Hibernating ribosomes help bacteria survive

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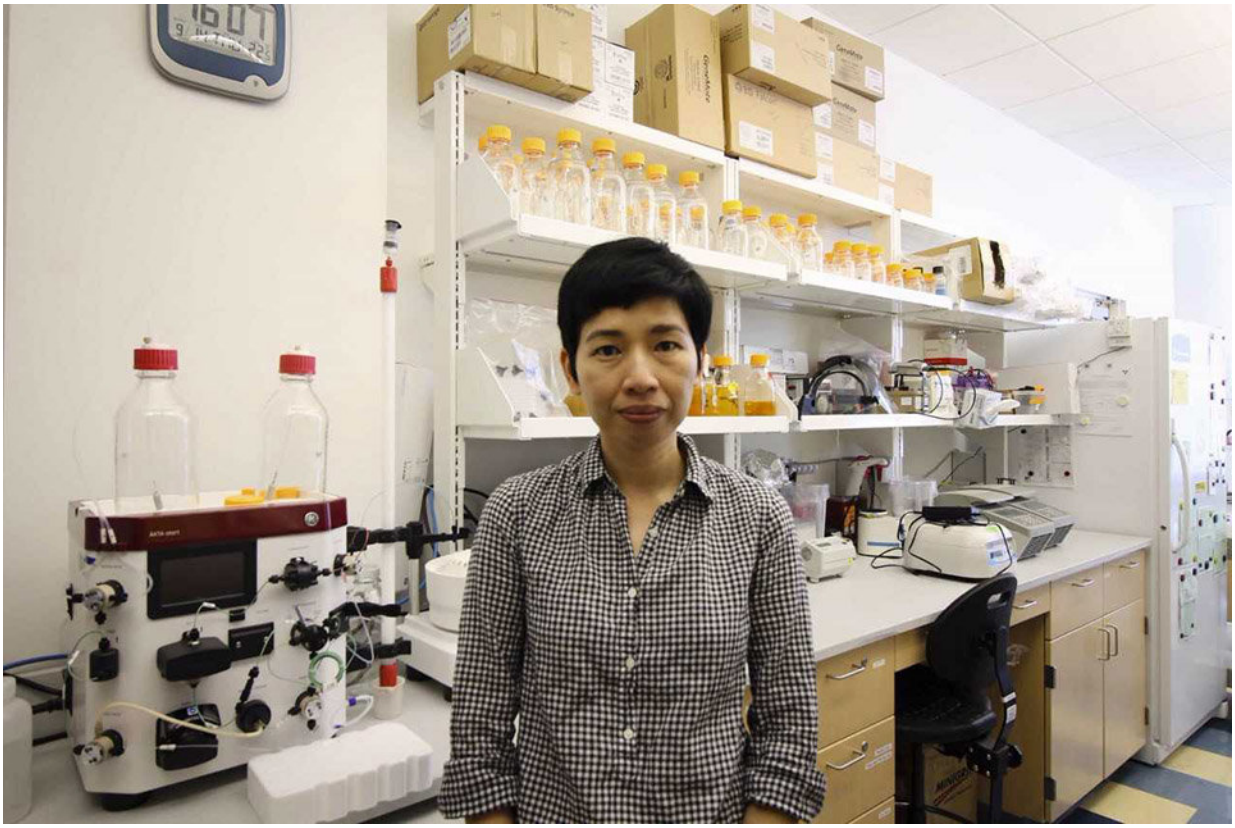

Mee-Ngan F. Yap, Ph.D., assistant professor of biochemistry and molecular biology at Saint Louis University. Credit: Saint Louis University / Ellen Hutti

In the second of two high-profile articles published in recent weeks, Saint Louis University scientist Mee-Ngan F. Yap, Ph.D., in collaboration with the laboratories of 2009 Nobel laureate in chemistry Ada Yonath at the Weizmann Institute of Science and Alexey Amunts at

Stockholm University, describe in *Nature Communications* new information about the structure of *Staphylococcus aureus* (or Staph) hibernating 100S ribosomes, uncovering secrets of how they turn off protein biosynthesis to conserve energy and survive under stressful conditions.

Ribosomes translate genetic code into proteins. However, protein synthesis consumes a lot of energy, and under stressful conditions, such as limited nutrient access, antibiotic stress or host colonization, some cells can suppress the translation process to conserve energy and help survival. In bacteria, ribosomes do this by switching to an inactive form called hibernating 100S ribosome.

The 100S complex - conjoined twins of 70S complexes - was first identified in bacteria over 50 years ago. Staph's cousin, the Escherichia coli (E. coli) bacteria, tends to form the inactive 100S structure when nutritional resources are scarce and returns to the active 70S structure within minutes after fresh nutrient sources appear. Gram-positive bacteria like Staph, on the other hand, contain 100S structures constantly, even when nutrients are plentiful.

Yap, who is assistant professor of biochemistry and molecular biology at Saint Louis University, says that the difference between the way the two bacteria hibernate is unexpected and suggests that Staph and other Gram-positive bacteria form their hibernating, 100S complexes in a species-specific way.

"In E. coli, two protein factors, RMF and HPF, are needed to enter the inactive phase," Yap said. "But only one protein, HPF, is needed for Staph.

"E. coli RMF and HPF bring the two 70S together by transforming the shape of 70S complexes into two compatible puzzle pieces without

direct contact of the two protein factors. In contrast, the Staph HPF staples the two 70S by direct attachment of two copies of HPF. As a result, the E. coli 100S ribosome is connected "head-to-head" while the Staph 100S ribosome is operated "side-by-side."

"The distinct shape of 100S ribosomes seems to be species-specific. When we knock the HPF out and eliminate it in Staph, they cannot survive as well and they are less infectious."

By hampering the formation of Staph's hibernation phase, scientists may be able to discover a unique Gram-positive-specific anti-bacterial treatment.

"In the long run, we may be able to target Staph or other Gram-positive bacteria with this species-specific approach," Yap said. "This may make it a good drug target."

More information: Donna Matzov et al, The cryo-EM structure of hibernating 100S ribosome dimer from pathogenic Staphylococcus aureus, *Nature Communications* (2017). DOI: 10.1038/s41467-017-00753-8

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