Intracellular signalling

Receptor-operated Ca channels

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THERE is hardly any tissue where receptor-operated calcium channels have not been postulated. Evidence from biochemical and tracer flux studies indicates that they are involved in many diverse cellular functions (see ref. 1 for a review). In contrast, electrophysiologists have had until recently only one well-characterized mechanism to explain receptor-mediated changes in Ca conductance: the second-messenger-induced modulation of voltage-activated Ca channels, which has been found in several systems^{2,4}. No such voltage-activated channels, however, have been found in cell types such as mast cells⁵ that are believed to possess receptor-operated Ca channels. But in the past few months, three more mechanisms of receptor-mediated Ca flow have been suggested. One is described by Kuno, Gardner and colleagues (ref. 6 and page 301 of this issue⁷); another was reported⁸ by Reuter and colleagues; and a third was proposed⁹ by Irvine and Moor.

Inositol (1,4,5) trisphosphate (InsP₃) is well established as a second messenger that releases calcium from intracellular stores^{10,11}. The report in this issue⁷ describes a second, independent effect of InsP₃ on calcium influx. In T lymphocytes, the authors observe current fluctuations resulting from opening and closing of very small, Ca-permeable channels directly activated by intracellular InsP₃. In their earlier work⁶, they observed a very similar channel in human T lymphocytes after activation by mitogen. The channel is not or is only marginally voltage-dependent and is blocked rather than activated by increasing calcium concentration, [Ca]_i, on its cytoplasmic side. The opening of this channel therefore cannot be caused by increased [Ca]_i, which shows that this is not an indirect consequence of Ca release from intracellular stores.

Such channels, which mediate what might be called a Ca-induced Ca influx, have recently been described⁸ by Reuter and colleagues. These authors observed a rise in [Ca]_i following peptide-induced neutrophil activation and the consequent opening of two types of nonspecific channels that are permeable to Ca and other cations. These channels are opened only by increased [Ca]_i and not by InsP₃ or by the peptide directly. This mechanism of Ca-mediated activation of Ca-conducting channels could be a widespread phenomenon that is used by cells to perpetuate an InsP₃-induced increase in [Ca]_i, which by itself is only transient.

The third mechanism of receptor-

mediated calcium inflow through the plasma membrane which has recently emerged also involves InsP₃. Irvine and Moor have shown⁹ that inositol (1,3,4,5) tetrakisphosphate (InsP₄), derived from InsP₃ by phosphorylation, may serve as a messenger on its own (see the recent discussion in News and Views¹²). When injected into sea urchin eggs, InsP₄ causes a raising of the fertilization envelope, a process which is dependent on the presence of extracellular Ca. This result suggests an InsP₄-activated channel.

The three mechanisms described (Ca-permeable channels directly opened by InsP₃; channels opened by an initial InsP₃-induced increase in [Ca]_i; and putative channels opened by InsP₄) will probably help to elucidate the role of calcium in many diverse cellular responses. It is now becoming clear that a phase of sustained increase in [Ca]_i dependent on external Ca can be separated from a transient phase independent of external Ca (mediated by InsP₃) in many types of electrically inexcitable cells. The channels described here have properties suggesting that they mediate such a sustained phase. Although they probably are the receptor-operated Ca channels that have long been searched for,

they are not Ca channels in the traditional sense. They lack ionic specificity, so that under physiological conditions the ion contributing most to the current is not Ca.

At first glance one is reluctant to accept three new mechanisms. But only a limited body of data is available at the moment. It will be interesting to see how many separate mechanisms will remain once they are more completely characterized. It is conceivable that the effect of InsP₃ on lymphocytes, which now seems to be a direct action of InsP₃, is in fact caused by InsP₄ generated by the cell from InsP₃. This possibility is considered by Kuno and Gardner⁷. On the other hand, Irvine and Moor mention⁹ that the action of InsP₄ is enhanced by prior Ca mobilization. This may provide a link to the channels described⁸ by Reuter and colleagues. □

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Archaeology

New perspectives on the history of ancient Maya civilization

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OUR understanding of ancient Maya civilization has undergone huge changes in recent years. Although the exciting breakthroughs in deciphering Maya hieroglyphic writing and in appreciating the ideological roles of the Maya elite have justifiably received much publicity¹, equally significant breakthroughs have been made in understanding the agricultural and adaptive foundation upon which Maya civilization was built^{2,3}. All these advances have caused significant changes in traditionally held views of the rise, development, and so-called 'collapse' of Classic Maya civilization. Thus, in contrast to older views, Classic civilization is now thought to have been composed of urban centres, supported by both extensive and intensive agriculture, closely linked economically, politically and ideologically, and subject to widespread raiding and conflict. Whereas Mayan civilization was considered unique, it is now believed

to have developed in a similar manner to other pre-industrial complex societies. The new pollen data presented by David Rue on page 285 of this issue⁴ should lead to further revisions of the traditional picture. Assuming Rue's interpretation of the pollen in his two samples is correct — and it appears both plausible and well argued — some re-examination of current views is called for.

For many years, the earliest Maya remains of settled farmers could not be securely dated before about 800 BC. Although many suspected that earlier remains existed, there were no data to support such suspicions until the major discoveries⁵ by Norman Hammond at the site of Cuello in Belize, which pushed this date back about 1,500 years to 2300 BC. Hammond has argued that the occupants of Cuello in the late third millennium BC were settled, pottery-making, maize agriculturalists who culturally were Maya. But