transformation (Table 1). This effect can be achieved by either homologous mouse type C replicating viruses or heterologous viruses capable of replicating in such cells (*8*).

The increased levels of Moloney sarcoma specific RNA might be achieved by increased rates of transcription of the MSV genome or decreased rates of degradation of the sarcoma specific RNA. In addition, as a secondary effect, increases of sarcoma RNA may occur by gene amplification of the MSV genome. Within an S+L− mink cell infected with helper virus the presence of helper virus reverse transcriptase may increase the copy number of integrated MSV or the pseudotype MSV rescued by helper virus may be superinfecting surrounding S+L− mink cells and thereby increase the copy number.

Whatever the molecular explanation, the results observed in cells exogenously infected with Moloney sarcoma virus and superinfected with the replicating type C viruses suggests a hypothesis concerning a similar possible phenomenon in cells that might be carrying latent oncogenic information not acquired by exogenous infection. Thus, it is possible that a usually nontransforming type C virus might act in vivo in a similar manner by leading to an increase in RNA from potentially oncogenic normal cellular or viral genomes during the replication of the nontransforming type C virus. Such a model would predict that some forms of leukemia or lymphoma caused by type C viruses (particularly those characterized by a long latent period and involving replicating but nontransforming viruses) might be due to effects on the levels of RNA of cellular genes by the replicating type C viruses rather than to a direct effect of a transforming gene of the viruses themselves on the growth potential of the cell.

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On Competitive Innervation of Goldfish Eye Muscles

The report by Scott (*1*), appears to contradict the conclusions we drew from similar experiments published in 1970 and 1972 (*2–4*). If her interpretation is correct, Scott's result would also throw doubt on other experiments on competitive reinnervation done by us (*5*), as well as on similar experiments she cites, done by others.

The question is whether the function of regenerated foreign nerve terminals in a multiply innervated striated muscle can be repressed when the muscle accepts further regenerating synapses from its embryologically appropriate nerve. When Scott repeated our procedure on goldfish eye muscles she observed behavioral repression of the function of foreign nerves supplying the superior oblique muscle in about the same proportion of cases we did, about one third of the animals. The behavioral test involves measurement of static ocular counterrotation in response to tilting the whole animal head up and head down. In Scott's experiment, electrical stimulation of both appropriate and inappropriate nerve trunks resulted in strong contraction of the superior oblique muscle, in apparent refutation of our conclusion that the foreign innervation had become ineffective in causing muscle contraction.

Regeneration of the antagonistic inferior oblique muscle is a problem in these experiments, as Scott points out. The behavioral method we used, however, can detect defects in coordination due to simultaneous contraction of antagonists (*3*, p. 139), and this cannot explain our results. We also checked all fish by dissection for regenerated muscles and found them in only two cases (*2*, p. 47; *4*, p. 153).

Why then should tests of innervation by the use of natural reflex activation of the oculomotor system give results that are incompatible with those from tests by electrical stimulation of motor nerves? We think it likely that the discrepancy arises because static vestibulo-ocular reflexes and direct electrical stimulation of muscle nerves in fact test the function of two separate classes of muscle fibers.

In a recent paper (*6*), we have described two patterns of innervation corresponding to the two kinds of muscle fibers found in these muscles. The larger fibers, comprising the bulk of the oblique muscles (*7*), have elongated nerve endings that come from a small number of parent nerve fibers and spiral round the fiber almost from one end to the other. These muscle fibers would contract almost synchronously along their whole length when an action potential was propagated along the extended nerve ending, and they appear to be designed to produce strong and rapid contractions. The smaller fibers, whose ultrastructure suggests that they are involved in tonic contraction, are very densely multiply innervated by nerve fibers that run transversely across the muscle fibers at intervals of about 50 μm and supply a nerve terminal to each one they cross.

