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on the end of a leash

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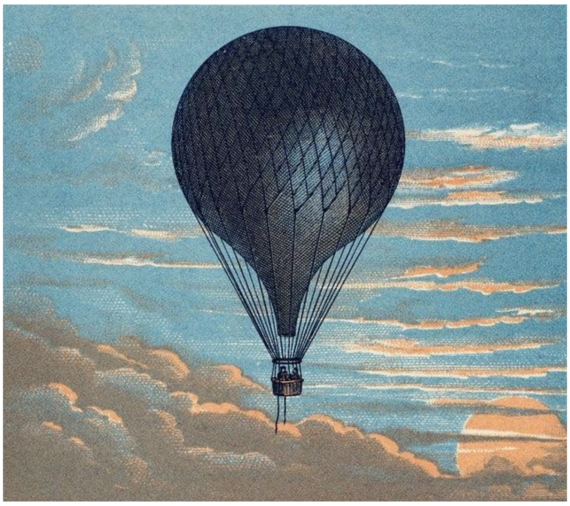
It has been a long time since I saw a plug hanging from the side of a bathtub. Remember the small triangular ring the chain dangled from, and the actual plug at the other end – usually a piece of black and slimy rubber that fitted perfectly into the plug hole. As a child, the perfection of the fit used to fascinate me and I would sit in the bath, pulling the plug out and pushing it back in again, fighting against the swirl and dynamics of flowing water. The system is straightforward enough. If you do not want the bath to empty, take something large, strong and watertight to fill the hole. You may think we are the inventors of the plug, but we are not. Filamentous fungi have been using the same kind of approach for millions of years to obstruct large holes, or septal pores, whose role is to let cytosol migrate from one part of the fungus to another. Sometimes it is necessary to seal the pores off, however. This happens thanks to organelles known as Woronin bodies which, just like the bath plug, are tethered close by.



'Le Ballon'

attributed to printer Eugène Pichot, 1883
perhaps by Jules Chéret (1836-1932)?

Filamentous fungi are so named because their cells – or hyphae – are long and filament-like. Hyphae are divided into compartments by septa, themselves an extension of the cell membrane. This sounds as though they have two separate cells, but it is not quite the case because indistinct parts of the cytosol can migrate freely through the septa, from compartment to compartment, thanks to large non-selective septal pores. Organelles as big as the nucleus can slip through. This may sound odd when the integrity of a cell does seem to be the best way to preserve life but it is a way of having the characteristics and benefits of a multicellular organism while keeping things relatively simple. There is a downside, however. If the cell membrane of a compartment is damaged, the cytosol will leak out unrestrained while probably letting unwanted matter drift in – unless septal pores are rapidly blocked. This is exactly what occurs.

Septal pores situated close to a recent wound are obstructed by organelles known as Woronin bodies (WB) – named after the Russian mycologist Mikhail Woronin (1838-1903) who was the first to describe them. Just big enough to be seen through a light microscope, WBs are very similar to peroxisomes. Peroxisomes are small single-membrane organelles that have a crystallized enzyme core and are found in virtually all eukaryotic cells where they are involved in a variety of metabolic reactions. WBs are only present in filamentous fungus, however, and the crystallized enzyme core is formed by a protein known as Woronin body major protein, or HEX-1. Why HEX-1? Because in *Neurospora crassa*, where this peculiar organelle was first observed, the protein spontaneously assembles into hexagonal crystals forming a matrix of oligomers.

HEX-1 seems to be unique to filamentous fungus. It has a peroxisome-targeting motif at its C-terminal, which is thought to target the protein to a peroxisome. Once inside, phosphorylation of HEX-1 triggers the self-assembly of HEX-1 monomers to form a large crystalline matrix which is not only stable but also particularly rigid. This initial formation would then bud from the peroxisome to form an actual Woronin body. Stability and especially rigidity are ideal properties for WBs to act as septal pore plugs – which need to be larger than the hole they must fill besides being inflexible. Other more 'flexible' organelles could cave in and gradually ease their way through septal pores under the pressure of the cytosolic flow caused by a wound.

Septal plugs cannot be left to float around freely, however. In hyphae, cytosol is continuously passing from one side of a compartment to another, creating a current strong enough to drag with it WBs – or any other cellular entity for that matter – towards septal pores. This would undoubtedly clog the pores which would compromise the necessary communication between compartments, thus harming the fungus. Like buoys in a harbour, WBs need to be tethered to something stable as they await to be used. A closer look at these peculiar organelles showed that WBs are indeed attached to the cell cortex – a region that lines the cell membrane on the cytoplasmic side – on the end of a long elastic tether, either close to the rim of septal pores, or much further away as is the case in *N.crassa* for instance. The long leash turns out to be formed by a protein (named leashin) where one end is associated with the cell cortex and the other is linked to a WB.

It is extraordinary to realise that such a simple and seemingly obvious system to plug holes has been thought up by cells. In the wild, filamentous fungi are prone to damage as many species grow in forests. In fact, they seem to thrive where there have been forest fires – an event which is becoming more and more frequent with climate change. When hyphae are wounded, cytosol leaks out of the wound in a gush. The strength of the gush is sufficient to drive WBs towards the closest septal pores to seal them off. Many scientists, however, think that sealing off is not merely passive since septal pores are sometimes also plugged in the absence of wounds, as presumably they must be unplugged too. This would imply that there is some kind of active regulation too, which would be used to regulate communication between compartments – a little like creating temporary cells.

Filamentous fungi seem to have found a way of remaining unicellular while establishing a near multicellular status with their septa and septal pores. Several filamentous fungi are pathogenic to plants and animals, causing serious mycoses or respiratory problems in humans for example, or killing off plants. Since the formation of Woronin bodies depends on the presence of HEX-1, the protein could present an ideal therapeutic target for diseases inflicted by filamentous fungi in humans, and it could also be used to make plant fungicides. In the meantime, is it not wonderful to know that, millions of years ago, Nature imagined what look like sophisticated balloons tied to the end of a tethered string to regulate the stream of life within cells?

Cross-references to UniProt

Woronin body major protein, *Neurospora crassa* : P87252

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