Sequence curiosity in v-*myc* oncogene

SIR—The DNA sequences of three avian acute transforming retroviruses that contain the v-*myc* oncogene[1-3] as well as the sequence of the chicken proto-*myc* gene[4] have recently been reported. We have now noticed that there is a codon where as a result of adjacent mutations, none of the three viral sequences codes for the amino acid residue that is coded for by the cellular proto-*myc* gene. This is position 61 numbered from the first ATG in chicken exon 2 (Fig. 1). Position 61 and its neighbours are conserved among proto-*myc* genes from chicken[4], human[5], mouse[6], and fish (R. Van Beneden, D. Watson and T. S. P., unpublished data).

Due to the relatively low number of amino acid differences between the viral and chicken *myc* sequences, it is rather unlikely that this has occurred by chance alone. Counting from the first ATG in exon 2, the chicken proto-*myc* locus codes for 416 amino acid residues. The number of amino acid substitutions between viral and chicken proto-*myc* is 7, 27, and 2 for MC29[1], MH2[2] and OK10[3], respectively.

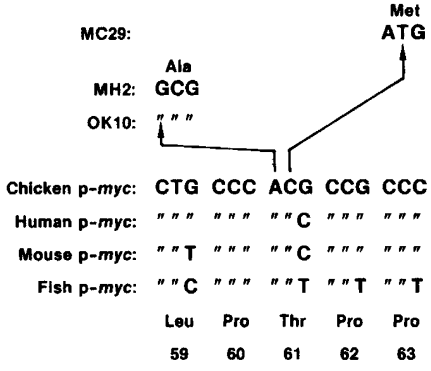

Fig. 1. Sequences of a segment of the *myc* gene from avian retroviruses and animal cells. The references for the sequences are given in the text. Except where noted, the viral sequences are identical to the chicken p-*myc* sequence for the segment shown. The codons are numbered from the first initiation codon in the second exon of chicken.

We calculate that there would be only one chance in 458 that all three viral sequences contain an amino acid substitution at a common position if the substitutions occurred randomly. We suggest as a possible explanation of this observation that substitutions at position 61 might lead to an increase in the oncogenic potential of the virus and thus would give the transformed cells a growth advantage.

We are currently evaluating this hypothesis by altering viral v-*myc* and animal proto-*myc* genes by site specific mutagenesis to determine if substitutions at position 61 indeed modulate oncogenic potential.

The occurrence of substitutions at a common location in the viral *myc* genes may be analogous to the findings in many laboratories that codon 12 of a *ras* gene is altered in viruses that contain *ras* sequences and in tumour DNAs that are capable of transforming NIH 3T3 cells (see ref. 7 for review). While each of the three viruses that contain the *ras* gene differ from the normal sequence by a G to A transition in the first position of codon 12, the mutations in transforming tumor DNAs occur in either the first or second position. For example, the first position of codon 12 of the c-Ha-*ras1* allele of rat is altered in Harvey murine sarcoma virus and Rasheed rat sarcoma virus while the second position in this codon is altered in rat mammary carcinomas induced by nitrosomethylurea. Similarly, the human c-Ki-*ras2* allele was found to be altered in the first position in a human lung carcinoma cell line and in the second position in a human colon carcinoma cell line.

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1. Reddy, E. P. *et al. Proc. natn. Acad. Sci. U.S.A.* **80,** 2500-2504 (1983).
2. Kan, N. C., Flordellis, C. S., Mark, G. E., Duesberg, P. H. & Papas, T. S. *Proc. natn. Acad. Sci. U.S.A.* **81,** 3000-3004 (1984).
3. Hayflick, J. *et al. Proc. natn. Acad. Sci. U.S.A.* **82,** 2718-2722 (1985).
4. Watson, D. K., Reddy, E. P., Duesberg, P. H. & Papas, T. S. *Proc. natn. Acad. Sci. U.S.A.* **80,** 2146-2150 (1983).
5. Watson, D. K., Psallidopoulos, M. C., Samuel, K. P., Dalla-Favera, R. & Papas, T. S. *Proc. natn. Acad. Sci. U.S.A.* **80,** 3642-3645 (1983).
6. Bernard, O., Cory, S., Gerondakis, S., Webb, E. & Adams, J. M. *EMBO J.* **2,** 2375-2383 (1983).
7. Varmus, H. E. *A. Rev. Genet.* **18,** 553-612 (1984).

Interferon and micRNA in cellular defence

SIR—Recently Coleman *et al.*[1] in a letter to *Nature*, proposed an original artificial micRNA (antisense RNA) system to prevent bacteriophage infection in *Escherichia coli*. A micRNA system has already been successfully used in mammalian cells[2] and micRNAs have been demonstrated to constitute normal prokaryotic mechanisms of regulation of gene expression at the translation level[3,4]. The frequent finding in viral genomes of sequences transducted from the cellular genome makes attractive the hypothesis that the endogenous anti-sense transcription active in genetic regulation may also operate in some viral infections. We should like to suggest a link between micRNA and the interferon system of defence against viral infections.

Interferon induction requires virus penetration; either single or double stranded viral RNA constitutes the critical factor in triggering the induction process. The activation of the cellular antiviral state by interferons involves complex mechanisms, as yet poorly understood, but it is now well established that a crucial step in the activation mechanisms is the presence of double-stranded RNA (dsRNA)[5]. dsRNA acts both as an affinity reagent and an activator for an enzymatic activity designated (2′–5′) A polymerase which in turn activates an endonuclease, resulting in preferential cleavage of viral mRNA[5].

Thus dsRNA is deeply involved both in the interferon induction and in the cellular metabolic pathways activated by interferon. This is a key point for our suggestion, that, upon virus infection and exposure to viral nucleic acids, the cell synthesizes micRNAs that are not only able to repress the translation of viral gene transcripts by binding to them but also thereby to constitute some of the dsRNAs that are involved both in interferon induction and in the cellular metabolic pathways activated by interferon.

Hybrids of a viral mRNA and an anti-mRNA in a partially double-stranded structure may also be preferentially cleaved by cellular enzymes which would account for the still unexplained discrimination between cleavage of cellular and viral mRNAs in interferon treated cells.

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1. Coleman, J. Hirashima, A. Inokuchi, Y. Green, P.J. & Inouye, N. *Nature* **315,** 601–603. (1985).
2. Izant, J.C. & Weintraub, H. *Cell* **36,** 1007–1015 (1984).
3. Mizuno, T. Chou, M.Y. Inouye, M. *Proc. natn. Acad. Sci. U.S.A.* **81,** 1966–1970 (1984).
4. Pestka, S. Daugherty, B.L. Jung, V. Hotta, K. & Pestka, R.K. *Proc. natn. Acad. Sci. U.S.A.* **81,** 7525–7528 (1984).
5. Nilsen, T.W. & Baglioni, C. *Proc. natn. Acad. Sci. U.S.A.* **76,** 2600–2604 (1979).

Non-repellent bird droppings

SIR—I would like to propose an alternative explanation for the observation reported by L. Roodyn (*Nature* **317,** 581) that after rain, bird droppings on the roof of his car were surrounded by a dry zone, while large drops of water were scattered about the rest of the surface.

He suggested a water repellent substance in the droppings. I suggest just the opposite.

Droppings contain a detergent (perhaps bile salts), so rain falling on the droppings spreads over the surrounding roof in a thin film, which evaporates rapidly. Meanwhile, rain falling on other parts of the water-repellent roof (perhaps treated with silicone wax) forms rounded droplets with low surface area in relation to volume, and therefore takes longer to evaporate. Thus the water-repellent area is the wet one, not the dry one.

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