demonstrated that wild-type p53 markedly suppresses MRP promoter activity to downregulate gene expression in both human and mouse cell lines. Only one report in the literature indicates a lack of association between MRP and abnormal p53 in gastric cancer, but this study reported 100% positivity for MRP [8], so would have been insufficiently sensitive to detect interclonal variation. We also found that all AML samples, i.e. those with wild-type as well as mutant p53 express at least some MRP, indicating that p53 inhibition of MRP is incomplete.

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Response from T. Tokunaga *et al*.

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We thank J. Turzanski and colleagues for their interest in our recent paper [1,2]. There are distinct differences from our study in the estimation of associations between various drug-resistant proteins including multidrug resistance-associated protein (MRP), P-glycoprotein (Pgp), lung resistance protein (LRP) and Bcl-family members and alterations in *TP53*. They carefully studied such associations in clones from patients with acute myeloid leukaemia (AML). Whereas, we examined the expression of *MRP* mRNA in 104 non-small cell lung carcinomas by reverse transcription–polymerase chain reaction (RT–PCR) and determined that all these cancers express MRP mRNA. Thus, we agree with Turzanski and colleagues that wild-type p53 is insufficient to inhibit native MRP expression. Nooter and colleagues [3] have postulated that a ubiquitous low level expression of *MRP* in various tissues plays an essential role in cellular physiology. To detect interclonal variation in *MRP* gene expression, we used Northern blotting [4] and immunohistochemical analyses [2]. Flow cytometric analysis is inadequate for solid tumour specimens that inevitably contain stromal tissues but contrastingly is a suitable and quantitative method for the analysis of single cell populations such as blood clones or clonogenic cancer cell lines. Turzanski and colleagues' results on the overexpression of MRP proteins associated with mutations of the *TP53* gene were convincing and encouraged us.

They additionally state that the expression of Pgp in acute leukaemia cells showed significant association with mutant *TP53*. We reviewed the association between Pgp overexpression and mutation of the *TP53* gene in 107 non-small cell lung cancers, 54 colorectal cancers, 30 osteosarcomas and 64 brain tumours. Regretfully, we did not confirm any significant association between them in any type of tumour. We previously reported that Pgp overexpression is related to acquired multidrug resistance in non-small cell lung cancer and osteosarcoma cell lines *in vivo*, whilst no marked overexpression was found in the expression of MRP protein [5,6]. These results suggest that alteration of MRP expression is probably found in cases with acquired *TP53* mutations.

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Transfection of the wild-type *TP53* gene into human leukaemia cells results in an alteration in the expression level of the *MRP* gene [7]. We are now studying whether the introduction of wild-type *TP53* into lung cancer cell lines can reverse multidrug resistance. Further studies are required to explain the mechanism by which p53 alters *MRP* gene expression.

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