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Evolution & Behavior

Scrambled frog eggs return to life

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ABSTRACT

Eggs have a highly organized spatial structure. Common sense tells us that if we scramble this structure, the life of the egg will probably end. Contrary to this expectation, we discovered that scrambled frog eggs can spontaneously re-organize into compartments that not only resemble cells, but also divide to produce copies of compartments like living cells in a developing embryo.

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When you make scrambled eggs for breakfast, you are probably not expecting any signs of life in the resulting mush, let alone development into chicken embryos. Indeed, it seems common sense that living things are organized structures, and once these structures are jumbled up, life would probably end.

Well, life is more resilient than we thought.

In our most recent research, we found that scrambled eggs from the African clawed frog *Xenopus laevis* spontaneously re-organize into individual compartments that each resembles a cell. These cell-like compartments are alive – they can divide to produce more compartments in the same way that real cells would replicate themselves in an embryo.

How is this possible?

Like all animal cells, the frog egg is made up of an internal juice called the cytoplasm which is enclosed by a 'skin' known as the plasma membrane. We initially wanted to learn how undiluted cytoplasm isolated from eggs undergoes death and decay. To be able to do so, we scrambled thousands of frog eggs and collected their cytoplasm, creating an egg extract. Cells typically contain nuclei in which their genetic material is stored. However, egg nuclei are mostly lost during the preparation of egg extracts. To make up for the loss of this cellular component, frog sperm nuclei were added into the egg extract. Subsequently, we spread a droplet of such egg extract on a microscope slide and watched how the homogenized egg juice would decay.

Then something utterly unexpected happened.

Though they were initially scattered, the nuclei sprang into action and rearranged themselves into a two-dimensional lattice. Microtubules, filamentous protein polymers that act like the skeleton of the cell, grew out in a radial pattern centered on the nuclei. Mitochondria, the powerhouse of the cell, and the endoplasmic reticulum, the internal lipid membrane structure that spans the cell, both migrated towards the nuclei. The collective rearrangements of these cytoplasmic components created compartments where they were enriched, and border zones where they were depleted. Within each compartment the components were arranged much like what one would expect from a typical cell. The initially featureless cytoplasm as a result ended up looking like a sheet of cells lined up like a honeycomb.

What is required for compartment formation? It is tempting to think that the added sperm nuclei orchestrated the re-organization of the homogenized cytoplasm. But that was not the case here, as egg extracts both with and without sperm nuclei gave rise to cell-like compartments with almost the same appearance. Rather than the nuclei, we found that the microtubule, its associated cytoplasmic motor protein called dynein, and energy (in the form of adenosine triphosphate, ATP) are crucial for this remarkable re-organization.

We then wondered whether these compartments are more than just something that look like cells. Can they do anything that living cells can do?

The answer is yes. One of the most important functions of a living cell is division – a process that produces more copies of itself after each cell cycle so that life can continue to exist. To see whether the compartments can divide, we made egg extracts with added sperm nuclei, but without the drug that would normally be added to block their cell cycle. The cell-like compartments emerged from the homogeneous extract as before, and then divided to produce more compartments. The division proceeded as one would expect from a real embryonic cell: One mother compartment with a single nucleus split into two equally sized, but smaller daughter compartments, each also containing a single nucleus. The division can go on for many cycles within a droplet of egg extract, partitioning it into a population of small compartments, in the same way an egg would eventually divide into a population of small embryonic cells.

This discovery is a demonstration that biological materials can retain striking vitality even when they are taken out of their original packaging. Despite the initial disruption, the cytoplasm can regenerate surprisingly normal structure by self-organization, and can restore some of the most important functions (such as cell division). In a way, this shows that the structure and function that define life are amazingly tenacious. It opens up many possibilities for science, engineering and medicine. One hypothesis is that this may be a conserved phenomenon across different species, and it can potentially tell us something about how early cellular life emerged on earth. The egg extracts may also become the basis for building artificial cells, allowing us to engineer therapeutic agents. Much further research lies ahead, but the future is promising.