100 YEARS AGO

The value and possibilities of wireless telegraphy as a journalistic adjunct are described in Saturday's *Times* by the special correspondent who established a wireless telegraph system at the theatre of war operations in the Far East with such success that both the belligerents regarded the enterprise as dangerous to their interests. The Japanese Government placed such limitations upon the free movements of the *Haimun* — the vessel chartered by the *Times* for its wireless telegraph service — that this means of communication was discontinued of necessity; and there seems little doubt that in future the use of all systems of wireless communication will be controlled by international law.

From *Nature* 1 September 1904.

50 YEARS AGO

A New Periodic Table of the Elements Based on the Structure of the Atom. **To demonstrate the periodicity in the properties of the chemical elements, Lothar Meyer chose the most direct representation: he plotted the elements in the order of their atomic weights on the abscissa, and the values of the property in question on the ordinate. At the same time, Mendeléef published the Periodic Law in the form of tables… During the following decades innumerable attempts were made to improve on Meyer and Mendeléef. All sorts of representations, trees with branches, concentric circles, spirals, figure-eights, and various three-dimensioned curves were tried;…behind all this was the hope to get nearer to the mystery of the periodic system if a more perfect arrangement could be found. But the scientific result of all these attempts was nil… It is somewhat astonishing to see that quite recently "A New Periodic Table of the Elements" has been published which is a revival of the old discarded attempts. The curves, for example, which represent the specific gravity of the elements, are based on one of the well-tried spirals and can, naturally, not avoid the old drawbacks… The author recommends even a cone-shaped periodic chart, another repetition of previous suggestions; whoever takes the trouble to follow the advice to cut the drawing out and to gum it together as a cone, will scarcely get any insight into the sequence of chemical elements which the usual tables do not give.**

From *Nature* 4 September 1954.

high-grade adenomas in mice carrying the transgene and the *Apc* defect contained foci of invasive carcinoma, whereas no carcinomas were seen in mice with only the *Apc* defect.

In the normal small intestine and colon, epithelial cells proliferate predominantly in the bottom of small pits called crypts, before becoming specialized and migrating upwards, where cells die and slough off (Fig. 1). In normal mice, Mazelin *et al.* found that *Dcc* was uniformly expressed throughout the intestinal epithelium, whereas netrin-1 expression was mostly restricted to the base of the crypts. This is consistent with the view that interaction of netrin-1 with its receptors might regulate survival versus cell death, with netrin-1 stimulating proliferation in the crypt and the absence of netrin-1 perhaps contributing to cell death at the surface.

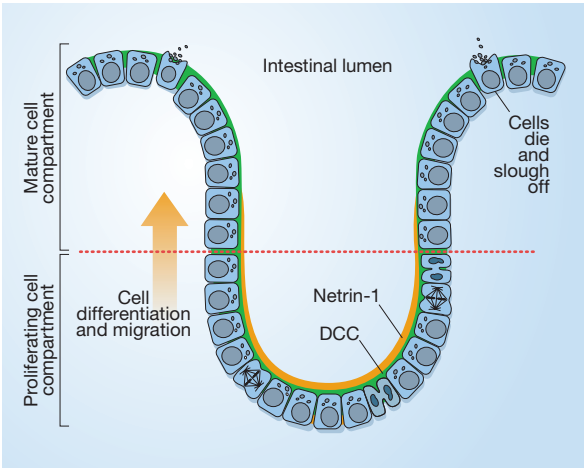

Figure 1 **Model for the role of netrin-1 and DCC in regulating cell survival and death in the intestine, based on Mazelin and colleagues' results[4]. In a normal intestine, cells proliferate at the bottom of pits called crypts. They then migrate upwards towards the surface. As they go, the cells stop proliferating, become more specialized, and ultimately die. Netrin-1 expression is mostly restricted to the base of the crypt, but expression of its receptor DCC is essentially uniform in all epithelial cells[4]. According to the dependence-receptor hypothesis, the findings imply that binding of netrin-1 to DCC might contribute to cell survival in the crypt. At the surface, the absence of netrin-1 leads to DCC-mediated cell death.**

With this paper, Mazelin *et al.* offer encouraging *in vivo* data to support the hypothesis that the DCC and UNC5H proteins function as dependence receptors for netrin-1. Yet there are some caveats. First, because there are other netrin-1 receptors[13,14], an excess of netrin-1 might promote cell survival in part through pathways independent of DCC and UNC5H. Second, in the genetically engineered mice there is a uniform gradient of netrin-1 in the intestinal lining, as well as overexpression of netrin-1 relative to its usual levels, which could lead to some doubts about the physiological relevance of the findings. However, Mazelin *et al.* did see increased cell death in intestinal crypts of mice deficient in netrin-1, implicating netrin-1 in the survival of normal intestinal cells.

Their findings are consistent with the notion that there might be strong selection for inhibition of DCC and UNC5H expression or function in colon and other cancers. The proteins might indeed function in tumour suppression, perhaps by inhibiting growth or causing the death of potential cancer cells in environments where the netrin-1 concentration is low. Conceivably, singular inactivation of *DCC* or *UNC5H* might be insufficient to promote tumour development. Concerted inactivation of both genes might be required for progressive outgrowth of cells in regions where netrin-1 levels are usually low, explaining why mice lacking one copy of the *Dcc* gene showed no overt predisposition to intestinal or other tumours[7].

To understand better the roles of DCC and UNC5H proteins as netrin-1 dependence receptors that regulate cell survival, it might prove useful to study other genetically engineered mice, such as mice with intestinal-specific deletions of the *Dcc* and/or *UNC5H* genes, or mice carrying *Dcc* or *UNC5H* mutations that are predicted to interfere with the receptors' ability to initiate cell death. Other dependence receptors have been identified[3] and yet others probably remain to be discovered, so further research should help to clarify whether alterations in dependence-receptor pathways have a more widespread role in cancer. ■

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