VIGYAN PATRIKA

Mistakes in protein synthesis can lead to phenotypic diversity

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How would you explain your paper's key results to the non-scientific community?

Popular media often portrays DNA as the 'code of life'. Like with any code, decoding is essential to make sense of the underlying information. DNA is decoded into RNA, and finally into protein molecules which perform most of the work in a living cell. Therefore, changes in DNA often result in changes in the coded proteins, altering cellular properties. However, the interesting fact is that proteins can still change without the code (DNA) being disturbed at all. This happens due to the mistakes made during decoding. Even though these mistakes are usually not transmitted across generations, they can still influence how a cell behaves and its fitness in various ways. However, this can only happen if the mistakes are 'visible', that is if they result in changing some cellular property. Very often, mistakes in protein synthesis (decoding) are corrected or buffered and never see the light of day, so to speak. The key result of our paper is that, such mistakes in protein sequences (mistranslation) not only alter the mean trait value but also increase the variability of some cellular properties that are important for cellular health. This means that now we have trait values in the population which did not exist previously. For example, consider a classroom with children's heights ranging from 3 feet to 4 feet, in turn resulting in specific physical height based capabilities. On adding new children, if we expand the children's height range from 2 feet to 5 feet, new height based capabilities emerge. For example, taller children may be able to reach switches and shelves that the others cannot (new trait values).

What are the possible consequences of these findings for your research area?

Variability in phenotypes is the raw material for evolution. Now that we know that mistranslation increases phenotypic variability, we can speculate that mistranslation can potentially influence evolution. This is a big step forward because like we discussed earlier, unlike DNA, proteins are not passed on from generation to generation. This means that mistakes at the protein level are usually confined to the single cell or generation in which they occur. However, by altering variability in fitness linked traits, they can still influence which cells will survive to represent the next generation, or which will perform the best.

What was the exciting moment (eureka moment) during your research?

This particular piece of work was complex and involved many twists and turns. There were two or three potential Eureka moments which fizzled out, as happens so often in research! Ultimately though I think the most exciting finding came through Godwin's single cell observations: the fact that mistranslating cells show wider (more variable) distributions of cell length and division times.

What do you hope to do next?

I look forward to establishing my own research group in India. My plan is to blend basic and applied science in my research, while delving into how non-DNA based changes can impact evolution.

Dr. Laasya is postdoc and DBT/Wellcome Trust early career fellow with Dr. Deepa Agashe, National Centre for Biological Sciences, Bangalore. As an independent postdoctoral fellow, she works in an Evolutionary Biology laboratory and blends molecular biology with evolution, investigating how errors in protein synthesis can influence bacterial adaptation, and even turn out to be good for the cell. She is also interested in studying antibiotic resistance and exploring its link with translation accuracy. She obtained her PhD from the Indian Institute of Science. During her doctoral research, she explored the molecular mysteries of bacterial protein synthesis. After her PhD, Laasya worked as a freelance science writer for a year. In the future, she intends to understand more about the contribution of non-genetic variation to adaptation and evolution.

Where do you seek scientific inspiration?
Every successful experiment is a confidence and enthusiasm booster! I find that discussions with mentors and colleagues along with quiet walks give me focus, as do occasional breaks from work to do something entirely different.

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How do you intend to help Indian science improve?
Indian science has expanded hugely in the last decade, particularly in terms of manpower. I hope to make use of this very skilled and diverse scientific community to establish collaborations and widen my own expertise. Increasing competition and expectations has also driven up levels of stress among students and postdocs. I therefore also hope to function as an empathetic and motivating mentor, and spread the excitement of doing science.

Reference
Samhita, L., K Raval, P., Stephenson, G., Thutupalli, S. and Agashe, D. (2021), The impact of mistranslation on phenotypic variability and fitness. Evolution. https://doi.org/10.1111/evo.14179

Dr. Deepa Agashe lab: https://adaptationlab.in/

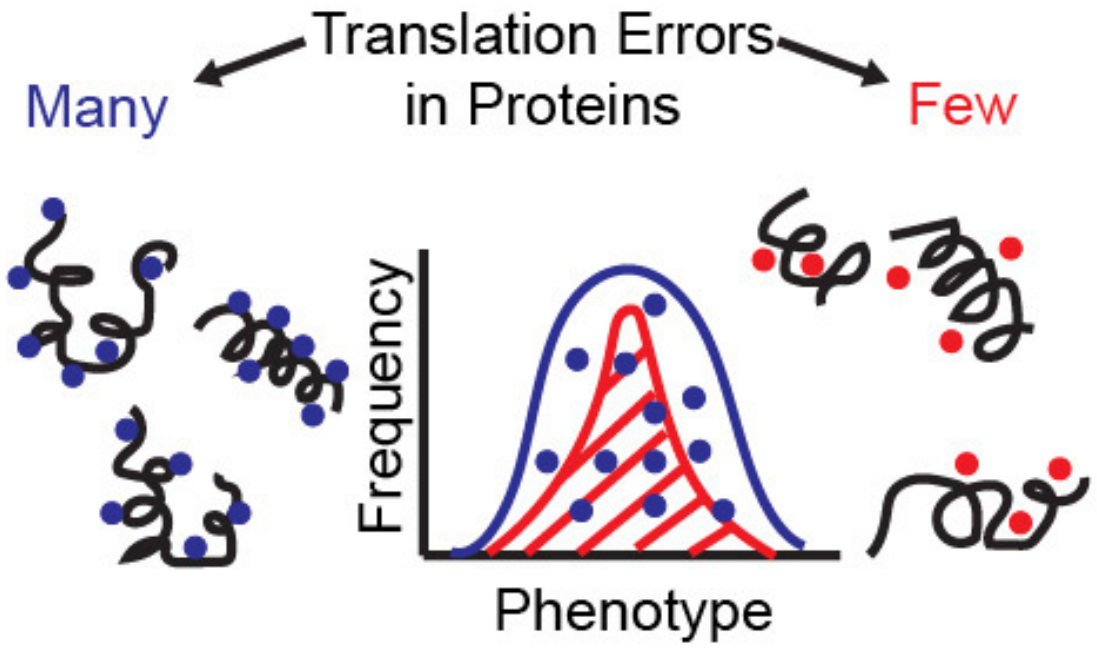

Figure 1: Translation errors. Image credit: Dr. Deepa Agashe.