Table 1. Base pairing between RNAs

(1)*5′ UCUUCCGUGG 3′†	(1′) 5′ ACGGGGG 3′
3′ GGAAGGCGUC 5′‡	3′ UGCCUUU 5′‡
(2) 5′ CGA^{A} CCCA 3′	(3) 5′ UACCG 3′
3′ CGU$_{C}$ GGGU 5′	3′ AUG|GC 5′
| §	
(4) 5′ GAUCC 3′	(5) 5′ CGAAC 3′
3′ CUAGG 5′	3′ GCΨTG 5′

* Numbers correspond to those in Fig. 1.

† In each pairing, the upper strand shows a part of the sequence of VA RNA$_I$ and the lower strand shows a part of the sequence of 18 S rRNA (1, 1′), the junction of the first and second leader sequences (2), the junction of the second and third leader sequences (3), the T-loop of initiator tRNA (4), or the T-loop of elongator tRNA (5).

‡ These sequences are complementary to each other, and might make a stem of hairpin structure at the 3′-end of 18 S rRNA.

§ The vertical bars show the junctions of the spliced tripartite leader sequence (2, 3).

Fig. 1 and Table 1]. The junction of the first and second leader sequence has seven complementary nucleotides out of eight to the nucleotides of the loop and the stem terminus. The junction of the second and third leader has five consecutive nucleotides that are complementary to the nucleotides of the relevant loop. Therefore, binding of VA RNA$_I$ to the tripartite leader sequence of the late mRNA is also possible. Another notable sequence is 5′ GAUCC 3′, in the stem of VA RNA$_I$ (2 mol/mol), which occurs in the neighbourhood of the loops [(4) in Fig. 1]. This sequence is complementary to the 5′ GGAUC 3′ sequence of the TΨC-loop of mammalian initiator tRNAs. The nucleotides in the D-loop may also contribute to the binding of the initiator tRNA to mRNA (Ganoza *et al.*, 1985). Therefore, binding of the tRNA to VA RNA$_I$ as well as to mRNA should also be possible. Additionally, the 5′ CGAAC 3′ sequence included in region B [(5) in Fig. 1], which corresponds to one of the promoter sequences for VA RNA$_I$ (Fowlkes & Shenk, 1980), is complementary to the 5′ GTΨCG 3′ sequence in the elongator tRNAs. The elongator tRNA which is bound adjacent to the initiator tRNA may possibly also bind to both mRNA and VA RNA$_I$. In the case of VA RNA$_{II}$, it has only two complementary sequences for the junction of leader 1 and 2, and for TΨCG.

The initiation complex proposed here involves the 18 S rRNA of the smaller ribosomal subunit which binds VA RNA$_I$, VA RNA$_I$ which binds the tripartite leader sequence, and initiator tRNA which binds to both VA RNA$_I$ and to the initiation codon of mRNA. The next elongator tRNA may also bind both VA RNA$_I$ and mRNA. It is plausible that the sequences that are complementary to the junctions of the tripartite leader sequence, 18 S rRNA, initiator tRNA, or elongator tRNA, are in the single-stranded loops, in the stem termini near the loops, or near the 3′- or 5′-terminus when VA RNA$_I$ is in its proposed conformation in solution (Monstein & Philipson, 1981). When protein synthesis begins and a short peptide is made, the tripartite leader may leave the first ribosome and may find a different one. The complex of mRNA with VA RNA$_I$ should not be so stable that it freezes the ribosome. The sequence at the junction of the second leader and third leader sequences is the same as the second leader terminal region (5′ CGGUA 3′) in the absence of splicing. However, when normal splicing does not occur, the length of the RNA chain between the second leader sequence and the initiation codon may be too long to allow formation of the stable initiation complex. In fact, the spacing and even nucleotide sequence between the sequence proposed by Shine & Dalgarno and the initiation codon greatly affect the efficiency of protein synthesis in *Escherichia coli* (Shepard *et al.*, 1982; DeBoer *et al.*, 1983).

Experimental investigations to determine whether the specific interactions of RNAs described herein are functional are obviously possible and involve the substitutions of nucleotides in VA RNA$_I$ or in the tripartite leader sequence, or the inhibition of protein synthesis by oligonucleotides complementary to the relevant sequences of VA RNA$_I$ or of the tripartite leader.

Akira MURASUGI

Meiji Institute of Health Science, 540 Naruda, Odawara 250, Japan

DeBoer, H. A., Hui, A., Comstock, L. J., Wong, E. & Vasser, M. (1983) DNA **2**, 231–235

DeWachter, R. (1979) Nucleic Acids Res. **7**, 2045–2054

Fowlkes, D. M. & Shenk, T. (1980) Cell **22**, 405–413

Ganoza, M. C., Marliere, P., Kofoid, E. C. & Louis, B. G. (1985) Proc. Natl. Acad. Sci. U.S.A. **82**, 4587–4591

Kaufman, R. J. (1985) Proc. Natl. Acad. Sci. U.S.A. **82**, 689–693

Kitajewski, J., Schneider, R. J., Safer, B., Munemitsu, S. M., Samuel, C. E., Thimmappaya, B. & Shenk, T. (1986) Cell **45**, 195–200

