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Press Release

Issued: 9th September 2020

UNDER STRICT EMBARGO until 16:00 BST Wednesday 9th September

Caffeine shot delivers wakeup call on antifungal drug resistance

The management of fungal infections in plants and humans could be transformed by a breakthrough in understanding how fungi develop resistance to drugs.

It was previously thought that only mutations in a fungi's DNA would result in antifungal drug resistance. Current diagnostic techniques rely on sequencing all of a fungi's DNA to find such mutations.

Scientists from the University of Edinburgh have discovered that fungi can develop drug resistance without changes to their DNA – their genetic code.

The new research, published in *Nature,* finds that resistance can emerge in fungi without genetic changes. Instead the fungi exhibit epigenetic changes – alterations that do not affect their DNA – suggesting that many causes and cases of antifungal resistance could have been previously missed.

Each year fungal diseases affect billions of people globally, causing an estimated 1.6 million deaths.

Infections resistant to treatment are a growing problem, particularly in patients with weakened immune systems such as those with HIV. Few effective antifungal drugs exist.

Overuse of agricultural fungicides is also leading to increasing resistance in soil borne fungi. Fungal disease results in the loss of up to a third of the world's food crops annually.

The team of scientists from the University of Edinburgh's Wellcome Centre for Cell Biology studied the emergence of resistance in a yeast, *Schizosaccharomyces pombe*, by treating it with caffeine to mimic the activity of antifungal drugs.

The team discovered that the resulting resistant yeast had alterations in special chemical tags that affect how their DNA is organized. Some genes became packed into structures known as *heterochromatin*, which silences or inactivates underlying genes, causing resistance as a result of this epigenetic change.

This discovery could pave the way for new therapies to treat resistant infections by modifying existing epigenetic drugs or developing new drugs that interfere with fungal heterochromatin.

Improved fungicides to treat food crops could limit agricultural losses and also reduce the number of resistant fungal strains in the environment that continue to fuel increased infections in humans.

Professor Robin Allshire, who led the study at the Wellcome Centre for Cell Biology, Institute of Cell Biology, School of Biological Sciences, said: "Our team is excited about the possible implications that these findings may have for understanding how plant, animal and human fungal pathogens develop resistance to the very limited number of available and effective antifungal drug treatments."

Sito Torres-Garcia, Darwin Trust of Edinburgh funded PhD student and first author of the paper, said: "Our study shows for the first time that fungal cells can develop drug resistance by altering how their DNA is packaged, rather than altering their DNA sequence."

The study was funded by Wellcome and The Darwin Trust of Edinburgh.

For further information please contact: Rhona Crawford, Press and PR Office, 0131 650 2246, rhona.crawford@ed.ac.uk