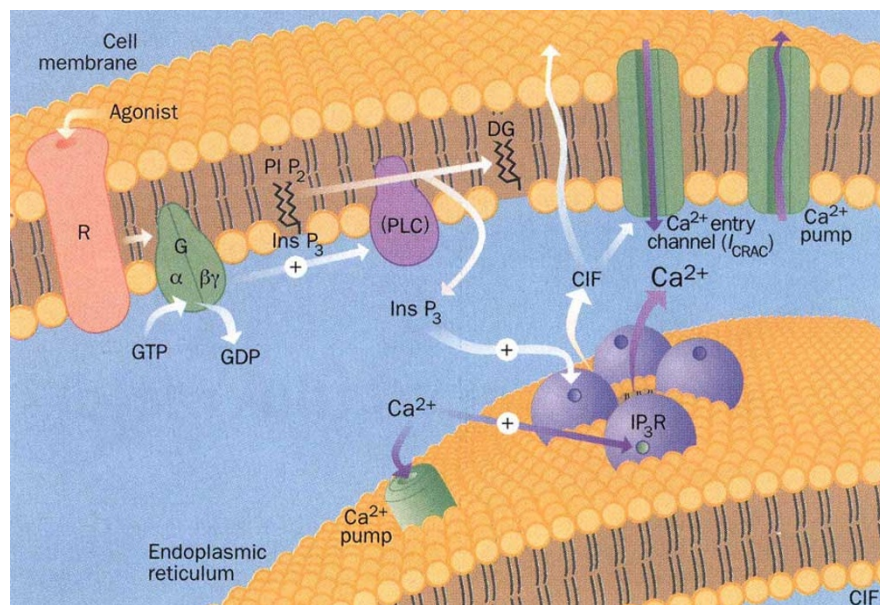


perimental manoeuvres. CIF moves from organelles to cytoplasm, and even across the cell membrane into the supernatant, where it can stimulate adjacent cells. A clever set of cross-desensitization experiments has determined that CIF is not a recognized conventional second messenger.

Independent electrophysiological experiments seem to bear out some of the

there is early evidence from I_{CRAC} (ref. 9) and calcium measurements¹⁰ which hints at the involvement of small G proteins as the coupling messenger. I_{CRAC} is not the only channel admitting calcium at hyperpolarized potential after calcium release⁷. Finally, other proposed direct coupling schemes between the ER inositol-trisphosphate receptor and the plasma-membrane repletion channels^{11,12} have



CIF, or calcium influx factor, is apparently released from intracellular organelles when calcium stores are depleted. CIF opens calcium influx pathways, probably ion channels, to admit calcium back into the cytoplasm where Ca-ATPase transporters then pump it back into the cell's stores. In many cells, calcium is released from the endoplasmic reticulum (ER) via activation of the inositol trisphosphate (InsP_3) receptor. Many GTP-binding protein receptors are coupled to phospholipase C to break down phosphatidylinositol bis phosphate (PIP_2) into diacylglycerol (DG) and InsP_3 . InsP_3 opens a receptor/channel on the ER membrane to allow calcium to flow out of the ER into the cytoplasm.

main characteristics of the mobile factor. Using *Xenopus laevis* oocytes expressing 5HT_{1C} receptors, Parekh and colleagues show that an I_{CRAC} -like current is enhanced by okadaic acid, a serine/threonine phosphatase inhibitor (class 1A, 2A). Furthermore, when a piece of plasma membrane is ripped from the cell the intrinsic mechanism runs down, but if the excised patch is crammed back into the cytoplasm at a different cellular location, the patch may once again respond. This indicates that a diffusible phosphorylated calcium influx factor is inactivated by intrinsic phosphatases, supporting key aspects of CIF.

Is CIF the long-sought factor? Are there alternative mechanisms? The two reports published here will almost certainly not settle the issue. First, CIF has been only partially characterized and a crucial experiment, the activation of I_{CRAC} by CIF in an electrophysiological assay, has not yet been done. Also, after longer incubation periods in okadaic acid, refilling of stores is apparently uncoupled rather than enhanced¹⁸. Furthermore,

yet to be tested experimentally. Only time will tell if CIF will join the ranks of unexpected, new second messengers such as nitric oxide and cyclic ADP ribose. In the meantime, these results will provide new tools and stimulate further experiments to elucidate one of the cell's most important control mechanisms. □

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DAEDALUS

How to be loved

ONE of the saddest facts of human life is that the demand for love greatly exceeds the supply. Hence such diverse phenomena as agony columns, romantic novels, philosophy, creative art, domestic pets, and crime. The artist, it is said, is belatedly seeking the love and approval he did not get in infancy. And it is the children of broken homes and fostering agencies who, starved of early love, develop into thugs and vandals.

In this connection, Daedalus recalls the strange psychiatric syndrome of free-floating anxiety. The sufferer isn't anxious *about* anything; he's just anxious. Similarly, many teachers encourage their pupils to feel free-floating self-esteem, despite having nothing much to be esteemed for. And we all envy the free-floating celebrity enjoyed by those popular figures who aren't celebrated for anything: they're just celebrities. So, says Daedalus, what we need is a way of inoculating children with free-floating belovedness — the sense of being loved or having been loved, not by anyone in particular, just loved in the abstract.

This apparent spiritual problem may in fact be biochemical. Simple anaesthetics can abolish from the brain its magical property of consciousness. Anxiolytics and tranquillizers can conquer the dark forces of misery and loosen the grip of obsession. So DREADCO's biochemists are now seeking the molecular basis of belovedness. They are studying the brains of young hooligans knifed or shot by their fellows, and comparing them with those of happy and stable citizens who, less deservedly, have also met with fatal accidents. Somewhere in this complex comparison, they hope to spot the key enzyme level or neurotransmitter-ratio which, once properly set, gives its owner the ontological security of feeling that he has been loved.

DREADCO's 'Be-Loved'® will be loaded into the child's own T-cells. They will then be injected back into him, to carry the drug through the blood-brain barrier. It will then trip the vital biochemical switch normally tripped by growing up in a secure family. The resulting permanent sense of belovedness and self-worth will be an enduring inoculation against crime. It should be given pre-emptively: ideally at parental separation, and certainly no later than first conviction. Be-Loved will be vastly expensive — it will push the state of the art to develop. But it will easily be paid for by the wholesale closure of police and social services departments. The entire underclass of their clientele will be transformed into stable, hard-working, complacent, artistically untalented citizens.

David Jones