Reversible oxygen-sensing 'switching' mechanism discovered

September 10 2012

Bacteria that cause disease in humans have a 'reversible switching mechanism' that allows them to adapt to environments lacking oxygen, scientists at the University of East Anglia (UEA) have found.

Published today in the journal Proceedings of the National Academy of Sciences, the findings provide a new insight into how bacteria sense and adapt to oxygenated atmospheres, and uncover a new 'antioxidant' pathway by which certain types of damaged proteins can be repaired.

The research focussed on the regulatory protein fumarate and nitrate reduction (FNR), which senses the presence of oxygen in the environment and 'switches' off and on specific genes in pathogens such as *E. coli* when there is no oxygen present – conditions often found in the human intestinal tract.

It was conducted by researchers at UEA, the University of Georgia and the University of Sheffield

Oxygen is sensed by FNR through a special cofactor – called an iron-sulfur cluster – that undergoes conversion from one form to another, smaller one, thereby causing the protein to change shape (the 'switch') and leading to the turning off of genes associated with growth without oxygen.

Joint lead author Prof Nick Le Brun, from UEA's School of Chemistry, said: "This study has revealed important new details of FNR's switching

mechanism, demonstrating that the cluster conversion can go in reverse, so that the switch is a reversible one.

"This also highlights a new general mechanism by which this type of protein can be repaired if it gets damaged – which can often happen, as iron-sulfur clusters are highly reactive towards oxygen and other species that are associated with oxidative stress, which is linked to a whole host of diseases, as well as ageing."

The findings could have a number of implications for the developments of new antibiotics and the study of iron-sulfur cluster proteins, which are found in all types of cells where they play crucial roles in many processes including respiration, DNA replication and DNA repair.

The clusters can also be damaged by oxidative stress – conditions that cause damage to cellular components that lead to the activation of specific defence responses – which is thought to be involved in the development of many diseases including cancer, Parkinson's and Alzheimer's.

More information: 'Reversible cycling between partially cysteine persulfide-ligated clusters and cysteine-ligated clusters in FNR' is published today by *Proceedings of the National Academy of Sciences*. www.pnas.org/content/early/201 … /1208787109.abstract

Provided by University of East Anglia