Shape-inducing chemical identified

Every creature has humble beginnings as a single, fertilized cell. That cell divides in two, and those two become four, and before long there is born a highly differentiated being, with hundreds of different kinds of cells — bone, blood, nerve, skin — all of them growing in just the right places and in just the right shapes.

This process of differentiation and pattern formation, called morphogenesis, remains one of the least understood areas of modern biology. Put simply: How does a developing cell "know" where it is in the embryo, and so "know" what kind of tissue it's supposed to become?

One popular theory postulates the existence in the embryo of one or more "signal substances" called morphogens. Such a substance, the theory goes, would form a chemical gradient as it diffused from its source—just as a brightly colored dye, when added to water, would become diluted as it began to spread. Embryonic cells — depending on their distance from that source — would be exposed to different concentrations of the chemical, triggering them to develop into different types of cells. But do morphogens really exist? Until recently they've remained the developmental biologist's Holy Grail.

Now, Harvard Medical School researchers Christina Thaller and Gregor Eichele have identified what appears to be the first morphogen — a derivative of vitamin A called retinoic acid. The research, reported in the June 18 NATURE, follows more than 20 years of speculation that morphogens may play a role in cell differentiation.

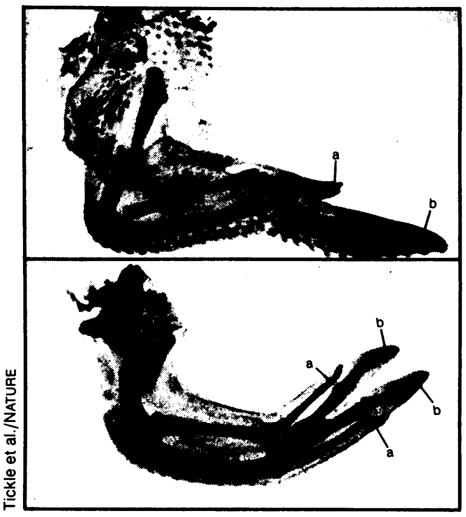
Earlier experiments with chick-embryo limb buds — the tiny clumps of undifferentiated cells that eventually develop into wings or legs—had shown that the transfer of some tissue from the back margin of a bud to the front margin could induce the growth of additional digits in a pattern mirroring the normally occurring digits. Ordinarily, the front margin of a limb bud becomes the little finger or little toe, while the back margin turns into a thumb or big toe. According to the morphogenic theory, there must be some substance produced in the back of the bud that at high concentrations causes smaller digits to develop, and at diluted concentrations (toward the front of the bud) allows for the development of big toes or thumbs. It was unclear, however, what factor in the transplanted tissue stimulated this programmed growth.

The link between retinoic acid levels and limb differentiation was first recognized in 1982, when researchers showed that they could induce the same type of mirror-image pattern by implanting retinoic-acid-soaked bits of paper into the front part of a limb bud. But it remained to be proved that limb buds contained a natural supply of retinoic acid and, if so, that it was present in a naturally occurring gradient.

To settle the issue, Thaller and Eichele dissected more than 5,500 limb buds of chick embryos and used extremely sensitive gas and liquid chromatography techniques to measure the retinoic acid concentrations in different parts of the buds. Their findings confirmed the presence of a retinoic acid gradient, with concentrations about the same as have been shown to induce limb differentiation when applied artificially. As expected, the retinoic acid concentrations were highest along the back margin and lowest along the front margin, supporting the researchers' supposition that retinoic acid is produced in the posterior part of the limb bud and diffuses from there.

The discovery has implications beyond chick embryo development. Earlier experiments have shown that limb morphogenesis in humans is probably regulated by the same substance or substances that regulate morphogenesis in chickens. "All extremities of vertebrates are homologous, or derived from a common ancestral form," Eichele told SCIENCE NEWS, "so many of the very fundamental mechanisms like pattern formation have been conserved completely." Meanwhile, he says, although retinoic acid's role as a morphogen appears to be confirmed, the actual biochemical mechanism of its action has yet to be discovered. To affect morphogenesis, he says, retinoic acid must somehow communicate with the DNA in a cell's nucleus, where it can have some effect on gene expression or on the stabilization of genetic messages.

— R. Weiss



Tickle et al./NATURE

Chick wing (top) displaying a normal digit pattern (a, b) and one with "mirror image" digits (a, b, b, a) caused by application of retinoic acid to the limb bud's front margin.

Déjà vu: Acid rain in China

If you can picture what it was like in Tennessee about 65 years ago, you get a sense of the present air-pollution situation in parts of China. Recent measurements show that precipitation in China tends to have high concentrations of sulfate and calcium ions but relatively low acidity. These levels are similar to those observed around Knoxville, Tenn., in the early 1920s.

This conclusion emerges from a recent comparison of precipitation composition in China, the eastern United States and a remote area in Australia. The report, published in the June 19 SCIENCE, also notes that the sulfate levels in China's rainwater may be high enough to cause "significant and severe ecological changes." The study was conducted by James N. Galloway of the University of Virginia in Charlottesville, Zhao Dianwu of the Institute of Environmental Chemistry at the Academia Sinica in Beijing, and their colleagues.

Rainfall composition in China reflects the country's reliance on coal combustion for electricity generation, home heating and cooking. The available coal generally has a high sulfur content, and it is usually burned in small furnaces or stoves with no pollution controls. With so many low-to-the-ground sources, pollution is kept close to its origin. Sulfate concentrations in Guiyang City, China, for instance, are about six times higher than present levels in New York City. In contrast, the small number of motor vehicles keeps nitrate levels lower than in comparable U.S. areas.

In rural and suburban areas, calcium-rich soils, the extensive use of limestone for building and the emission of alkaline materials by furnaces helps lower rainfall acidity. Precipitation in rural China also has a high concentration of ammonium ions, generated by excretory wastes used as fertilizer. As a result, pH values in China are generally higher than those in the eastern United States.

"The reduction of the acidity, however, does not necessarily reduce the potential for acidification of aquatic and terrestrial ecosystems," the researchers say. The hazard depends more on sulfate concentration than on the acidity of the rainfall itself. Although the potential for ecological deterioration in China is unknown, they say, other areas of the world have suffered damage "at levels of atmospheric deposition of sulfur- and nitrogen-containing compounds that are less than those currently existing in China."

— I. Peterson