RÉSUMÉ

### Frosty reception

WHEN the Roman historian Silius Italicus, describing Hannibal's epic journey over the Alps, wrote of the troops' terror at the sight of the mountains "covered with ice and hail that never thaws", he was taking a rather elastic view of events, it seems. His poetic licence is exposed in *Climatic Change* (**22**, 139–150; 1992) by J. Neumann, who has taken a close look at tree-ring data for sub-Alpine conifers to show that the climate in 218 BC, the year of the crossing, was if anything milder than in this century. There may have been snow falls in September at the time of the crossing (other historians mentioned this), but no glaciers in the vicinity. But Italicus was not being entirely inventive: during his lifetime, 250–320 years later, the climate had chilled considerably, and the glaciers may have advanced.

### The mycoplasma factor

ARE mycoplasmas the elusive cofactors that, with HIV-1, some think are necessary to cause AIDS? Last year S.-C. Lo *et al.* isolated a mycoplasma, dubbed *M. penetrans*, from the urine of AIDS patients. They now show (*Lancet* **340**, 1312; 1992) that antibodies to the organism occur in 40% of AIDS patients and 20% of asymptomatic HIV-1-positive patients, but in only 0.3% of uninfected controls (and in none of a group of HIV-1-negative, immunocompromised individuals). As AIDS patients mount poor immune responses, and often do not make antibodies to other mycoplasmas such as *M. fermentans*, the true incidence of *M. penetrans* in AIDS sufferers may be even higher than these figures suggest. Further studies of this organism, using, for instance, PCR of 16S RNA sequences, will no doubt follow.

### Weeping wine

OENOPHILES will be no strangers to the sight of droplets running down the inside of a glass of fine wine. Kelvin understood the basis of the effect — differential evaporation of water and alcohol in the film that rises under capillary forces from the edge of the liquid, causing a gradient in concentration and thus surface tension — but the details have been accorded little attention. Now J. B. Fournier and A. M. Cazabat (*Europhys. Lett.* **20**, 517–522; 1992) have identified the "tears of wine" as a fingering instability analogous to others, such as the thermal Marangoni effect, which are also the result of surface-tension inhomogeneities. Merging of the tears produces a self-similar profile in the advancing film. As the effect should also be found in engineering operations that involve liquid mixtures with markedly different surface tensions, the results have implications that go beyond the wine cellar.

MUSCLE DEVELOPMENT

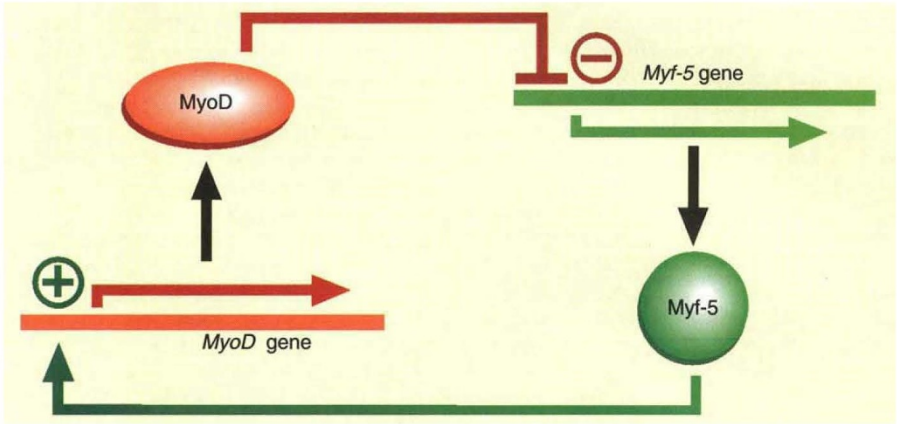
# Running without regulators

*Simon M. Hughes*

FIVE years ago, the cloning of *MyoD*, a gene that is sufficient to convert fibroblasts into muscle cells, caused quite a stir[1]. Many hoped that *MyoD* would prove to be the elusive master-regulator, a switch able to commit a cell to a particular fate and keep it there. The story now turns out not to be so simple, though it may be more intriguing. Two papers in *Cell*[2,3] show that muscle can form in the absence of either *MyoD*, the original myogenic 'determination' gene, or *Myf-5*, the currently favoured candidate in the same gene family.

The *MyoD* gene seemed to be a master-regulator because, in addition to its myogenic activity in cells in tissue culture, it is expressed exclusively in skeletal muscle and activates transcription from the E box DNA motif found in the regulatory regions of most known muscle-specific genes. Moreover, consistent with a switching role, it can activate its own expression by a positive feedback loop. But the unique position of *MyoD* as a master-regulator of myogenesis came under threat when three homologous members of the myogenic helix–loop–helix (mHLH) transcription factor family were discovered. The myogenin, Myf-5 and MRF4 (also known as Myf-6/herculin) proteins each have much the same characteristics as MyoD (see ref. 4 for review). The *Myf-5* gene, being expressed before the others, became the favoured putative master-regulator. The question became, do the genes cooperate in a regulatory network or does each have a subtly distinct function *in vivo* (or both)?

That the mHLH genes were the key to myogenic commitment then came into doubt when it was discovered that none of their products are detectable in mouse limb buds at a time when muscle precursors are known to be present: could the somitic cells (which populate the limb bud) express mHLH proteins transiently before migration into limbs; do they migrate to the limb before induction of myogenesis; or are other molecules responsible for myogenic commitment?




Possible negative feedback control loop for *MyoD* and *Myf-5*. There is evidence for each separate step, though in different cells. The model is not dependent on whether the mHLH proteins act directly or indirectly on the mHLH genes. Any increase or decrease in either transcription factor activity or gene expression for either *MyoD* or *Myf-5* is immediately self-correcting. Such systems are intrinsically more stable to perturbation than the simple auto-inductive positive feedback loops that have been ascribed to mHLH genes. Together with the myogenin and MRF4 proteins, it is possible that each of several pseudo-stable set points for expression of mHLH genes could maintain a distinct muscle cell state.

Furthermore, experiments in frogs and nematodes showed that some mHLH genes are expressed in cells that are not committed to myogenesis. These clues suggested that the mHLH proteins were unlikely to act alone as master-regulators of myogenesis, so their role had to be tested by manipulations of their expression *in vivo*.

Enter Braun, Rudnicki and their friends[2,3], who have modified the *Myf-5* and *MyoD* genes by homologous recombination in embryonic stem cells and produced mice in which, although aberrant transcripts are made, no functional protein should be present. Disappointingly (at least for those who like simple stories), both mice have muscle, so neither gene is the master-regulator of myogenesis. Mice with the *Myf-5*$^{ml}$ mutation die at birth, but not of defective muscles. They suffer from a delayed appearance of somitic muscle accompanied by a failure of rib formation and, hence, an inability to breathe. Braun *et al.*[2] speculate that the rib defects may be due to failure of an inductive interaction between myogenic tissue and adjacent