inside-positive) and normal polarization of the bottom (inside-negative) results in a voltage gradient across each cell, top-to-bottom, of about 90–100 mV ('bottom-positive'). The stacking of hundreds of such cells, like batteries in a series, generates the stunning potential of about a hundred volts characteristic of these organs. The abundance of acetylcholine receptors in the cells was essential to their cloning[2], and similarly Jentsch took advantage of the abundance of Cl^- channels in using them as the source of mRNA.

The electroplax Cl^- channel, like the erythrocyte anion exchange protein, band 3, is inhibited by the drugs based on modified stilbene disulphonates such as DIDS. However, a relatively high concentration — in the micromolecular range — is required for inhibition. Surprisingly, the two main DIDS-binding proteins in electroplax membranes are the α subunit of the (Na^+ + K^+) ATPase and a second protein Jentsch and colleagues cloned a few years ago but which is not a subunit of a Cl^- channel[3]. This highlights the potential hazards in using an inhibitor of relatively low affinity and specificity to purify a channel (or any other) protein.

The cloning strategy that was ultimately successful involved functional expression of the protein in *Xenopus* oocytes. Injection of total electroplax mRNA induces expression of a voltage-sensitive Cl^- channel, and Jentsch *et al.* selected cDNAs that, when hybridized to total mRNA, removed (hybrid-depleted) the channel-inducing activity. Moreover, an RNA transcript of the full-length cDNA *in vitro* induced expression of Cl^- channel activity. The encoded protein of 805 amino acids, has 12 (or 13) presumed membrane-spanning α helices and in sequence does not resemble any known protein.

The cloned channel protein is voltage-sensitive; that is, it is slowly activated when the membrane is hyperpolarized. Perhaps surprisingly, the channel does not contain a sequence resembling the presumed 'voltage gating helix' (helix 4) in voltage-dependent K^+ and Na^+ channels, where every third residue is arginine or lysine[4]. However, these cation channels open when the membrane is depolarized.

The cloned channel protein has many properties in common with the major electroplax Cl^- channel studied in detail by Miller and his associates in reconstituted lipid bilayers[5]. In particular, once the channel is opened the flux of Cl^- ions increases with membrane depolarization. Single-channel recording will be required to determine whether the two are identical (there may be a regulatory subunit). Both the electroplax Cl^- channel and one from kidney have two Cl^- diffusion pathways, and the electroplax channel is thought to be a homodimer. The opening and inactivation of the two Cl^- 'proto-channels' are coupled to the chloride transmembrane electrochemical gradient — a novel mechanism of channel gating[6] — and it will be of some interest to see whether this property is intrinsic to the cloned Cl^- channel protein.

An important question is the relationship of this channel to the apical Cl^- channel in airway and sweat duct (and other) epithelial cells which is defective in cystic fibrosis (CF)[7,8]. The cloned 'CF gene' product is almost certainly not a Cl^- channel, but a protein that regulates channel activity, even though expression of a wild-type gene in a CF epithelial cell reverses the defect in Cl^- transport[9,10].

Can one use molecular hybridization with the electroplax channel cDNA to clone the mammalian 'CF Cl^- channel'? Can it be used to clone other interesting Cl^- channels, such as those in coated vesicles[11] or in the apical membrane of the gastric oxyntic cell[12] that, together with an ATP-driven H^+ pump, are required to establish a pH gradient? Attempts of this sort with other ion transport proteins might be instructive. When Kopito and I cloned the erythrocyte anion exchange protein[13], we thought we could use the cDNA as the probe to isolate clones for anion channel proteins. This approach did yield two other cDNAs encoding anion exchangers but no anion channels[14]. The cDNA encoding the *Drosophila Shaker* voltage-sensitive K^+ channel has been used to clone a large number of insect and mammalian K^+ channel proteins[15]. But this large 'superfamily' does not include two key types of K^+ channel proteins, those activated by ATP or by Ca^{2+} ions. Thus, once one clones a new type of channel protein or transporter, one can rather quickly clone its close relatives, yet increasingly sophisticated expression cloning strategies will be needed to clone entirely new types of membrane proteins. How many families of anion channels exist is an open and pressing question. □

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DAEDALUS

Only connect

BRITAIN, like many other countries, suffers chronically from road congestion. Existing roads can be upgraded and new ones built, but every stretch of extra road is jam-packed from the moment it is opened. Daedalus now proposes to double or triple our road capacity almost at a stroke.

He points out that in a fast stream of traffic, each car is separated from the next by at least ten car-lengths of empty road. This gap gives each driver the chance to see and react to the brake lights of the car ahead, should it decelerate unexpectedly. Simply by halving the reaction time of the drivers, the cars could pack twice as tightly, and road capacity would double.

The obvious technology for this job is the short-range infrared link used to control television sets. An infrared brake light, coded not merely to say that the brake was on, but to relay the changing speed and deceleration of the vehicle, could easily be detected by the car behind. Faster than any human driver, it could apply the appropriate brake force to avoid collision. In the process, of course, it would transmit its actions to the car behind it, and the message would pass down the traffic stream. A forward-shining infrared 'acceleration light', telling each car the speed and acceleration of the one behind, would complete the system. The stream of traffic would become a virtual train, its cars coupled tightly by invisible elastic couplings.

The technology should be quite simple. Many modern cars have power brakes and electronic engine management systems that lend themselves to remote control; the new fittings would be mainly cheap electronics with few expensive mechanics. Two vehicles equipped with the system would establish communication by a 'handshake' of the sort used by fax machines, and would then close up to their safe distance. A dashboard light would warn each driver of the connection, and his instinctive alarm at the tight spacing should soon wear off. Drivers should soon learn to switch rapidly between normal and 'automatic' safe distance perception, just as they switch rapidly between the different safe driving rules for single and multiple carriageways.

Once brought to market, the new system should spread fast. Drivers without it, painfully aware that their car was being shunned by those around, will be shamed by this continuous public demonstration of their disregard for safety, wasteful use of road space, and lack of the latest motoring gadget. All over our newly capacious motorway network, the 'trains' of self-satisfied, tight-packed motorists will increase in length and frequency. Soon only the odd unmodified banger will stagger along in enforced isolation, a pariah of the roads.

David Jones