It is now known that the static ocular reflexes are a function of the smaller tonic muscle fibers (*8*). In a test of innervation by electrical stimulation of the nerve trunk, however, the bulk of the muscle tension would come from the larger muscle fibers. Large fibers will also be the main contributors to any sample of junctional activity gathered by an intracellular microelectrode because they are easier to penetrate and hold. The majority of small muscle fibers are 5 μm or less in diameter, and it must be very hard to record from inside them.

If the above is true, Scott's results may mean that there is selective competitive innervation of the population of small, multiply innervated muscle fibers, which leads to repression of previously functional foreign synapses, but that

there is no effective competitive repression of innervation of the large muscle fibers that are normally innervated from a very few motoneurons. This would reconcile the conflict between the behavioral and electrophysiological methods of testing muscle reinnervation and is consistent with our original suggestion that multiple innervation, with a possibility of mutual interaction between closely spaced foreign and correct synapses on one muscle fiber (*9*), is the prerequisite for competitive repression of transmission from foreign nerve terminals.

The physiology of the proposed repressive process and its recognizable ultrastructural features, if any, are still unknown.

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Several lines of evidence indicate that Mark and Marotte's newly proposed hypothesis cannot reconcile the discrepancy between the apparent repression of foreign innervation observed in behavioral tests and the demonstration of functional foreign innervation on reinnervated muscle fibers in the goldfish (*1*). In additional tests of eye rotation behavior (*2*) I have observed that the disappearance of reversed reflexes is not always the ultimate outcome of appropriate nerve regeneration, despite what has been previously suggested (*3*). In some animals both reversed and normal reflexes occur, and these results indicate that both the foreign and the original nerve can drive the superior oblique muscle in the intact animal. It has not yet been demonstrated with physiological experiments (*4*) that only the slow fibers of fish extraocular muscles are involved in the production of static eye rotation. My behavioral observations [like those of Mark and co-workers (*3*)] cannot distinguish between the two types of muscle fibers. They do, however, indicate that whatever fibers are responsible for the observed behavior can be functionally innervated by both foreign and appropriate nerves.

Since the two populations of fibers are anatomically separate within the superior oblique muscle, I have been able to record extracellularly from small populations composed exclusively of one type of fiber, and my data show that both fast and slow muscle fibers can become, and remain, innervated by both foreign and appropriate nerves. In addition, I have recorded with a single intracellular electrode the activity of both foreign and appropriate synapses in individual fibers for periods of up to 7 months after the initial surgical nerve cross; the mean quantal content of excitatory junctional potentials from foreign synapses is not significantly different from that of excitatory junctional potentials in control fibers. I found no evidence of functional repression of foreign innervation on either population of muscle fibers (*2*). These data are consistent with a recent report of continued functioning of both foreign and appropriate innervation on perch gill muscle (*5*), the fibers of which are polyneuronally, multiterminally innervated and do not spike. These characteristics suggest that perch gill muscle fibers are similar to the slow fibers in goldfish superior oblique muscle. It therefore appears that the presence of dense innervation of single fibers is not sufficient to guarantee repression of foreign synapses following reinnervation by the appropriate nerve. There is also strong evidence against repression of foreign innervation on focally innervated mammalian muscles (*6*). Although there is evidence of functional displacement of foreign innervation on newt (*7*) and salamander (*8*) muscle, without morphological data it cannot be concluded that this represents synaptic repression as it was originally defined (*3*).

In studies of synaptic interactions it seems important to apply the term "synaptic repression" only to a competitive situation that results in loss of function in synapses that retain normal morphological characteristics. The gradual reduction of the number of terminals on single muscle fibers that occurs during embryonic development (*9*) is not synaptic repression as defined above. Functionless but apparently intact synapses have been produced without interneuronal competition in animals treated with botulinum toxin (*10*), and may occur in animals suffering from certain hereditary disorders, such as motor end-plate disease (*11*). True synaptic repression, however, has not been demonstrated.

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