stand how processed material can be mixed up from the hydrogen-burning region to the surface of low mass stars by means of meridional circulation.

No consensus now seems possible on the meaning (or, in some cases, even the reality) of colour and abundance gradients within clusters other than ω Cen (K. Freeman; M. Chun; G. Da Costa). The question of whether or not the absolute brightnesses of RR Lyrae variables are correlated with their metal abundances is 'controversial.' It is important because these stars are one of our standard candles, whose brightness partially determines the extragalactic distance scale, and so Hubble's constant and the age of the Universe. W. Liller and V. Clube strongly advocated a relationship (partially based on recent photometry by B. Carney) in which the RR Lyraes in clusters of lowest metal abundance are about one magnitude fainter than those in clusters of high Z. A constant brightness for these stars, independent of cluster composition, was equally strongly supported on both observational and theoretical grounds by P. Demarque, R. Kraft, and F. Hartwick.

The various problems of globular cluster astronomy are probably in as good shape as we can expect, considering that (although some of the clusters were recorded by Messier) the first classification of them by radius and central concentration was begun only about 50 years ago by H. Sawyer Hogg, who was an active participant at the Institute. □

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# Bacterial gene into monkey cells

*from John Jenkins*

One of the long term aims of genetic engineering recently came a step closer to reality, with the stable propagation in mammalian cells of a hybrid DNA molecule containing a mammalian tumour virus chromosome and a bacterial gene. The successful development of such vectors for introducing and propagating genes in mammalian cells offers the hope of eventually being able to study the control of expression of eukaryotic genes in a system not too far removed from their natural environment. Even further in the future is the possibility of using such vectors to introduce particular genes to correct inborn genetic defects.

The idea itself is not new. In 1972, Jackson *et al.* (*Proc. natn. Acad. Sci. U.S.A.* **73,** 2904; 1972) described the construction of a hybrid molecule from simian virus 40 (SV40) and bacteriophage λ DNA, and such hybrids can replicate in suitable host cells (Ganem *et al. Cell* **7**, 349; 1976). The problem is that replication of the hybrid virus kills the host. A new development gets round this problem by tailoring or 'crippling' the SV40 so that the genes responsible for cell death are cut out before the hybrid is made.

SV40 can behave in two different ways when it infects a cell, and its genome can be divided into two regions on this basis. In rat cells, the entire virus genome is inserted into the host chromosome and the cells change many of their growth characteristics. This transformation requires the expression of only about half the SV40 genome making up what is known as the early region. The second type of infection, of monkey cells for instance, requires expression of most of the genome. In this case, the remainder of the viral genes are functionally expressed and about 36 h after infection mature virus particles appear, followed by the lysis of the host cells. Cell types that support this lytic cycle of infection are termed permissive, while those which transform but fail to produce mature virus are called nonpermissive.

In order to cut out the genes responsible for lytic infection, (Hamer *et al. J. molec. Biol.* **112,** 155; 1977) cleaved the circular virus DNA at two points within the late region, using the restriction enzymes *Hpa*II and *Eco*RI. The large fragment from this, containing the origin of DNA replication and the early region genes, was ligated to a DNA fragment containing an *E. coli* tRNA suppressor gene. In order to get large amounts of the hybrid DNA it was necessary to first grow it up in monkey cells in the presence of a helper virus which possessed functional late region genes. Purified hybrid DNA from this lytic cycle was then used in the present series of experiments (Upcroft *et al. Proc. natn. Acad. Sci. U.S.A.* **75,** 2117; 1978).

The hybrid DNA was found to transform nonpermissive rat cells, and analysis of total cellular DNA from infected cultures showed the presence of about three copies of non-integrated hybrid genome per cell. Some copies might have integrated with the host DNA and been maintained as such but the evidence for this was not conclusive. Infected monkey cells, which with wild type SV40 support the production of mature virus, were found to contain amounts of nonintegrated, superhelical hybrid DNA which was stably propagated when the cells were cloned.

There are several advantages to this system of nonlytic propagation using a crippled vector. First, the recombinant DNA is never expressed as an infectious virus particle simply because it does not possess the necessary genes. This satisfies some of the safety considerations involved in this type of work. Second, since assembly of a complete particle is not needed, the amount of DNA that can be 'carried' on the SV40 vector is probably increased, and third, the host cells remain viable, which offers the chance of long term studies on the maintenance and expression of 'foreign' DNA sequences in a mammalian system.

Hamer *et al.* looked for expression of the bacterial gene in the original lytic infection and found that although the sequence was transcribed into RNA, no functional supressor tRNA was detectable. This is not surprising in view of the different types of processing of tRNA that probably take place in bacterial and eukaryotic cells (Knapp *et al. Cell* **14,** 221; 1978; O'Farrell *et al. Nature,* **274,** 438; 1978). This may not be a problem when the gene 'insert' is from a more closely related donor. Rumour has it that correct transcription and expression of globin genes cloned in an SV40 vector in mammalian cells has been achieved in Paul Berg's laboratory at Stanford.

There are a variety of sequences that could usefully be worked on in a system of this kind, but many of them will probably have to wait until more has been done to reduce the possible hazards of working with a tumour virus. The vector in these experiments could still transform cells, and it may be necessary to remove this ability before the SV40 is sufficiently 'crippled' to use with genes that might confer a selective advantage on the hybrids.

Other routes exist for getting genes into mammalian cells, for example, by cell fusion and selection (Szybalski *et al. Natn. Cancer Inst. Monogr.* **7,** 75; 1962; Littlefield *Science,* **145,** 709; 1964) and such genes may be expressed in adult animals (Illmensee *et al. Proc. natn. Acad. Sci. U.S.A.* **75,** 1914; 1978). But in terms of simplicity and flexibility the tumour virus vector could be a winner. □

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