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'Grignard superseded after 60 years'

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Do acidic proteins turn you on?

A couple of very significant straws in the wind have just blown into that intractable field of genetic control in higher organisms. They take the form of papers in *Biochemical and Biophysical Research Communications* and *Nature* respectively, and make an already attractive theory of the way genes are switched on and off in mammalian chromosomes look even better. Briefly, this theory suggest that the pattern of gene expression is determined by small quantities of acidic protein present in the chromosomes. It predicts that a change in the gene pattern should be accompanied (indeed, preceded) by an alteration in the content of such acidic proteins in the nucleus. The two papers report that this is in fact just what can be observed in mammalian cells which have certain of ther genes switched on by steroid hormones.

The acidic protein idea stemmed from the large volume of work that has been performed on histones over the past few years, notably by James Bonner and his colleagues in California. Histones are basic proteins which form roughly half the bulk of chromosomes (most of the rest being DNA), and have become increasingly implicated in genetic control. The traditional view of histones was that many different varieties might exist, each able to recognize and "shut off" a specific region of DNA. But as the histone work progressed it became abundantly clear that histones are in fact distinguished by being remarkably constant in structure, far more so than almost any other type of protein. The view then shifted to the idea that histones are blanket gene repressors, and are told which genes to cover—or which genes *not* to cover—by some other molecule.

For the past couple of years an amicable controversy has been bumping along concerning the identity of these specificity-determining factors. The Bonner school has favoured the small fraction of RNA that can be found associated with chromosomes. The opposite view, documented most effectively by John Paul of the Beatson Memorial Hospital, Glasgow, and his former research colleague Stewart Gilmour (now working in Canada), is that the key molecules are acidic proteins (see "What makes cells different?", by Stewart Gilmour, *New Scientist,* vol. 42, p. 346).

Another group holding the acidic protein view is that of Ching-Sung Teng and Terrell Hamilton at the University of Texas, Austin. This team is interested in the action of the hormone oestrogen on the uterus, and last year, for instance, reported *in vitro* work which strongly hinted that in this organ acidic proteins play a role in displacing histones from DNA, thus exposing or switching on certain genes. In a new paper in *BBRC* (vol. 40, p.1231) they have now extended the work—and the conclusions—to the living animal.

Using a radioactive labelling technique, they studied the proteins made in the nuclei of rat liver or uterus cells after the animal had received an injection of oestrogen. Their main finding is that 12 hours after the hormone treatment, the incorporation of label into the acidic protein from uterine cells was stimulated by 75 per cent, while the same measurement made in liver cells showed a stimulation of less than 6 per cent. The 12-hour mark is also distinguished by being the time which gene activation by oestrodiol is at its maximum. Teng and Hamilton claim their results provide "clear evidence that the synthesis of a specific nuclear acidic protein is involved in gene activation induced by (oestrogen) acting on its specific target organ, and further, that this effect of the hormone is organ-specific.

Although Teng and Hamilton's work was published earlier, it was completed and their paper submitted to *BBRC* well after the parallel investigation of Keith Shelton and Vincent Allfrey of Rockefeller University, New York, was accepted for publication by *Nature.* Their paper eventually appeared last week (vol. 228, p. 132), and reports studies made on rat liver cells after the animals had received an injection of the steroid hormone hydrocortisone. Again, clear evidence of acidic protein stimulation was gathered, and Shelton and Allfrey have even managed to fractionate the main protein involved.

John Paul, although encouraged by these new developments, also warns against reading too much into them. Although there seems little doubt that the hormones do increase the levels of an acidic protein in the nucleus, the evidence that this protein is responsible for activating genes is still only circumstantial. Shelton and Allfrey's success in fractionating a specific protein might prove to be especially important in settling the cause-and-effect relationships of the protein and gene activation. But in any case, what Teng and Hamilton call the "remarkable congruence" between the two studies provides important support for the idea that the specificity of gene switching lies in the chromosone's acidic proteins.

Grignard superseded after 60 years

Victor Grignard won his Nobel Prize in 1912 for discovering the reaction between magnesium and an alkyl halide (RX) in ether. The resulting "Grignard reagent", RMgX, can then be reacted with a wide variety of aldehydes, ketones, and other carbonyl compounds to give alcohols of every description. For nearly 70 years this reaction has been a mainstay of synthetic organic chemistry, mostly in research laboratories but also to some extent in industry. But now it looks as though Grignard may be superseded at last by a simple, one-step process discovered by P. J. Pearce, D. H. Richards, and N. F. Scilly of the Explosives R and D Establishment, Waltham Abbey (*Chemical Communications,* 1970, p.1160).

Like many classic discoveries, this one resulted from following up a reaction which "went wrong". The procedure is simple. A mixture of a carbonyl compound and an alkyl halide is added dropwise to a suspension of lithium pieces in tetrahydrofuran, keeping the temperature at 0°C. The authors record yields as high as 96 per cent. The mechanism of the reaction is being studied, and an attempt to replace lithium with the much cheaper sodium is being made. Manufacturers of alcohols, as well as laboratory chemists, should keep an eye on this one; the high-tonnage cumenephenol process started in a similar way.

Feeding garbage into the Mouth of Hell

The ultimate monster to devour all the waste that man creates on the Earth's surface may be the Earth itself—or so an American geologist and a civil engineer now suggest. Writing in *Nature* (vol. 228, p. 154) R. C. Bostrom and M. A. Sherif of the University of Washington, Seattle, point out that one consequence of the now well substantiated concept of sea-floor spreading, is that some 60 cu.km of new crust is being added to the surface of our planet every year. Since the Earth's volume presumably remains constant the up-welling of new material along the 40 000-odd km of ocean ridges must be compensated somewhere by a comparable volume of sinking material.

The picture of the ocean floors now in fashion supposes them to be rigid plates constantly being forced apart along the ridges by the addition of new material; where neighbouring plates abut, often along a continental margin, the plate on one side is forced down, underthrusting the other. Its material descends deep into the Earth's mantle. The more active of such "zones of subduction" often shaken by strong earthquakes and delineated by oceanic trenches, could form the world's virtually bottomless garbage cans. Fast sedimentation would assist burial initially.

If, as Bostrom and Sherif believe, the economics of such a method of disposal were favourable, it would seem to provide a happy solution to the problems of nuclear waste and unwanted nerve gas shells, quite apart from the enormous bulk of relatively non-toxic refuse. Disarmament committees might come to regard it as the symbolic goal of all their efforts, and revolutionaries as a fitting destination for old and useless politicians.

As its proposers conclude, the only eventual outcome would be, "the discovery of a distinctive, and perhaps puzzling, suite of metamorphic rocks". But what if, desperate for raw materials, we should need to mine our former refuse tips long before then?