



**Figure 1 Morphogen movement.** How a gradient of Hedgehog (Hh) protein might form, as proposed by Eaton and colleagues<sup>1</sup>. **a**, Lipoprotein particles are made in the fat-body and distributed throughout a fruitfly larva, coming into contact with the imaginal discs. **b**, A blow-up of an imaginal disc close to its anterior (A)–posterior (P) boundary. Posterior cells secrete Hh, producing a gradient of Hh-charged lipoprotein particles and a counter gradient of uncharged particles. **c**, Blow-up of A and P cells, showing some of the steps that produce and transduce the Hh gradient. 1: The Hh precursor cleaves itself and is added to cholesterol to form Hh–Np. 2: Palmitic acid is added. 3: The protein is transported to the plasma membrane. 4: The Dispatched protein might help to load Hh into lipoproteins. 5: Loaded particles diffuse somewhat, with the help of heparan sulphate proteoglycans (HSPGs) and the Shifted (Shf) protein<sup>19,20</sup>. 6: Charged lipoproteins bind to receiving cells, aided by the Hh receptor Patched (Ptc) and possibly HSPGs and low-density-lipoprotein receptors (LDLRs). 7: The signal is transmitted to the nucleus.

with HSPGs, which are also important in lipid metabolism<sup>8</sup>. Thus, HSPGs might affect morphogen diffusion, at least in part, by interacting with their lipoprotein carrier. Consistent with this idea, diffusion of a form of Hh that cannot be modified by lipids is independent of HSPGs<sup>7</sup>.

Another fascinating potential link concerns how target cells might bind and take up morphogen–lipoprotein complexes. Lipoproteins have their own receptors, the low-density-lipoprotein receptors (LDLRs), and certain members of this protein family are essential for receiving the Wg signal<sup>9,10</sup>. But it is not clear whether they interact directly with Wg<sup>11</sup>. Perhaps instead they bind the lipoprotein moiety of Wg–lipoprotein particles. Other LDLRs might similarly contribute to morphogen activity<sup>12,13</sup>.

Yet another exciting possibility concerns the mechanism that delivers Hh and Wg from the membranes of the cells that produce them to lipoproteins. Perhaps morphogens associate reversibly with lipoproteins, thus generating a source of morphogen-charged

particles close to morphogen-producing cells. Alternatively, a more active mechanism may exist. Consistent with this notion, the protein Dispatched — a member of the sterol-sensing receptor family — is essential for the release of cholesterol-modified Hh from Hh-producing cells, but is not required for the release of a non-cholesterol-modified form<sup>14</sup>. Thus, Dispatched might be involved in charging lipoproteins with Hh. A similar mechanism involving lipid rafts — specialized regions of the cell membrane — has also been suggested for Wg secretion<sup>15</sup>.

Despite the many possibilities suggested by this model, more questions are raised, in part because both fields have been so productive. How efficiently are peripheral tissues, such as the lumens of *Drosophila* imaginal discs, bathed by lipoproteins? Are lipoproteins the sole carriers for Hh and Wg, or are other mechanisms, such as the formation of micelle-like Hh multimers<sup>16</sup>, also involved? Because Wg and Hh sometimes act on the same cells, do individual lipoprotein particles carry both morphogens at the same



**100 YEARS AGO**

On Sunday, the President of the French Republic entertained the King at the Elysée at a dinner party, at which 120 guests were present. The guests included distinguished authors, artists, musicians, and other representatives of intellectual activity, almost exclusively members of the Institute of France. By inviting leaders of literature, art, and science to meet the King, graceful recognition was given of the high place occupied by the muses in the polity of the Republic. In the days when sheer muscular force was the mainstay of a nation, bodily strength and prowess were rightly regarded as recommendations for Court favours; but now that brain-power instead of muscle determines the rate of national progress, the State that desires to advance must foster all the intellectual forces it possesses. This principle is well understood in France, and is also clearly recognised in Germany, where every man who makes notable contributions to knowledge of any kind, assists industrial progress, or creates works of distinguished merit, whatever they may be, is sure to receive personal encouragement from the Emperor. The presence of these leaders of thought is a striking characteristic of the German Court; while, on the other hand, their absence, and the overpowering influence of military interests, are distinguishing features of Russian, and, let us add, of British Court functions.

**ALSO:**

Satisfactory progress and general prosperity form the key-note of the report of the Zoological Gardens at Giza for the past year. The report is illustrated by the reproduction of a most interesting photograph of an aardvark, or ant-bear, slightly marred by the effect of a shadow by the side of the nose. From *Nature* 4 May 1905.

**50 YEARS AGO**

“Mathematical Association Annual Meeting.” The first item in the afternoon session was a discussion of “The Disadvantages of a Mathematical Education”, led by Mr. W. O. Storer (Department of Education, University of Birmingham); Mr Storer thought that the logical training supposedly given by mathematics might be arid, and that mathematical insistence on accuracy might lead to intellectual arrogance. Some members were reluctant to accept these inferences. From *Nature* 7 May 1955.