Antibiotic resistance: 'Sleeping' bacteria that can survive drug treatment identified

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'Sleeper cells', which can survive doses of antibiotics and lie resting in a dormant state, may hold a key to understanding antibiotic resistance, research has found.

Dr Stefano Pagliara, a biophysicist at the University of Exeter, has developed a novel way of identifying cells likely to survive antibiotics, even before the drug treatment.

The research, published in the journal *BMC Biology*, lays the foundation for understanding the special properties of bacteria that can survive being treated with antibiotics, so that new ways of targeting them can be developed.

Antibiotic resistance is one of the most pressing public health challenges and threatens the ability to effectively fight infectious diseases including pneumonia and tuberculosis.

After dosing bacteria with ampicillin, the Exeter University team found that the vast majority of the 1.3 per cent of cells that survived were live but non growing.

Dr Pagliara has dubbed them 'sleeper cells' because they look dormant and resemble the cells that have been killed by antibiotics, but are potentially dangerous with the ability to 'wake up' and re-infect humans or animals.

The Exeter University research team found that the two types of cells surviving antibiotics, 'sleeper cells' and persister cells, have similar features suggesting the two populations of cells are linked. Their unique fluorescence meant they could both be spotted even before being dosed with antibiotics.

But because 'sleeper cells' are non growing, standard detection methods cannot differentiate them from dead cells, giving the false impression that far fewer cells have survived a course of antibiotics.

The Exeter University team, including Dr Rosie Bamford and Ashley

Smith, used a miniaturised device which enabled them to isolate and study single bacteria over time. This device could be used to study any bacteria posing a threat to human or animal health.

Using fluorescence to light up individual cells, they identified the viable but dormant 'sleeper cells', which looked as if they are dead or dying after being treated with antibiotics. The other type of surviving cells known as persister cells - which accounted for less than one third of surviving cells - started regrowing after the course of antibiotics ends.

Cells which survive treatment with antibiotics can all eventually divide, leading to a relapse of infection while increasing the risk of antibiotic resistance development.

Dr Pagliara, a senior lecturer in the Living Systems Institute at the University of Exeter, said:

"Antibiotic resistance is one of the serious health challenges of our age. The cells we identified elude antibiotic treatment and pose a serious threat to human health. In fact, unlike persister cells which quickly resume growth after the antibiotic course ends, 'sleeper cells' remain non-growing for prolonged periods of time, and elude detection using traditional methods."

"Our research should make it easier to develop biomarkers to isolate these cells and open up new ways to map the biochemical makeup of bacteria that can escape antibiotics, so we can find ways of targeting them effectively."

Dr Pagliara is planning a programme to identify and isolate individual 'sleeper cells' for a thorough analysis with next-generation sequencing to see how they express genes differently than those that are not resistant to antibiotics.

Provided by University of Exeter