

from a sub-clone of M β G2, is a 230-base pair fragment which extends from a *Bam*HI site at amino acid codon 99 to a *Hind*III site near the middle of the intervening sequence; this probe (designated IVS-A) contains the most distal 18 base pairs of the 5' coding sequence and the proximal 220 base pairs of the intervening sequence. The second probe depicted in Fig. 1, a *Bam*HI to *Pst*I fragment of approximately 600 base pairs (designated IVS-B), also contains the distal 18 base pairs of the 5' coding sequence but extends through the intervening sequence to within 75 base pairs of the 3' coding sequence. The third probe, an approximately 1,500-base pair *Bam*HI to *Xba*I fragment (designated IVS-C) contains in addition to the distal 18 base pairs of the 5' coding sequence, the entire intervening sequence, 3' coding sequence, 3' transcribed but untranslated region, and approximately 600 base pairs of genomic flanking sequence.

To identify sequences in the mouse genome homologous to these probes, murine embryonic DNA was purified, fragmented with *Eco*RI and fractionated by RPC-5 column chromatography. Aliquots from the RPC-5 fractions were electrophoresed, blotted on to nitrocellulose paper and then annealed to a ³²P-labelled probe^{16,20}. The results of hybridisations with the three probes are shown in the third (IVS-A), fourth (IVS-B) and fifth (IVS-C) panels of Fig. 2. The identical appearance of these three panels is notable, as is their identity with the second panel (β -globin), where the probe was the ³²P-labelled β -globin structural gene sequence cloned in plasmid pCR1 (ref. 21). The two discrete bands observed with the β -globin structural sequence as probe (and hence, those bands in the same positions in the IVS-A, IVS-B and IVS-C hybridisations) represent the two non-allelic β -globin genes: the upper, less intense band is the 13-kilobase β^{min} (M β G3); the lower, more intense band, the 7-kilobase β^{maj} (M β G2). The last panel (α -globin) demonstrates the band pattern of mouse α -globin sequences; in this experiment, the probe was the ³²-labelled α -globin structural gene sequence cloned in pCR1 (ref. 21). Note that three α -globin genes are detected and that there is no homology between any of these and the β^{maj} probes (compare IVS-A, B and C to α -globin). The top panel (EtBr) does not depict an autoradiogram but is simply an example of a gel strained with ethidium bromide and photographed before blotting and hybridisation; note the large amounts of DNA of heterogeneous size in each RPC-5 fraction, each lane containing of the order of 10⁴ genomic fragments.

Before drawing conclusions from the above experiments, we should consider the ability of our probes to detect homologous sequences. From a comparison of the partial sequences of M β G2 (β^{maj}) and M β G3 (β^{min}) as well as heteroduplex studies, we are certain of at least 50 base pairs of homology between probes IVS-A or IVS-B and β^{min} (ref. 16; D.A.K., unpublished data); it is evident from Fig. 2 that this degree of hybridisation is detected. We know, however, from unrelated experiments, that IVS-A barely detects an 18-base pair homologous sequence (H.I.M., unpublished data). The minimum size of homologous sequences resolved in these experiments is, therefore, approximately 20–50 base pairs.

We conclude that the long intervening sequence of the mouse β^{maj} gene shares detectable homology in the mouse genome with only the β^{min} gene. We cannot rule out short sequences which might be more widely shared among intervening sequences and serve as recognition sites for processing. It is possible that rather than similarity or identity of primary sequence, there are within the intervening sequences characteristic conformations conferred on the mRNA precursors by secondary and tertiary structures. Alternatively, the sequences surrounding the intervening sequence may provide the specificity required for the elimination reaction. Such a possibility is especially suggested by what is known of yeast tRNA intervening sequences^{12,17}. These differ among tRNA precursors, whereas the conformations of the tRNA molecules themselves are probably quite similar. Further, recent evidence involving a portion of a putative intervening sequence in the chicken ovalbumin gene suggests that it is

present only in the ovalbumin gene¹⁸. Ultimately, a comparison of the structure of all these elements should permit us to define the critical features required for splicing.

Note added in proof: We have recently determined the entire nucleotide sequence of the mouse β -globin major gene (Konkel *et al. Cell*, in the press) and find short closely homologous sequences at the borders of both small and large intervening sequences.

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Errata

In the article 'The tau heavy lepton—a recently discovered elementary particle' by M. L. Perl, *Nature* **275**, 273–278, in line 6 on page 274 for reaction (2) read reaction (3). In line 13 for equation (1) read equation (2).

In the letter 'Viral sequences related to a human skin papillomavirus in genital warts' by G. Orth *et al.*, *Nature* **275**, 334–336, on page 335 right-hand column line 6 should read ... are close to those ...

The title to the letter by Jones, Kindman and Knowles, *Nature* **275**, 564, should read: 'Stereochemistry of phosphoryl group transfer using a chiral [¹⁶O, ¹⁷O, ¹⁸O] phosphate monoester: the stereochemical course of alkaline phosphatase'.