1. What question(s) does the paper address? *Put another way, why was the study performed?* In addition, what is the hypothesis? If multiple hypotheses are provided, you only need to list one. Do so in a single, succinct sentence.

Traditional antibiotics attack bacteria through breaking bonds in the peptidoglycan that compose (gram positive) cell walls. In this way, structurally weakened cell walls give way to pressure, and weakened cells die. The work of Ramadoss *et al.* highlights the key issue: antibiotic development has nearly stopped because bacteria adapt so quickly. The purpose of their research was to identify an alternative target for antibiotic activity.

The hypothesis of their paper is that targeting bacterial trans-translation protein tagging presents a viable option for research as trans—translation is not found within eukaryotic cells. Thus, antibiotics that affect bacterial cells should be relatively harmless to humans.

1. What are the main conclusions of the paper?

A primary compound, KKL-35, inhibited trans-translation. The high-throughput screen identified several other broad-spectrum inhibitors. These results indicate that trans-translation is a viable target for antibiotic targeting.

More specifically, researchers found that KKL-35 and other compounds terminated trans-translation via luciferase-based assay. The luciferase construct inserted into the protein of interest (luctrpAt) produced luciferase (and thus, fluorescence) if trans-translation was inhibited, but otherwise exhibited no fluorescence if trans-translation was not inhibited.

6) Why are the conclusions important?

For bacterial targets that are otherwise immune to traditional antibiotics, there are currently no alternatives. The pharmaceutical industry has largely abandoned the research into antibacterial molecules, as the cost is so high and drug-resistance develops immediately. This research opens the possibility to a new class of antibiotics. In a world of seven billion people, and bacterial infections that remain unresponsive to first-line antibiotics, the human race needs some sort of possibility to combat rising resistance.