Redox regulation of cell signalling

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SIR — We have been investigating the structural basis of the interaction between nitric oxide (NO) and the *ras* oncogene product p21 to gain insight into how redox signalling is achieved in cells. Our approach is one way to address the more general problem of finding a molecular target for redox-active environmental toxicants and free radicals. We report here that we have identified the site of molecular interaction between NO and $p21^{ras}$ that is responsible for the initiation of signal transduction.

In our earlier studies we found that a single *S*-nitrosylation event on full-length $p21^{ras}$ produced enhanced guanine nucleotide exchange[1]. Our present *in vitro* studies used $p21^{ras}$ lacking the carboxy-terminal 23 amino acids, as this form of the protein has identical biochemical activity to the wild-type enzyme[2]. To identify the exact site of *S*-nitrosylation, we cleaved $p21^{ras}$ with cyanogen bromide, which yielded three fragments, each containing one cysteine residue. Fragment 1, containing Cys 51, has a relative molecular mass (M_r) of 7,203; fragment 2, containing Cys 80, has M_r 4,540; and fragment 3, containing Cys 118, has M_r 6,225.