Jet lag uncovered by mould

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Studying red bread mould may teach us how our own internal clock works. This is exactly what the Centre for Organelle Research (CORE) at the University of Stavanger, Norway is doing.

By experimenting with the fungus' response to light and darkness, researchers explore its reaction to different substances, food and temperatures.

“The fungus may give us a clue about how higher-ranking organisms such as humans respond to changes in circadian rhythms. It is a fascinating fact that many of the diurnal principles are shared by humans and fungi,” says Ingunn W. Jolma, who is doing her PhD on regulation of biochemical oscillators at CORE.

Adapting to change

Once every 24 hours, the red bread mould produces a new generation of spores called conidia. The mould is governed by a 24 hour circadian rhythm, controlled by its genes. This circadian rhythm will proceed, even if the fungus is kept in constant darkness in a laboratory. Lacking light as a zeitgeber or time giver, the fungus adjusts its period length to approximately 22 hours. The researchers have carried out different experiments, in which they have altered the duration of the fungus’ exposure to light and darkness. The mould has adapted to the new patterns, although it may need some time to adjust. It is, in fact, suffering from jet lag.

“Jet lag is actually a phase change. If the fungus is transferred to a different time zone, it will adapt to its new environment and the new time. As with humans, this process will take some time, and the fungus may become a little stressed. The great thing about the internal clock is that the fungus will adapt its crucial cellular processes to its new environment,” says Jolma.

Red bread mould – neurospora crassa in Latin – originates from the tropics, but has relatives elsewhere. In Norway, the fungus thrives in the filamentous fungus aspergillus. Among these is a species which grows on cheese that has been left too long in the fridge.

As its genome has been fully mapped, the red bread mould is widely used in research on circadian rhythms. The fungus is also non-

pathogenic, which means that it does not pose any health risk to people exposed to it.

Unstable sleeping patterns

The CORE researchers have carried out experiments by adding various substances to the red bread mould. In one experiment they added lithium – which for many years has been used to treat bipolar disorders. Bipolar patients often suffer from unstable sleeping patterns, and lithium is reported to remedy this problem.

“A stable sleeping pattern helps us function better. We all have experienced sleep-disrupted nights, and we know how tough this can be,” Jolma says.

After being exposed to lithium, the mould’s circadian rhythm was prolonged. As the scientists examined the fungus’ protein level, they found that the clock protein Frequency become much more stable after lithium had been added. In other words – lithium slows down the protein’s disintegration process, which is turn extends the day.

Governed by genes

The inner clock is controlled by our genes, and all organisms have several clock genes. They produce a blueprint called mRNA, which in turn forms protein. As more protein is formed, it eventually binds to DNA and stops reproducing. This is called negative feedback. After some time, the protein starts to disintegrate, and the process will start anew.

On the other hand, positive feedback enables protein to increase its reproduction. As the mould’s protein content varies during a 24 hour

cycle, it is theoretically possible to measure its protein level and thereby establish the time of day.

“The internal clock in both humans and fungi has this system of positive and negative feedback loops in common. By understanding how these processes operate in fungi, we may apply an equivalent principle to uncover how the clock works in humans,” says Jolma.

The inner clock governs our sleeping patterns, as well as body temperature, blood pressure, blood thickness and metabolism. Since our clock is ruled by genes, we may remove all external influences or time givers, and the organism will still follow its given patterns. The ‘natural’ circadian rhythm among humans is 25.5 hours on average, albeit with large individual differences. This means we will adapt to a 25.5 hour cycle, when deprived of time givers such as lightness and dark.

Fluorescent fungi

All organisms are able to switch its genes on and off, depending on the time of day. The researchers at the University of Stavanger apply different methods for tracing the mould’s circadian rhythm. Just recently, they took up a method which has been in little use on red bread mould. They employ a so-called reporter gene – a gene which measures easily measurable enzymes. In this particular case, it is easily measurable because it emits a luminous product. The reporter gene employed is called luciferase – the same gene which makes a firefly fluorescent.

The partner protein luciferin is added to the mould’s nutrients, and as soon as the gene is ‘switched on’, the mould starts emitting light. After the gene is switched off, the light-producing process stops.

The fungus is grown in the dark, and observed by a specially equipped camera. By studying the images, the scientists can follow the mould’s

circadian rhythm under different conditions.

The red bread mould study is basic scientific research, aimed at yielding new insights and theoretical knowledge.

“Our discoveries may eventually enhance our understanding of phenomena such as jet lag, adverse health effects of shift work, and illnesses related to the circadian rhythm of our cells,” Jolma concludes.

Provided by University of Stavanger