γ-exon. An ICER-specific exon between the Q2 region and γ-exon contains the translational initiation site. The ICER gene product, therefore, encodes a 120-amino-acid protein from the carboxy terminus which includes the DNA-binding domains of CREM, but not the amino-terminal phosphorylation domain (P-box) or the two glutamine-rich domains. Like other CREM isoforms, ICER shows plained by desensitization of receptors or by other steps upstream of cAMP, because it is seen in the presence of cAMP analogues. Instead, it could be that ICER expression, which peaks at a time corresponding to the declining phase of the NAT, leads to repression of NAT/regulator gene expression (Fig. 2). Because ICER itself is induced by cAMP treatment in the pineal, one would im-

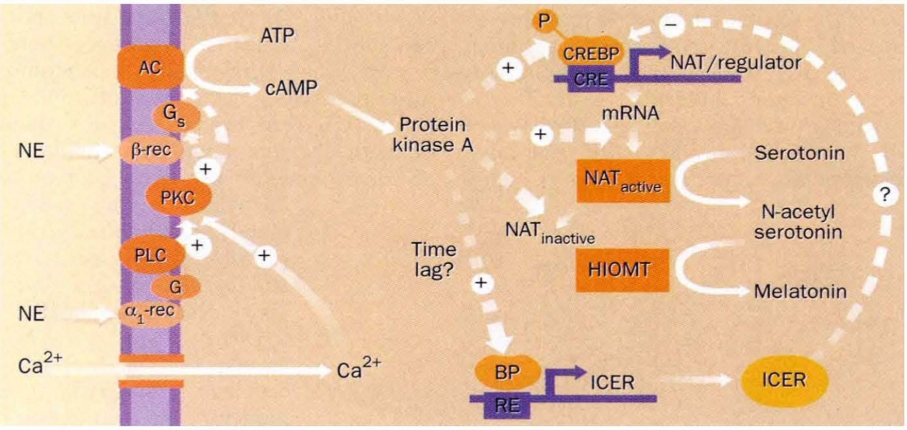

FIG. 2 Proposed scheme for adrenergic regulation of pineal melatonin biosynthesis and ICER gene expression. AC, adenylate cyclase; G, G protein; rec, receptor; NE, norepinephrine; PKC, protein kinase C; PLC, phospholipase C; CREBP, CRE binding protein; HIOMT, hydroxyindole-O-methyltransferase; BP, binding protein; RE response element. Adapted from refs 2,3.

differential splicing of the two alternative DNA-binding domains and of the γ-exon. But ICER is the first example of a CRE-binding protein that does not have the P-box, which means that the level of expression may be the main determinant of its activity.

In some elegant experiments, Stehle *et al.* show that ICER is a powerful repressor of cAMP-induced transcription (the most potent of the CREM family yet tested). It also appears that ICER is the predominant form of CREM expressed in most tissues, the highest levels being found in neuroendocrine cells such as those of the pineal, pituitary and adrenal glands.

In the rat pineal, ICER is under circadian control. As with NAT, ICER mRNA is induced at night and peaks about 6 – 9 hours after lights off. The nocturnal elevation of ICER mRNA is under adrenergic regulation because it is blocked by superior cervical ganglionectomy and by β-adrenergic antagonists. Furthermore, treatment with β-adrenergic agonists or with cAMP analogues in organ culture mimics the nocturnal induction of ICER, showing that elevation of cAMP can induce ICER gene expression.

The time course of ICER expression in the pineal both suggests what ICER may do and can explain a long-recognized paradox in the pineal. Continuous treatment of pineal glands with norepinephrine or dibutyryl cAMP causes an increase in NAT which reaches a plateau after 6 – 12 hours and then decreases to baseline levels[9]. That decrease cannot be explained agine that ICER should also negatively regulate its own gene expression. If so, the inability to induce ICER expression in the pineal during the day[1] may reflect ICER autorepression.

So far, only a few examples of circadian clock control of transcription have been described[10]. Along with the *period* gene of *Drosophila*[11], ICER now provides an example in which circadian regulation of gene expression is accompanied by a feed-back loop. Perhaps in cases of dynamic gene regulation, simple unidirectional regulation such as the use of an activator may not be adequate. Rather, it may be that we will come to see the importance of negative feedback loops in which both positive and negative regulation of rhythmic gene expression occurs using a 'push-pull' mechanism. □

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DAEDALUS

Traffic pressure

MANY racing cars are designed to have 'negative lift'. The airflow over them pushes them down on the road, increasing the traction of their tyres. Daedalus is now taking this idea to extremes. His new 'suckercar' has a massive extractor fan to suck air from underneath it. The force holding it down on the road can exceed its own weight. So it can adhere to a vertical wall, and can even run upside-down across a ceiling.

The design is largely a direct inversion of conventional hovercraft practice. The fan of the suckercar consumes very little power; a mere 0.02 atmospheres of underpressure can exert the required force, and a skirt brushing the road all round the vehicle restricts inward leakage of air. The fan, however, is continuously variable. At every instant, it delivers the exact adhesive suction required.

On the open road, the fan runs quite slowly, giving just enough adhesion to hold the car's smooth, energy-efficient tyres firmly down on the tarmac. During braking, acceleration or cornering, it sucks harder to prevent skidding. In an emergency, it can suck the car down so ferociously as practically to anchor it to the road. This powerful adhesion could be vital in a crash. A firmly anchored suckercar could not be overturned or kicked along by a collision, and its occupants would be safe from whiplash and other accelerational injuries.

On a wet or icy road, quite vigorous suction is needed to maintain traction. But in serious flooding or in deep soft snow, the fan can be reversed. It then blows downwards, lifting the vehicle and permitting it to make slow but safe progress as a true hovercraft.

The suckercar comes into its own on vertical or inverted surfaces. The full power of the fan is needed to hold the vehicle in place. But it can then navigate the most forbidding mountainsides and overhanging cliffs. Elevated motorways will suddenly double in capacity as their undersides become available; sucker traffic will crowd the hitherto wasted walls and roofs of road tunnels. Sucker fire engines and ambulances will be able to drive straight up the sides of stricken tower blocks, park safely under full suction, rescue people from the top floors, and drive down again.

Weak or pot-holed roads may be a problem. The suckercar's 'negative air-cushion' should be too weak to inhale manhole covers or loose cobbles; but open drains and deep pot-holes may gust air unpredictably into it. Daedalus is fitting fast-acting servos linked to a constantly pumped reserve vacuum tank. For a crucial moment, it can suck as hard as such cavities can blow. David Jones