

Professor Jeff Cole

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[School of Biosciences \(/schools/biosciences/index.aspx\)](/schools/biosciences/index.aspx)

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Postgraduate supervision

For a list of possible PhD projects offered by Prof Cole:

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Research

Research Theme within School of Biosciences: [Molecular and Cell Biology \(/research/activity/cellbiology/index.aspx\)](/research/activity/cellbiology/index.aspx)

Research description

1. Genetic regulation of anaerobic bacterial metabolism of nitrate and nitrite

Oxygen, nitrate and nitrite regulate the synthesis of many enzymes required for bacteria to grow anaerobically. Such 'global responses' involve transcription factors such as FNR, NarL and NarP which respond to signals generated by oxygen, nitrate and nitrite. How are these various regulatory signals coordinated to achieve regulated gene expression? How are the promoters of the genes organised and how do the factors interact with RNA polymerase? This is a joint project with Professor Steve Busby.

2. The molecular and genetic basis of bacterial resistance to human defence mechanisms.

How gonococci invade and survive in the human body have been studied in Birmingham for many years. We are currently interested in the biochemical mechanisms that enable gonococci to adapt to oxygen starvation to explain how they survive both in vivo and in vitro when starved of oxygen. . Microarrays will be used to determine how many operons are regulated by two transcription factors that regulate expression of genes essential for anaerobic survival.

3. Unresolved sources, sinks and pathways for the recovery of enteric bacteria from nitrosative stress

We are attempting to resolve many controversies concerning the sources and mechanisms of reduction of nitric oxide by enteric bacteria, and how nitrosative damage is repaired. The membrane-associated nitrate reductase is the major source of NO generated from nitrite, but at least one other source remains to be identified. Nitrite reductases are primarily detoxification systems that decrease rather than increase the accumulation of NO in the cytoplasm: whether they also catalyse NO formation is unresolved. As none of the three enzymes that reduce NO account for the majority of the rate of NO reduction, additional mechanisms remain to be discovered. Little is known about the biochemistry of damage repair. We are trying to show that the enigmatic hybrid cluster protein is part of a repair pathway rather than a hydroxylamine reductase, as annotated in many genome databases.

4. New bacterial hosts and strategies for generating difficult recombinant proteins in bacteria

Almost any gene can be cloned into a plasmid for expression in a bacterial host, but membrane proteins or proteins that require secretion or extensive post-translational modification often accumulate as unfolded proteins in inclusion bodies. As part of the BBSRC BRIC project and in collaboration with GSK, we are developing novel E. Coli hosts and protocols to produce these difficult proteins in both shake flask and fed-batch fermenters.

Publications

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