

Newsdesk

Prospects for inhibiting angiogenesis

A recent paper (*Cell* 1997;88:277-85) has shown that a novel angiogenesis inhibitor TNP 470 has the ability to induce tumour growth regression without causing drug resistance. Anticancer therapy is plagued with problems of drug resistance, which relate to the ease with which the tumour cell genome can change expression. An alternative approach is to target the tumour blood supply since the endothelial cells should have a more stable genome. In preliminary studies TNP470, a synthetic inhibitor of angiogenesis, was found not to induce drug resistance on repeated use as tumours regressed and recurred. Now, the same group of researchers has reported on a similar lack of drug resistance to a natural angiogenesis inhibitor, endostatin, which is a 20 000 Da C terminal fragment of collagen type XVIII produced by haemangiopericytoma. Endostatin specifically inhibits proliferating endothelial cells but has no effect on resting endothelial cells. In addition, all treated tumours regressed to microscopic size and, with cycling endostatin therapy, no macroscopic or microscopic tumours were found. Remarkably, all tumours eventually became dormant even when the endostatin treatment was stopped. The potential value for ophthalmic use is immediately obvious, particularly if endostatin can be administered locally and repeatedly without loss of potency. Apart from its obvious use in the treatment of intraocular malignancy, both topical and intraocular application might have wide use in conditions such as proliferative diabetic retinopathy, rubeosis iridis, and corneal vascularisation, particularly if there is no "bystander" cell damage.

Antigen presentation

Although immunologists have for decades been focusing on how antigen presenting cells present foreign and self protein antigens, many of us have often wondered about all those other molecules which make up microorganisms and mammalian tissues—such as lipids, glycolipids, and other molecules, especially since they appear to be important components of adjuvants and therefore have the ability to induce inflammatory and immune responses. Now it appears that antigen presenting cells have the ability to present antigen via their CD1 molecules, a family of cell surface proteins distinct from MHC molecules and located on chromosome 1. However, they do show considerable structural similarity to MHC class I molecules in that they have three heavy extracellular α chains linked to β 2 microglobulin. CD1 antigens appear to be particularly important in present-

ing mycobacterial antigens to a restricted set of T cells. The role of CD1 restricted antigen presentation in immunity generally is only now being unravelled (see *Current Biology* 1997;7:R508-10) but some interesting observations have been made already, such as the high expression of CD1 on dendritic cells in skin granulomas from patients with leprosy who demonstrate effective immunity to this organism.

Developments in scleral contact lenses

Medical indications for contact lens use constitute the main drive towards developing better tolerated scleral contact lenses. A recent meeting addressed specifically the value and need for effective scleral contact lenses (International Scleral Lens Conference, 27 November, London). The aim of the conference was to disseminate information on a new type of rigid gas permeable (RGP) scleral lens (the sealed RGP lens) which has the advantage of minimising the anoxia associated with other types of contact lens and thus reducing long term complications which are found with PMMA ventilated lenses. A wide range of topics were aired, starting off with the question of "Why not just fit a corneal lens?" (Buckley, London). A study at Moorfields of 911 eyes (640 patients) showed that a primary indication for RGP scleral lenses was primary corneal ectasia. Other more general indications included post-keratoplasty and other ocular surface disease, but they were also useful in some cases of aphakia and other refractive indications. Some basic information on biomaterial polymer chemistry (Parker) and procedures for fitting of these lenses (Pullum, London; Christie, London) was provided, while a "wet lab" instruction session was given by S McPherson (Aberdeen) and P Terry (Oxford). These lenses were considered to have many advantages not least of which was their use in very advanced keratoconus or severe corneal surface irregularity, where they were seen as a viable alternative to surgery. The opinion was that too few ophthalmologists were aware of these lenses or did not have access to contact lens specialists experienced in their use.

Galletti wins the Minerva prize

The Minerva Foundation has named Italian scientist Claudio Galletti the winner of its Golden Brain Award 1997 for his work in the field of visual neuroscience. This annual award is given to a researcher who has made a fundamental contribution to our knowledge of mechanisms underlying the physiology of vision. Galletti's work has been in two areas of

visual science: the first was the discovery of certain cells whose function is to track objects in space (position cells). The differentiating feature of these cells is that their receptive field remains constant when the eyes move, in contrast with other cells whose receptive fields move with the direction of gaze (retinal slip). The importance of these cells was recently emphasised with the report of a patient with a bilateral parietal cortical defect which manifested itself in a selective loss of this ability to compensate for retinal slip (see *Newsdesk BJO* 1998;82:8). Galletti is also known for his work in dissecting the links between visual tasks and reaching behaviour. This was discovered following studies of the region of the brain which received information from the position cell. In the same region of the parietal cortex there are cells related to arm movement which he believes allow complex adjustments needed to reach successfully for objects. Defects in this area may underlie a condition known as optic ataxia in which patients have an inability to grasp objects accurately.

Mucosal immunology and the eye

The eye in its unique position at the interface of several different immunological systems was the centre of attention of a recent meeting reporting on various aspects of the mucosal immune system (*Mucosal Immunology and Ocular Disease*: Ertal, October 1997). Under discussion were surface defence mechanisms, especially IgA, the ocular mucosa compared with other mucosal surfaces, mechanisms of tolerance induction via the ocular mucosa compared with ocular immune privilege, and the potential for vaccine administration via mucosal immunisation protocols. Some interesting observations were made, such as the inverse correlation between surface IgA and cell mediated immunity when tolerance was induced; that contrary to previous notions the intraocular compartment appears to have access to the cervical lymph nodes; that Fas/FasL is an important mechanism in immune privilege within the eye owing to constitutive expression of Fas by ocular cells; and that many mechanisms of tolerance were mediated via a final common pathway involving IL10. Immunosuppression via mucosal tolerance regimens has reached the clinical trial stage and although the results in multiple sclerosis, rheumatoid arthritis, and uveitis are not spectacular, they have been sufficiently promising to encourage further research in this area. In particular, this type of approach has possible application in corneal transplantation since it has been shown that tolerance to alloantigens can also be induced via mucosal surfaces.



Br J Ophthalmol 1998 82: 109
doi: 10.1136/bjo.82.2.109

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