutionary genetic conflicts and speciation. Although this atmosphere provided the best opportunity to make new discoveries, Malik and Smith also credited Zanders' ability to bridge the strengths of both labs for the ultimate success of the project.

"Despite speciation being one of the most intriguing problems in biology, one that even Darwin termed the "mystery of mysteries", our ability to understand how new species form will be greatly enhanced by new model systems in which we can fully understand the genetic and molecular basis underlying hybrid dysfunction," Malik said. "The prospect of using these discoveries to understand the genetic basis of chromosome dysfunction and human disease is exciting, and it's a foreseeable outcome of such basic research."

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