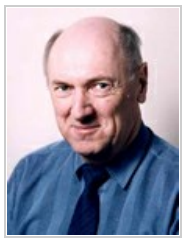
Professor Jeff Cole

Emeritus Professor of Microbiology

School of Biosciences (/schools/biosciences/index.aspx)



Contact details

Telephone +44 (0)121 41 45440 (tel:+44 121 41 45440)

Fax +44 (0)121 41 45925

Email j.a.cole@bham.ac.uk (mailto:j.a.cole@bham.ac.uk)

School of Biosciences
University of Birmingham
Edgbaston
Birmingham
B15 2TT
UK

Postgraduate supervision

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

www.findaphd.com/search/customlink.asp?inst=birm-Biol&supersurname=Cole (http://www.findaphd.com/search/customlink.asp?inst=birm-Biol&supersurname=Cole)

Research

Research Theme within School of Biosciences: **Molecular and Cell Biology (/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

Snyder, L. A. S., Cole, J. A. and Pallen, M. J. (2009) Comparative analysis of two *Neisseria gonorrhoeae* genome sequences reveals evidence of mobilization of Correia Repeat Enclosed Elements and their role in regulation. BMC Genomics 2009, **10:**70.

Squire, D. J. P., Xu, M., Cole, J. A., Busby, S. J. W. and Browning, D. F. (2009) Competition between NarL-dependent activation and Fis-dependent repression controls expression from the *Escherichia coli yeaR and ogt promoters. Biochemical Journal* ***420****: 249-257.* and promoters. Biochemical Journal : 249-257.

Sevastsyanovich, Y., Alfasi, S., Overton, T., Hall, R., Jones, J., Hewitt, C. and Cole, J. (2009) Exploitation of GFP fusion proteins and stress avoidance as a generic strategy for the production of high quality recombinant proteins. FEMS Microbiology Letters **299**: 86-94.

Sevastsyanovich, Y., Alfasi, S. and Cole, J. (2010) Sense and nonsense from a systems biology approach to microbial recombinant protein production. Biotechnology and Applied Biochemistry **55:** 9-28.

Li, Y., Hopper, A., Overton, T. W., Squire, D. J. P., Cole, J. and Tovell, N. (2010). Organisation of the electron transfer chain to oxygen in the obligate human pathogen, *Neisseria gonorrhoeae*: roles for cytochromes c_4 and c_5, but not cytochrome c_2, in oxygen reduction. Journal of Bacteriology **192**: 2395-2406.

Marteyn, B., West, N., Browning, D., Cole, J., Shaw, J., Palm, F., Mourniers, J., Prévost, M.-C., Sansonetti, P. & Tang, C. (2010) Modulation of *Shigella* virulence in response to available oxygen *in vivo*. Nature. **465:** 355-358.

Alfasi, S., Sevastsyanovich, Y. R., Griffiths, L., Hall,R. and Cole, J. (2011) Use of GFP Fusions for the isolation of *Escherichia coli* strains for improved recombinant protein production. Journal of Biotechnology **156**: 11-21.

Marietou, A., Griffiths, L. and Cole, J. (2009) Preferential Reduction of the Thermodynamically Less Favorable Electron Acceptor, Sulfate, by a Nitrate Reducing Strain of the Sulfate Reducing Bacterium, Desulfovibrio desulfuricans 27774. J. Bacteriol. In press.

Jia, W., Tovell, N., Clegg, S., Trimmer, M. and Cole, J. (2008) Site-directed mutagenesis and physiological experiments reveal a single channel for nitrate uptake and nitrite transport by Escherichia coli NarU and a role for NirC in nitrite uptake. Biochemical Journal. In press.

Browning, D. F., Cole, J. A. and Busby, S. J. W. (2008) Regulation by nucleoid-associated proteins at the Escherichia coli nir operon promoter. J. Bacteriol. In press.

Clarke, T. A., Kemp, G. M., Wonderen, J. V., Cole, J, A., Cheeseman, M., Butt, J., Richardson, D. J. and Hemmings, A. M. (2008) Role of a conserved glutamine residue in tuning the catalytic activity of Escherichia coli cytochrome c nitrite reductase. Biochemistry 47: 3789-3799.

Cole, J. A. and Richardson, D. J. 18 August 2008, posting date. Chapter 3.2.5, Respiration of Nitrate and Nitrite. In A. BÃ¶ck, R. Curtiss III, J. B. Kaper, P. D. Karp, F. C. Neidhardt, T. NystrÃ¶m, J. M. Slauch, and C. L. Squires (ed.), EcoSal-Escherichia coli and Salmonella: cellular and molecular biology. http://www.ecosal.org. ASM Press, Washington, D.C.

Overton, T. W., Whitehead, R., Li, Y., Griffiths, L. and Cole, J. (2008) Sense and nonsense from whole genome microarray data in the analysis of microbial physiology. Biotechnologia 80: 15-30.

