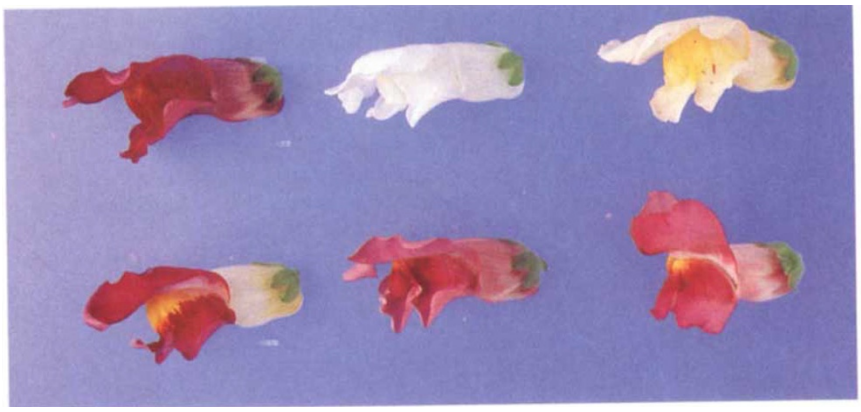
A portable palette



THE first issue of *The Plant Journal* comes adorned with a multicoloured display of mutant flowers prepared by Rosemary Carpenter and colleagues of the John Innes Institute in Norwich (**1**, 59–69; 1991). The new pigmentation mutants are generated by inserting transposons at key sites in the genes of *Antirrhinum majus*. Transposons are mobile genetic elements that can insert themselves at random in the genome, inactivating genes whose coding sequence is disrupted by the insertion or activating others when a promoter or transcriptional activator fortuitously results from the mutation. The phenolic pigment anthocyanin is responsible for the colour of *Antirrhinum* flowers, and strategic insertion of the transposons Tam*1,2,3,4* into genes encoding enymes active in anthocyanin synthesis gives the variety of flowers shown.

As the red wild-type flower (top, left) develops, anthocyanin synthesis normally follows a temporal and spatial pattern which defines different areas of the flower corolla. Synthesis starts in a ring at the base of the tube and in the lobes; the tube then realizes its full colouring. The other flowers result from transposon mutagenesis in different loci. The *nivea* locus encoding a synthase for the pigment precursor chalcone gives an albino bloom (top, centre) when it carries Tam*4* in its first exon: the mutant chalcone synthase is incapacitated by being longer than it should be. A Tam*1* insert in *incolorata* gives tinged ivory flowers (top, right) which result from a later block in the pigment synthesis pathway. Disruption by Tam*2* of *delila*, a gene that regulates the spatial distribution of anthocyanin, results in a bloom with coloured lobes and an ivory tube (bottom, left). The gene affected in the last two flowers, *daphne*, participates in the synthesis of flavones, the co-pigments that add brilliance to the anthocyanin colour. Here the flavones are missing, hence the dullness of the flowers. With the genetic engineer's increasing dexterity in manipulating pigmentation, who says the leopard still cannot change its spots? □

CELL BIOLOGY

The Janus factor

R. M. Warn

SCATTER factor and hepatocyte growth factor are two proteins with very different origins from which it would have been rather hard to deduce a common link. However last year Gherardi and Stoker[1] proposed, on the basis of sequence similarity of the N-termini, that the two were either similar molecules or even identical. The second proposal is now confirmed by Weidner *et al.*[2] who demonstrate, by a variety of criteria, that they are the same protein, and also give a chromosomal location — region 11.2–21 on the long arm of chromosome 7 — for the human factor.

Scatter factor was originally identified as a protein secreted by fibroblasts which disperses epithelial colonies of a variety of cell types in culture[3]. Subsequently it was found that smooth muscle cells also secrete the factor and endothelial cells too are scattered by it[4]. Scattered cells are highly motile, continuously extending processes by mechanisms reminiscent of neuron growth cones and retracting them in similar manner to the snap-back of fibroblast processes[5]. But scatter factor was not found to act as a mitogen for at least one kidney epithelial line susceptible to colony dispersion[6].

In contrast, hepatocyte growth factor was first recognized as a constituent of the serum of patients with fulminant liver failure[7] and that of partially hepatectomized rats[8], and was further found to be a potent mitogen of hepatocytes in culture. It was therefore initially recognized as a growth factor involved in liver regeneration. No effects on cell motility were reported for the assay systems used. The two molecules were only realized to be the same when sequence data became available. The final demonstration is that fibroblast scatter factor stimulates primary hepatocytes to divide and recombinant hepatocyte growth factor causes dispersion *in vitro* of a variety of epithelial colonies[2,9].

The molecule, which perhaps should now be known as HGF–SF, is a heterodimer; purified human factor shows several forms and consists of a large and a small subunit with relative molecular masses of 54,000–65,000 and 31,000–35,000 respectively. The large subunit contains four kringle modules, domains that are present in a variety of proteins including plasminogen and plasminogen activator and that are implicated in protein–protein interactions[10]. The smaller subunit resembles the catalytic subunit of plasmin and other serine proteases, with the difference that the histidine and serine residues of the active site are replaced and so the molecule shows no protease activity.

Only a few months ago, the receptor for HGF–SF was identified by two groups[11,12], and it turns out that the receptor is the product of the c-*met* proto-oncogene; c-*met* has been a receptor in search of a ligand for some time, having been first identified in 1984 (ref. 13). It is a membrane-bound tyrosine kinase of relative molecular mass 190,000, and thus has significant structural and functional features in common with the receptors of other growth factors, including platelet-derived and epidermal growth factors.

Now that HGF–SF is known to be a single entity, what conclusions can be drawn concerning the dual nature of the molecule? That certain growth factors promote cell motility has been known for some time (see refs 9 and 14 for reviews). But it is remarkable that HGF–SF can stimulate the motility of some epithelial cells without having any effect on mitosis. What kinds of signal cascade are activated by c-*met* and how they can be varied to have differential effects on cell division and motility are now questions of some interest.

Finally, what is the potential significance of the regulation of cell division and motility by HGF-SF in tumorigenesis, where both cell growth and movement are frequently grossly altered? The molecule induces the migration of transformed and non-transformed epithelial cells into collagen matrices, mimicking the effects of tumour cells in *vitro*[15]. Thus HGF–SF may initiate or enhance the metastatic