in these or other activities of the Special Programme should contact the Director, Special Programme for Research and Training in Tropical Diseases, World Health Organisation, Geneva, Switzerland, for further information.

Virus precursor shedding from mammary tumour cells

from A. J. McClelland

In 1976 Ritzi *et al.* made the intriguing observation that mice with murine mammary tumour virus-induced mammary tumours had much greater amounts of the major mammary tumour virus (MuMTV) structural glycoprotein gp52 in their blood than did mice with no mammary tumours. This was true even when the tumour-free mice were productively infected with MuMTV and had very high levels of gp52 in their milk. Ritzi's work raised several interesting questions. How are the MuMTV glycoproteins synthesised and assembled, what is the mechanism and biological function of gp52 secretion by mammary tumour cells and are there differences in the synthesis and assembly of MuMTV in normal and transformed cells?

Thanks to the establishment of continuous MuMTV-producing mammary tumour cell lines (Ringold *et al. Virology* **65,** 135; 1975; Sarkar *et al. Virology* **77,** 12; 1977) some answers to the first question at least have been found. It appears that the MuMTV glycoproteins are derived from a single precursor molecule, designated pre-gp70 (molecular weight 70,000) which is then cleaved to form the glycoproteins used in virus assembly (Racevskis & Sarkar *J. Virol.* **25,** 374; 1978; Schochetman *et al. Virology* **85,** 168; 1978; Dickson & Atterwill *J. Virol.* **26,** 660; 1978). Even more interesting is the unexpected discovery that the MuMTV glycoprotein precursor is shed from the surface membrane of the tumour cells in which it is synthesised.

Racevskis and Sarkar's discovery, that both gp52 and its precursor, pre-gp70, were present in virus-free culture medium from MuMTV-producing cells was unexpected because it was the first time that a glycoprotein precursor had been found in cell culture medium and because cell surface labelling studies had shown that, unlike MuMTV gp52, pre-gp70 is not present on the surface of MuMTV-producing cells.

Since pre-gp70 is shed into the medium of MuMTV-producing tissue culture cells, yet is apparently not available for surface labelling, two populations of pre-gp70 may exist. One population, destined to provide mature proteins for MuMTV assembly, may be cleaved before reaching the cell surface to produce gp52. The gp52 is then inserted into the cell membrane and leaves the cell only when it is incorporated into a virus particle. The second population of pre-gp70 molecules are shed from the cell without ever becoming integrated into its surface membrane. In that context, it is interesting to note that pre-gp70 has not been reported to be packaged within mature MuMTV particles.

The anti-gp52 serum that Ritzi used (*Proc. natn. Acad. Sci. U.S.A.* **73,** 4190; 1976) reacts with both gp52 and pre-gp70 and thus the glycoprotein that was detected in the plasma of tumour-bearing mice might have consisted of gp52 alone, gp52 and pre-gp70 or even pre-gp70 alone. The discovery that pre-gp70 is shed from mammary tumour cells in tissue culture could therefore explain the observation of Ritzi *et al.* but the mechanism by which MuMTV glycoproteins are shed from cells and the biological significance of shedding are still unknown. However, one can reasonably speculate that shedding helps MuMTV-producing tumour cells to escape from the immunological defences of the host. Immunisation studies have shown that gp52 is the most potent immunogen for protecting mice from exogenous MuMTV infection and subsequent tumorigenesis (Sarkar & Moore *Cancer Res.* **38,** 1468; 1978). It is therefore possible that the release of large quantities of gp52, and possibly pre-gp70, into the plasma provides a means of complexing (and thus, in effect, neutralising) cytotoxic antibodies against the glycoprotein, thereby increasing the survival advantage of MuMTV-producing tumour cells.

Whatever the biological function of glycoprotein shedding, it provides a unique opportunity to investigate two apparently different pathways of pre-gp70 transport and/or processing. It is still not known if MuMTV-producing normal mammary gland cells cultured *in vitro* would shed viral glycoproteins. If it is found that such normal cells do not exhibit the shedding phenomenon, membrane changes taking place in the transition from normal to tumour cells might be studied using MuMTV glycoprotein shedding as a marker for cell transformation. □

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Versatile accelerators

from R. G. P. Voss

The range of uses to which small accelerators are now put is astonishing. These were covered exhaustively in a recent conference in Texas on the application of small accelerators*. The word 'small' is perhaps misleading: there were progress reports on the two very large tandems being built in the United Kingdom and in the United States, at Daresbury and Oak Ridge respectively, and experiments carried out on the 800 MeV proton linear accelerator at LAMPF and the 20 GeV electron linear accelerator at SLAC were reported. Perhaps, as someone remarked, even small accelerators are big in Texas.

Amongst the many different fields, one topic inevitably attracted considerable interest: the application of accelerators to medical purposes. Several papers dealt with the production of radioisotopes by cyclotrons, tandems, and linear accelerators. Information was given on targets, yields, the subsequent radiochemistry, the various uses of the isotopes, and instrumentation to detect localised radioactivity in the human body. Considerable work has been done in recent years at Los Alamos with pions produced by the proton linear accelerator. This is a huge machine, 850 m long, and its suitability for widespread use in medical work is obviously restricted. As a consequence a smaller accelerator, a mere 120 m long, is now being developed. It is known as PIGMI (Pion Generator for Medical Irradiations) and is now in its third year of development, with emphasis on being less expensive ($10M) and more reliable than accelerators for pure research.

A related field of great interest is that of computed tomography, and developments following from the original EMI CT scanner were presented. Work on proton CT at Los Alamos was described by W. F. Hanson (Oak Ridge Associated Universities) and R. R. Highfill and M. E. Phelps (University of California at Los Angeles) gave a paper on positron tomography. By detecting the annihilation radiation from positrons one can make an *in vivo* study of physiological processes in specific regions of the body. The need for positron-emitting radioisotopes (such as ^{11}C, ^{13}N, ^{15}O, ^{18}F) with short half-lives means that

*5th Conference on the application of small accelerators, North Texas State University, Denton, Texas, 6–8 November 1978. Abstracts are published in the Bulletin of the American Physical Society, volume 23, number 8, 1978.

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