



FIG. 2 *a*, *In situ* analysis of the expression of the gene *MTCEK1* in intestinal epithelia of non-transgenic (left) and transgenic (right) mice. *b*, Protective effect of the cysteine biosynthetic pathway on diet-induced hair loss in mice. Age-matched non-transgenic (top) and transgenic (bottom) mice were placed on a synthetic diet in which the combined sulphur amino acids were reduced to 0.1% (w/w) of the total diet, but supplemented with 0.12% (w/w) Na_2S . Throughout the experiment, the drinking water of the mice was supplemented with 25 mM ZnSO_4 . Photographs were taken after 7 days. Hair loss was observed in the non-transgenic mice but not in the transgenic animals.

The gene *pMTCEK1* (ref. 5), which encodes the enzymes serine acetyl transferase and *O*-acetylserine sulphhydrylase, was transferred to transgenic mice by conventional microinjection⁶, breeding lines were established and expression of the transgene was demonstrated by northern blots and enzyme analyses. The pre-

sence of a functional biosynthetic pathway was confirmed by incubating dissected intestinal tissue with radioactive Na_2S and examining the synthesized amino acids. The results demonstrate a substantial peak of radioactivity in transgenic tissue incubations in the position at which cysteine (measured as cysteic acid) migrates (Fig. 1).

The expression of the *MTCEK1* gene in the intestinal epithelium of the transgenic mice was verified by an *in situ* analysis using an antisense bacterial *cysE* sequence RNA probe (Fig. 2*a*). The *cysE* mRNA could only be detected in the cells of intestinal epithelia from the transgenic mice.

The operation of the new biochemical pathway *in vivo* was demonstrated by placing the transgenic and control mice on a synthetic diet deficient in sulphur-containing amino acids but supplemented with Na_2S (refs 7, 8). Control mice showed either an extensive hair loss on the back and sides (three mice) or a marked 'dishevelled' quality in their coats (nine mice). On the other hand, all the transgenic mice (14) retained a normal hair coat with no sign of hair loss or change in coat quality. A comparison of a transgenic and a control mouse is shown in Fig. 2*b*. Because the hair loss in the controls could be reversed by supplementation of the diet with sulphur amino acids, we interpret our observations as indicating that the operation of the cysteine biosynthetic pathway in the transgenic mice has provided these animals with sufficient cysteine to prevent the diet-induced hair loss.

These results demonstrate that a functional biochemical pathway can be transferred from bacteria to mammals, can use endogenous substrates and co-factors for its effective operation and is capable of preventing some of the phenotypic effects associated with specific nutrient deprivation.

Further details of these results are

available on request from the authors and will be published in detail elsewhere.

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Smokeless fire

SIR — Summerlin¹ objects, in Scientific Correspondence, to the suggestion by Rodu and Cole² that smokers switch to using smokeless tobacco as a habit that would be significantly less harmful to them than active smoking. Summerlin bases his objection on the risk to users.

But smokers are not the only patients to whom health-care providers have responsibilities. Wells, in the most recent quantification of deaths due to second-hand smoking³, suggests "that in 1985 an estimated 62,000 ischemic heart disease deaths in the United States were associated with exposure to environmental tobacco smoke". He had previously estimated⁴ that in the same year 3,000 lung-cancer patients and 11,000 patients with "other cancers" died in the United States because of second-hand smoking. That is a grand total of 76,000 estimated deaths, rather than 30,000 estimated cases of oral cancer.

A massive shift towards the use of oral tobacco by smokers would considerably cut the tens of thousands of deaths caused by tobacco-smoke pollution. On balance, it would seem that health-care providers owe more to their non-smoking patients than is owed to active smokers who might choose to switch to oral tobacco.

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Scientific Correspondence

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