Logan, J. & Shenk, T. (1984) Proc. Natl. Acad. Sci. U.S.A. **81**, 3655–3659

Mathews, M. B. (1980) Nature (London) **285**, 575–577

Monstein, H.-J. & Phillipson, L. (1981) Nucleic Acids Res. **9**, 4239–4250

Schneider, R. J., Weinberger, C. & Shenk, T. (1984) Cell **37**, 291–298

Shepard, H. M., Yelverton, E. & Goeddel, D. V. (1982) DNA **1**, 125–131

Shine, J. & Dalgarno, I. (1975) Nature (London) **254**, 34–38

Steitz, J. A., Wahba, A. J., Laughrea, M. & Moore, P. B. (1977) Nucleic Acids Res. **4**, 1–16

Wong, G. G., Witek, J. S., Temple, P. A., Wilkens, K. M., Leary, A. C., Luxenberg, D. P., Jones, S. S., Brown, E. L., Kay, R. M., Orr, E. C., Shoemaker, C. S., Golde, D. W., Kaufman, R. J., Hewick, R. M., Wang, E. A. & Clark, S. C. (1985) Science **228**, 810–815

Received 23 January 1989

The human *reg* gene encodes pancreatic stone protein

Terazono *et al.* [1] recently described the cloning and sequencing of a cDNA apparently derived from pancreatic islets following partial pancreatectomy. On the basis of its induction during regrowth of the pancreas and its apparent origin from islets the corresponding gene was termed *reg* (for regeneration) with the implication that the gene was involved in islet regeneration.

On searching the Dayhoff protein database with the translated sequence of the human homologue [1] it

became obvious that human *reg* encodes pancreatic stone protein. Pancreatic stone protein (PSP) has been reported to be the major constituent of pancreatic stones taken from patients with chronic calcifying pancreatitis and may account for 10% of the total protein in normal exocrine pancreas secretions [2]. This protein was purified and partially sequenced in 1986 [2] and completely sequenced in 1987 [3]. It has been previously reported that pancreatic stone protein has sequence similarity to animal lectins [4] and human thrombomodulin [5].

The *reg* gene, as sequenced, encodes for a protein with an *N*-terminal extension of 32 amino acids as compared to the form of PSP sequenced by De Caro *et al.* [3]. It was argued that this form, PSP S1, was generated from a longer form, PSP S2-5, by extracellular proteolytic cleavage. On the basis of the gene sequence [1], it was argued that there is a 21-amino-acid signal sequence. It is possible that the signal sequence is in fact 32 amino acids long; alternatively the 11 amino acids remaining could be removed by further processing.

Although the synthesis of PSP (encoded by *reg*) by acinar cells does not rule out its involvement in islet regeneration, more investigation of its function is required before this can be assumed.

Timothy A. STEWART

Developmental Biology, Genetech Inc.,
460 Point San Bruno Boulevard,
South San Francisco, CA 94080, U.S.A.

1. Terazono, K., Yamamoto, H., Takasawa, S., Shiga, K., Yonemura, Y., Tochino, Y. & Okamoto, H. (1988) J. Biol. Chem. **263**, 2111–2114
2. Montalto, G., Bonicel, J., Multigner, L., Rovery, M., Sarles, H. & De Caro, A. (1986) Biochem. J. **238**, 227–232
3. De Caro, A. M., Bonicel, J. J., Rouimi, P., De Caro, J. D., Sarles, H. & Rovery, M. (1987) Eur. J. Biochem. **168**, 201–207
4. Patthy, L. (1988) Biochem. J. **253**, 309–311
5. Petersen, T. E. (1988) FEBS Lett. **231**, 51–53

Received 13 March 1989

Normal plasma vitamin E concentration

After reading a recent article in this journal [1] I wish to point out the erroneous statement concerning 'normal plasma vitamin E concentration' in the Discussion section. Numerous surveys on human populations who did not take vitamin E supplements showed the mean value of plasma tocopherol determined from 36 different studies to be around 0.9 mg/dl or 21 μM, with a range of 0.36–1.23 mg/dl or 8–28 μM [2]. Hence the concentration used (230 μM) in [1] is more than 10 times the 'normal' tocopherol value in plasma. Indeed, even with high oral vitamin E supplementation, plasma vitamin E could be expected to double or at best triple due to regulation of absorption [3].

Alvin C. CHAN

Department of Biochemistry, School of Medicine,
University of Ottawa, 451 Smyth, Ottawa,
Ontario, Canada K1H 8M5

1. Phoenix, J., Edwards, R. H. T. & Jackson, M. J. (1989) Biochem. J. **257**, 207–213
2. Farrell, P. M. (1980) in Vitamin E: a Comprehensive Treatise (Machlin, L. J., ed.), pp. 520–620, Marcel Dekker, New York.
3. Losowsky, M. S. *et al.* (1972) Ann. N.Y. Acad. Sci. **203**, 212–222

Received 15 February 1989