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A SPONGE-LIKE SINGLE-CELL ANCESTOR

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Genome link: Choanoflagellates are the closest living relatives of animals that appeared nearly a billion years ago. Thanks to recent genome sequencing efforts, they have been shown to possess some key processes, such as cell signalling, cell–cell adhesion, that were thought to be present only in multicellular animals. | Photo Credit: Getty Images/iStockphoto

The Smithsonian Institution, in the U.S., discussing the earliest form of life on earth, points out that an environment devoid of oxygen, and high in methane, was not fit for animal life, though it could 'host' microorganisms which could cope with the incoming sunlight and use it to generate energy for living. This was around 3.4 billion years (Byr)ago, about 1 Byr after the Earth itself was born. In the process, these microorganisms generated the gaseous waste product called oxygen. About 2 Byr later, thanks to this 'great oxidation event', the amount of oxygen on Earth became an important component of the Earths' surface, and amenable for animal life.

Using this oxygen as external energy, animal cells can produce their food for growth and multiply. In order to do so, their body anatomy and biology needed to change. (An excellent summary of the origin and the need for 'multicellularity' is given by T. Cavalier-Smith in *Proceedings of the Royal Society B,* February 5, 2017,<https://doi.org/10.1098/rstb.2015.0476>). He also points out why a unicellular organism, Choanoflagellate, can be used as the model to study the evolution and diversification of animals such as humans, consisting of multi-cell body parts such as tissues and organs. Choanoflagellates are the closest living relatives of animals that appeared nearly a billion years ago. Thanks to recent genome sequencing efforts, they have been shown to possess some key processes, such as cell signalling, cell–cell adhesion, that were thought to be present only in multicellular animals.

Over time, animal cells also evolved to produce increased amounts of molecules called reactive oxygen species (ROS), which are involved in many essential cell activities but toxic at high levels. The ROS play an essential role as signalling molecules in processes such as immunity, stress response and development. In addition, more complexity necessitates a substantial increase in the genome size of the animal with concomitant increase in all transactions in the cell: DNA, the genetic material in the cells of the various organs, their transcription of the information to messenger RNA (mRNAs), then translation of these into the amino acid sequences that make individual proteins in the cells through what are called tRNAs — at least one per amino acid. These increased number of tRNAs, from around 50 in a typical bacterium to a few hundred or more in animals, means they must be selected carefully with minimal errors.

If a wrong interpretation of the genetic code at the protein level occurs, it will lead to functional disorders and even diseases. (For example, substitution of one 'wrong' amino acid in place of the right one can change the shape, size or the solubility of the protein, leading to what Linus Pauling has called 'molecular disease'. One amino acid change in haemoglobin can lead to anaemia, one wrong amino acid in the proteins of the eye lens can lead to cataract). In order to avert such 'mistranslation' into the wrong amino acids in the resultant protein, cells do contain enzymes that help remove the incorrect amino acid. It is on this aspect of 'proofreading' enzymes in animal cells that a recent publication by Rajan Sankaranarayanan and his colleagues from the Centre for Cellular and Molecular Biology (CCMB), Hyderabad, has focused on. Their research findings titled: "Genomic innovation of ATD alleviates mistranslation associated with multicellularity in Animalia", are published in the journal *eLife,* on May 28, 2020 (Kuncha et al. eLife2020;9:e58118. DOI: https://doi.org/10.7554/eLife.58118).

This intriguing title made me talk to Dr Sankaranarayanan, and here is how he explained it. His group has found such a proofreading enzyme which is Animalia-specific called ATD, which removes the amino acid alanine (A) from tRNAs which are supposed to carry another amino acid threonine (T), thus restoring proper protein synthesis and hence normal function in the cell. They further showed that animal cells also carry another enzyme called ThrRS which performs similar activity as ATD, though at high ROS levels in the cell, this enzyme loses its activity. The enzyme, ATD, appears to be stable even at high ROS levels in cells.

These results were confirmed by them in the laboratory, using human kidney cells and mouse embryonic stem cells. Knocking out this gene from cells, using the newly available genome editing technology called CRISPR-Cas9, resulted in global protein misfolding leading to cell death. Strikingly, they could also identify the molecular reasoning behind the above phenomenon.

They show that indeed alanine was wrongly substituted for threonine in multiple places in proteins that are made in cells devoid of ATD. They will now have to check the specific role of ATD in tissues with high levels of ROS, such as testes and ovaries. The group points out that the increased number of a particular group of tRNAs, which resulted in the mistranslation problem in animals, may even have evolved the potential to be involved in other functions beyond translation, such as epigenetics, programmed cell death (apoptosis) and even fertility. These are to be examined in greater detail.

Lastly, does the proofreader ATD exist in the model animal Choanoflagellate and perform a similar function? The answer is yes, as Kuncha and coworkers write: “One such enzyme,called ATD, is only found in animals. ... Further studies found that ATD originated around 900 million years ago, before Choanoflagellates and animals diverged, indicating these enzymes might have helped to shape the evolution of animals”. In other words, this sponge-like single cell is the ancestor of all animals on earth, including us, humans. Truly a humbling thought!

What about plants and trees? That is another story.

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