Hunt, D. M., Saldanha, J. W., Brennan, J. F., Benjamin, P., Strom, M., Cole, J. A., Spreadbury, C. L. and Buxton, R. S. (2008). Single nucleotide polymorphisms causing structural changes in the CRP transcriptional regulator of the TB vaccine strain Mycobacterium bovis BCG alter global gene expression without attenuating growth. Infection and Immunity 76: 2227-2234.

Hemmings, A., Richardson, D., Clarke, T., Butt, J., Cheesman, M., Cole, J., van Wonderen, J., Kemp, G., Doyle, R.-Marie., and Tovell, N. (2008) Role of a conserved glutamine residue in tuning the catalytic activity of Escherichia coli cytochrome c nitrite reductase. Biochemistry 47: 3789-3799.

Overton, T. A., Justino, M. C., Li, Y., Baptista, J. M., Ana Melo, M. P., Cole, J. A. and Saraiva, L. M. (2008) Widespread distribution in pathogenic bacteria of di-iron proteins that repair oxidative and nitrosative damage to iron-sulfur centers. Journal of Bacteriology 190: 2004-2013.

Clarke, T. A., Mills, P. C., Poock, S. R., Butt, J. N., Cheeseman, M. R., Cole, J. A., Hinton, J. C., Hemmings, A. M., Kemp, G., Soderberg, C., Spiro, S., Van Wonderen, J. and Richardson, D. J. (2008) Escherichia coli cytochrome c-nitrite reductase NrfA. Methods in Enzymology. 437: 63-77.

Clarke, T. A., Cole, J. A., Richardson, D. J. and Hemmings, A. M. (2007) The structure of the pentaheme c-type cytochrome NrfB and characterisation of its solution-state interaction with the pentaheme nitrite reductase, NrfA. Biochemical Journal 406: 19-30.

Filenko, N., Spiro, S., Browning, D., Squire, D., Overton, T., Cole, J. and Constantinidou, C. (2007) The NsrR regulon of Escherichia coli K-12 includes genes encoding the hybrid cluster protein and the periplasmic, respiratory nitrite reductase. Journal of Bacteriology 189: 4410-4417.

Whitehead, R. N. and Cole, J. A. (2006) Different responses to nitrate and nitrite by the model organism Escherichia coli and the human pathogen Neisseria gonorrhoeae. Biochemical Society Transactions 34: 111-114.

Jepson, B. J. N., Mohan, S., Clarke, T. A., Gates, A. J., Cole, J. A., Butler, C. S., Butt, J. N., Hemmings, A. M. and Richardson, D. J. (2007) Spectrophotometric and structural analysis of the periplasmic nitrate reductase from Escherichia coli. Journal of Biological Chemistry 282: 6425-6437.

Whitehead, R. N., Overton, T. W., Snyder, L. A. S., McGowan, S. J., Smith, H., Cole, J. A. and Saunders, N. J. (2007) The small FNR regulon of Neisseria gonorrhoeae: comparison with the larger E. coli FNR regulon and interaction with the NarQ-NarP regulon. BMC Genomics 8: 35.

Desvaux, M., Cooper, L. M., Filenko, N. A., Scott-Tucker, A., Turner, S. M., Cole, J. A. and Henderson, I. R. (2006). The unusual extended signal peptide region of the type V secretion system is phylogenetically restricted. FEMS Microbiology Letters 264: 22-30.

Overton, T., Whitehead, R., Li, Y., Snyder, L. A. S., Saunders, N. J., Smith, H. and Cole, J. A. (2006). Coordinated regulation of the Neisseria gonorrhoeae truncated denitrification pathway by the oxygen-sensitive repressor, NsrR, and nitrite-insensitive NarQ-NarP. Journal of Biological Chemistry 281: 33115-33126.

Browning, D. F., Grainger, D. C., Beatty, C. M., Wolfe, A. J., Cole, J. A. and Busby, S. J. W. (2006) The Escherichia coli K-12 NarL and NarP proteins insulate the nrf promoter from the effects of IHF. Journal of Bacteriology 188: 7449-7456.

Nilavongse, A., Brondijk, T. H. C., Overton, T. W., Richardson, D. J., Leach, E. and Cole, J. A. (2006) The NapF protein of the Escherichia coli periplasmic nitrate reductase system: demonstration of a cytoplasmic location and interaction with the catalytic subunit, NapA. Microbiology 152: 3227-3237.

Cole, J. A. (2006) Periplasmic nitrate reduction. In The Periplasm. M. Ehrmann, Ed. American Society for Microbiology. Chapter 14, pp 247-259. Washington DC. USA.

Mohan, S. B. and Cole, J. A. (2006) The dissimilatory reduction of nitrate to ammonia by anaerobic bacteria. In Biology of the Nitrogen Cycle. H. Boethe, S. Ferguson and W. Newton, Editors. Elsevier. Amsterdam. Pp 93-106.

