system, a number of dwarfism and gigantism syndromes in man have been explained by mutations in one of the encoding genes. For example, a point mutation just on the carboxy-terminal side of the Pit-1 homeodomain causes a dominantly acting human combined pituitary-hormone deficiency of growth hormone, prolactin and thyroid-stimulating hormone[4], with a phenotype like that of the recessive Pit-1 mutant mouse. Consistent with its genetic dominance and similarity to the null phenotype, this mutant protein acts as an antimorph on testing for ability to transactivate a reporter gene while retaining the ability to bind DNA. Thus this mutation points to an amino-acid residue that can interfere with transactivation of downstream genes. Other less syndromic pituitary dwarfisms are caused by mutations in growth hormone itself, which can be treated with growth hormone injections, or in the growth hormone receptor, which cannot be treated in this way. So far, no pituitary dwarfism syndromes have been associated with mutations in GRF, though some have been treated with the hormone. There is some evidence that the molecule is expressed in the placenta as well as in the hypothalamus, and so might regulate other essential secretion and proliferation processes[5].

Some giants have also been explained in terms of the molecules in this signalling pathway. GRF was originally identified from a pancreatic tumour that secreted high levels of GRF and caused proliferation of somatotroph cells and excessive secretion of growth hormone, leading to acromegaly (chronic growth of hands, head and feet); and overexpression of GRF in transgenic mice causes gigantism[6]. Some human pituitary tumours that lead to acromegaly are caused by a dominant activating mutation in a G_s α-subunit which constitutively activates adenylate cyclase to cause proliferation of pituitary cells. But the same mutations in this gene cause the more pleiotropic multiple endocrine neoplasms in McCune–Albright syndrome[7]. This G_s α-subunit must function in a variety of tissues so that the activating mutation deregulates a number of signalling pathways.

The cloning of the GRF receptor provides another reagent with which to search for genetic linkage to particular dwarfism or gigantism disorders. As the GRF receptor is specific to the pituitary, loss-of-function mutations in it should lead to non-syndromic dwarfism that is resistant to GRF treatment. The *little* mouse mutant is a candidate GRF-receptor mutant. The *little* mutant does not respond to GRF but does respond to growth hormone, suggesting that it is defective in hypothalamic signalling[8]. In addition, the defect in growth hormone secretion can be bypassed with the adenylate-cyclase activator forskolin or the G_s activator cholera toxin, implying that the downstream signal transduction pathway is normal in this mutant. A key experiment is to show that the GRF receptor is closely linked to *little* and to look for allele-specific DNA sequence changes. Studies of human dwarfs showing similar responses to GRF and growth hormone should reveal loss-of-function mutations in the GRF receptor.

Dominant activating mutations in the GRF receptor would be expected to have the opposite phenotype, gigantism. Because the GRF receptor is a member of such a well-studied gene superfamily, an arsenal of results from yeast to man predict the function of GRF receptor domains and the consequences of mutations in those domains. For example, the carboxy-terminal cytoplasmic domain of the seven-helix transmembrane β-adrenergic and yeast α-factor receptors negatively regulates their coupling to G_s so that deletion of this domain causes hypersensitivity to their ligands[9,10]. Similar mutations in this domain of the GRF receptor would be expected to cause hypersensitivity to GRF which could lead to somatotroph hyperplasia or tumours. In fact, there are pituitary tumours that do not carry mutations in the G_s α-subunit. However, a number of these pituitary tumours do not increase cAMP levels, suggesting that they are caused by mutations in protein kinase A which decouple it from its normal regulator cAMP, or act downstream of this point. Still, there is a strong pointer to the GRF receptor mutations that should be searched for in acromegalic tumours or in very tall people.

Given the dramatic progress in explaining and treating the underlying causes of dwarfism and gigantism, soon the endocrinologists will outnumber the dwarfs. They will keep busy, I predict, by studying the more subtle genetic variations in those of us whose height is fewer standard deviations from the mean, and of course by treating those who wish to move along the curve. □

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DAEDALUS

Cold light

DAEDALUS is surprised that astronomy works at all. We see the stars and galaxies through a thin veil of interstellar gas. It may be very tenuous, but surely it should blot out almost all distant objects by its sheer enormous thickness? If the enigmatic 'dark matter' of the Universe is also interstellar gas, the problem becomes even more severe. One possible escape is that interstellar gas is very cold. Most of it should be at 3 K, the background temperature of the Universe. Many conductors become superconducting at this temperature; by analogy, Daedalus expects that many insulators become super-transparent. They cease to interact electromagnetically, and their optical extinction coefficients go to zero.

This idea could easily be tested by cooling an optical fibre of known extinction coefficient in liquid helium. With good fortune, it would become super-transparent, so that light launched into it would travel for ever. A super-transparent fibre, closed into a ring and separated from its light source, should trap some light in endless circulation. Break it open some time later, and you should see a little flash as the trapped light escapes.

Such an effect could transform information technology. Supercooled optical fibre, needing no intermediate booster amplifiers, could greatly simplify telecommunications. A camera or photometer that did not merely record the effects of light, but trapped an actual sample of it for later study, could also be appealing. But the major implications are in optical computing. If light can be trapped in endless circulation, it could form the long-sought optical memory for such a computer. The crucial circuit element would be a circular loop of super-transparent fibre coupled to some sort of nonlinear optical switch. The switch would be triggered by a light pulse that altered its refractive index, flipping it briefly from total internal reflection to full transmission. The optical pulse train to be stored would enter the loop; by the time it had completed a circuit the switch would be reflecting again, and it would be trapped in continual circulation. The memory element could be interrogated at any time by flipping the switch again, thus recovering the stored pulse train. Unlike conventional semiconductor memories, a super-transparent memory would draw no power, and would continue to hold data when the computer was turned off.

Daedalus is now dreaming up other uses for stored light. He likes the idea of storing samples of summer sunlight for release in winter; but the volume of fibre required looks forbidding.

David Jones