Immunology

Contrasuppressor cells and oral tolerance

from R.B. Taylor

AMONG the subtle regulatory tasks required of the immune system is adjustment of the modality and magnitude of an immune response to suit the anatomical locality in which it is to take place. A good example of this ability is oral tolerance — immune responsiveness to antigens at mucosal surfaces with a much reduced response to systemic challenge with the same antigens¹. The value of this mechanism is probably to prevent systemic allergic responses to food antigens without compromising local defence of the mucosae. The demands of such subtle functions should have prepared us for the further complexities in immunoregulatory mechanisms that continue to be revealed. One of these, which has now come to stay, is the contrasuppressor circuit². I. Suzuki and co-workers, on page 451 of this issue, now report data implicating contrasuppression in the maintenance of oral tolerance³.

As so far defined in mice, this circuit comprises T lymphocytes called contrasuppressor cells whose end function is to neutralize the inhibitory action of T-suppressor cells on the T-helper cell population. One of the cells necessary for contrasuppression has a distinctive surface phenotype and the property of adherence to *Vicia villosa* lectin. These cells have been found in various lymphoid organs including Peyer's patches and seem to play a part in selection of the modality (contact sensitivity or antibody production) of the response to the trinitrophenyl hapten^{2,4}. In man there is evidence of contrasuppression in cultures of peripheral blood lymphocytes responding to an antigen from the oral bacterium *Streptococcus mutans*. The cells responsible for this activity were shown to bind antigen and *V. villosa* lectin and carry the surface markers T8, T3 and Ia (see ref. 5 for review).

The work now reported by Suzuki *et al.*³ builds on the earlier finding in the same laboratory that oral tolerance could be induced in C3H/HeN mice but not in the congenic strain C3H/HeJ which differs at a locus determining the ability to respond to bacterial lipopolysaccharide. In the present work, mice of both strains are subjected to prolonged oral immunization with sheep red blood cells (SRBC). Oral tolerance develops in the C3H/HeN mice but can be broken by transfer of T-cell fractions enriched for contrasuppressor cells taken from the spleens of the C3H/HeJ mice — to result in the development of anti-SRBC antibody-forming cells of all

the major isotypes in the recipient spleen. Very small numbers of contrasuppressor cells (5×10^4) are effective. Oral tolerance to SRBC is also shown by C3H/HeN spleen cells *in vitro*, and is similarly abrogated by the inclusion of contrasuppressor cells in the cultures. On the basis of various methods to enrich or deplete the active cells, it was concluded the contrasuppressor cells resemble those originally described. The fact that oral tolerance to SRBC is lost in the presence of contrasuppressor cells indicates clearly that T-helper cells are present but controlled by suppressor cells. If this suppression is neutralized by the contrasuppressor cells then T-helper cells can become active.

The phenomenon of local immune responses in the gut coexisting with oral tolerance has been described as "an island of responsiveness in a sea of suppression".

Astronomy

A hidden quasar revealed

from C. Martin Gaskell

IT has long been realized that the quasar phenomenon encompasses many orders of magnitude in luminosity, ranging from the brightest quasars, which far outshine the galaxies they are in, down to the mildly active nuclei (often called mini-quasars) of relatively normal galaxies like our own, that have luminosities comparable with the brightest stars. Despite the enormous range in energy output (a factor of at least 10^{10}) there are many features that all these active nuclei possess in common; the most important is a spectrum with (roughly) constant energy per decade of frequency in the entire range from millimetre wavelength radio waves to X-ray (and probably γ -ray) energies. Does this mean that all such 'active' galactic nuclei are manifestations of the same basic quasar mechanism? The answer in recent years has been an increasingly firm yes. And R.R.J. Antonucci and J.S. Miller¹ have now made observations greatly strengthening our belief in the unity of quasar activity.

The quasar family is divided into several genera and species on the basis of the strength and nature of the radio emission and the optical emission line spectrum. One of the more important species is the Seyfert 2 galaxy. A Seyfert galaxy has emission lines whose Doppler broadening

The challenge now is to find out what elements of the system are sufficiently localized to determine the geography of this island. Restricted migration of contrasuppressor cells from the gut seems unlikely as these cells are found in the spleens of the C3H/HeJ mice after oral immunization. Instead one may need to look at the populations of cells which, once primed, return to the mucosae to function in local immunity. It may be that there is a defect in the return of T-suppressor cells relative to the other types. The growing interest in mucosal immunization is to be welcomed because the mucosal route is after all the commonest, whereas intraperitoneal immunization rarely occurs outside the laboratory — except perhaps in the bull-rings of Seville⁶. □

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exceeds the velocities of normal interstellar gas and stars in the rest of the galaxy. Khachikian and Weedman² sub-divide Seyfert galaxies into two classes: Seyfert 1, where ionized gas moves very rapidly (velocities of a few per cent of the speed of light); and Seyfert 2, where the ionized gas moves only slightly faster than the stars in a typical galactic nucleus (an order of magnitude slower than in Seyfert 1 galaxies). Seyfert 1 galaxies are clearly closely related to the bright quasars. The dense rapidly moving gas producing the strong broad emission lines (the so-called broad-line region) is an intimate part of the quasar phenomenon. It is found at radii as small as a few light days from the energy source in some Seyfert 1 galaxies³ (only a few times bigger than the Solar System) and is seen in all bright quasars. Why is it not seen in Seyfert 2 galaxies? There are two probable reasons: either the dense gas is somehow hidden; or it is absent, in which case Seyfert 2 galaxies could be fundamentally different from bright quasars.

In the past few years it has been realized that Seyfert 1 galaxies can masquerade as Seyfert 2 galaxies either by temporarily turning off their photoionizing continuum (see, for example, ref. 4) or, in some cases by having a lot of dust obscuring their innermost regions^{5,6} (dust is certainly pre-