Constantinidou, C. C., Hobman, J. L., Patel, M. D., Penn, C. W., Cole, J. A. and Overton, T. W. (2006) A reassessment of the fumarate and nitrate reduction regulon and transcriptomic analysis of the effects of nitrate, nitrite, NarXL and NarQP as Escherichia coli adapts from aerobic to anaerobic growth. Journal of Biological Chemistry 281: 4802-4808.

Overton, T. W., Griffiths, L., Patel, M. D., Hobman, J. L., Penn, C. W., Cole, J. A. and Constantinidou, C. (2006) Micro-array analysis of gene regulation by oxygen, nitrate, nitrite, FNR, NarL and NarP during anaerobic growth of E. coli: new insights into microbial physiology. Biochemical Society Transactions 34: 104-107.

Filenko, N.A., Browning, D. A. and Cole, J. A. (2005) Transcriptional regulation of a hybrid cluster (prismane) protein. Biochemical Society Transactions 33: 195-197.

Burlat, B., Gwyer, J. D., Poock, S., Cole, J. A., Hemmings, A. M., Cheeseman, M. R., Butt, J. N. and Richardson, D. J. (2005) Cytochrome c nitrite reductase: from structural to physico-chemical knowledge. Biochemical Society Transactions. 33: 137-140.

Jepson, B. J. N., Marietou, A., Mohan, S., Cole, J. A., Butler, C. S. and Richardson, D. J. (2006) Evolution of the soluble nitrate reductase: defining the monomeric periplasmic nitrate reductase subgroup. Biochemical Society Transactions 34: 122-126.

Jia, W. and Cole, J. A. (2005) Nitrate and nitrite transport in Escherichia coli. Biochemical Society Transactions 33: 159-161.

Marietou, A., Richardson, D., Cole, J. and Mohan, S. (2005) Nitrate reduction by Desulfovibrio desulfuricans: a periplasmic nitrate reductase that lacks NapB, but includes a unique tetraheme c-type cytochrome, NapM. FEMS Microbiology Letters 248: 217-225.

Elvers, K. T., Turner, S. M., Wainwright L. M., Marsden, G., Hinds, J., Cole, J. A., Poole, R. K., Penn, C. W. and Park, S. F. (2005) NssR, a member of the Crp-Fnr superfamily from Campylobacter jejuni, regulates a nitrosative stress-responsive regulon that includes both a single-domain and a truncated haemoglobin. Molecular Microbiology 57: 735-750.

Browning, D. F., Grainger, D. C., Beatty, C. M., Wolfe, A. J., Cole, J. A. and Busby, S. J. W. (2005) Integration of three signals at the Escherichia coli nrf promoter: a role for Fis protein in catabolite repression. Molecular Microbiology 57: 496-510.

Clegg, S., Jia, W. and Cole, J. A. (2006) Role of the Escherichia coli nitrate transport protein, NarU, in survival during severe nutrient starvation and slow growth.

Microbiology 152: 2091-2100.

Turner, S.M., Moir, J.W.B., Griffiths, L., Overton, T.W., Smith, H. and Cole, J.A. (2005) Mutational and biochemical analysis of cytochrome c2, a nitric oxide-binding lipoprotein important for adaptation of Neisseria gonorrhoeae to oxygen-limited growth. Biochemical Journal 388: 545-553.

Clarke, T., Dennison, V., Seward, H., Burlat, B., Cole, J. A., Hemmings, A. and Richardson, D. J. (2004) Purification and spectropotentiometric characterisation of Escherichia coli NrfB: a deca-heme homo-dimer that transfers electrons to a deca-heme periplasmic nitrite reductase complex. Journal of Biological Chemistry 279: 41333-41339.

Spreadbury, C. L., Pallen, M. J., Overton, T., Behr, M. A., Mostowy, S., Spiro, S., Busby, S. J. W. and Cole, J. A. (2005). Point mutations in the DNA- and cNMP-binding domains of the homologue of the cAMP receptor protein (CRP) in Mycobacterium bovis BCG: implications for the inactivation of a global regulator and strain attenuation. Microbiology 151: 547-556.

Mohan, S. B., Schmid, M., Jetten, M. and Cole, J. (2004). Detection and widespread distribution of the nrfA gene encoding nitrite reduction to ammonia, a short circuit in the Biological Nitrogen Cycle that competes with denitrification. FEMS Microbial Ecology 49: 433-443.

Lundberg, J. O., Weitzberg, E., Cole, J. A. and Benjamin, N. (2004) Nitrate, bacteria and human health. Nature Reviews Microbiology 2: 593-602.

Browning, D. F., Cole, J. A. and Busby, S. J. W. (2004) Transcription activation by remodelling of a nucleoprotein assembly: the role of NarL at the FNR-dependent Escherichia coli nir promoter. Molecular Microbiology 53: 203-215.

Brondijk, T. H. C., Nilavongse, A., Filenko, N., Richardson, D J., and Cole, J. A (2004) The NapGH components of the periplasmic nitrate reductase of Escherichia coli K-12: location, topology, and physiological roles in quinol oxidation and redox balancing. Biochemical Journal 379: 47-55.