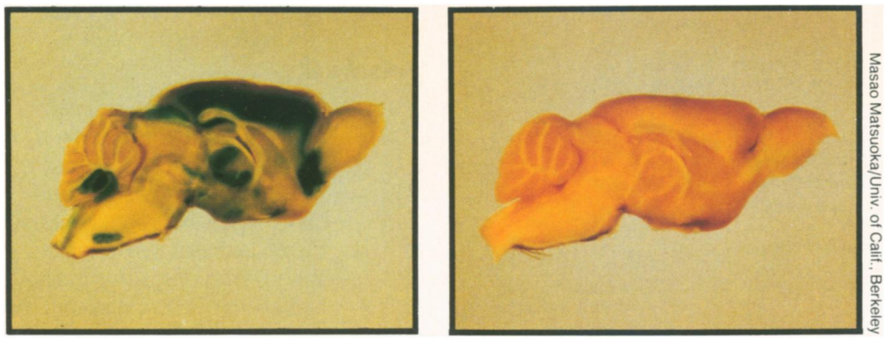
Genes May Shuffle in Developing Brain

In 1987, immunologist Susumu Tonegawa of the Massachusetts Institute of Technology won the Nobel Prize for showing that white blood cells mix and match a handful of genes to make the interchangeable parts that form the millions of different antibodies used by the body to ward off infection. However, researchers have failed to find evidence of this gene-shuffling phenomenon – called somatic, or body-cell, DNA recombination – in cells other than those of the immune system. Until now.

Nerve cells also possess the ability to dice and splice their own genes, reports an international group led by Hitoshi Sakano of the University of California, Berkeley, who worked with Tonegawa on some of the Nobel laureate's most famous experiments. Sakano and his colleagues find that neurons in the brains of mice can rearrange their genes using the same mechanisms as white blood cells. Moreover, the rearrangement accelerates during the development of young mouse pups. The group describes its work in the Oct. 4 SCIENCE.

Researchers in the group hesitate to conclude that this gene rearrangement plays a role in the specialization of the brain's different regions during early life. But they say they plan to investigate whether the shuffling process helps initiate the brain's development by turning some genes on and others off.

To make their discovery, the team created genetically engineered mice whose cells contained a backwards copy of a marker gene. In its correct orientation, this gene produces an enzyme that can cause cells to turn blue. The researchers flanked the inserted marker gene with two stretches of DNA involved in the gene rearrangement of white blood cells. They reasoned that if neurons could recombine their own genes, some of the cells would cut out the marker gene and flip it over, causing the gene-shuffled cells to stain a telltale blue.



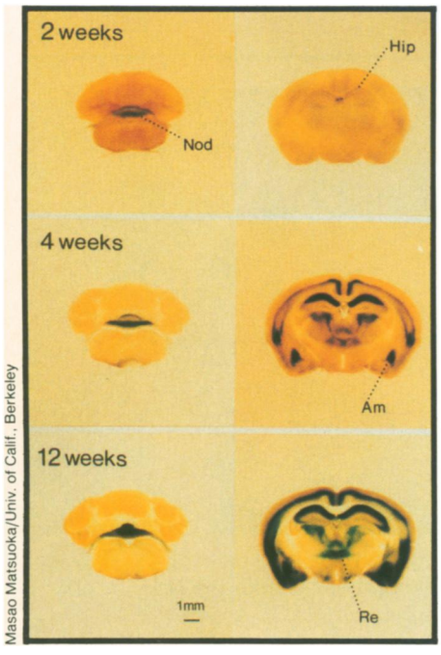
Masao Matsuoka/Univ. of Calif., Berkeley

Bluish tint appears in mouse brain regions containing the rearranged marker gene (left), but not in a brain lacking the gene (right).

To the researchers' surprise, brain neurons in the transgenic mice did reorient the marker gene. Sakano's team detected the blue stain in 78 particular areas of the mice brains – most of which they knew served to link sights, smells, sounds or pain with an appropriate response, such as eating or fleeing. The brains of older pups stained more darkly, the researchers noted, and also contained a larger number of stained regions, suggesting that neuron genes rearranged more often as a young animal matured.

"We've shown that genes can recombine in the brain," says Berkeley immunologist Linda Kingsbury, a member of Sakano's group. But she cautions that the team cannot tell how often the phenomenon occurs in normal neurons, because they studied a foreign marker gene flanked by splicing sequences used by white blood cells. "It may be that the sequences we put in are not used at all in the [normal] brain," she says.

David T. Larue of Berkeley, a neuroanatomist on the team, adds that researchers cannot determine whether gene rearrangement plays a role in brain development until they can find that one of a neuron's own genes is shuffled before birth and as a mouse pup matures. Until then, "we won't know if this is occurring as part of any real developmental sequence," he says.



Masao Matsuoka/Univ. of Calif., Berkeley

Slices from the hindbrain (far left) and midbrain (left) reveal larger bluish areas of gene rearrangement as mouse pups mature after birth. Abbreviations denote specific brain regions.

Nevertheless, "one can't help but feel very excited and intrigued by [Sakano's team's] results," says David G. Schatz of Yale University. Two years ago, Schatz and several colleagues reported identifying the gene that activates the genetic swap in immune-system cells. Schatz's team also found that the gene, named recombination activating gene-1, is turned on in neurons. But he cautions that Sakano's team needs to rule out the possibility that the brain DNA might recombine randomly. "It's absolutely essential that their experiments be repeated in other strains of mice," Schatz says. – *C. Ezzell*

Saturn's white spot: Driven by the sun?

A puzzling white spot mars Saturn's normally featureless face about every 30 years. Astronomers now report data suggesting that a seasonal change in solar heating may trigger storms that produce this short-lived phenomenon.

The most recent giant spot erupted over Saturn's equator last October, catching many astronomers by surprise (SN: 10/13/90, p.228). But Agustin Sanchez-Lavega and his colleagues were ready. They had predicted the spot's occurrence based on the frequency of the last four to blemish the ringed planet. By June 1990, the researchers had one telescope in Japan and three more in France trained on Saturn, awaiting the spot's debut.

Their 48 nights of observations, made over a range of visible-light and near-infrared wavelengths from late September through November, provide the most detailed information yet on the phenomenon, asserts Sanchez-Lavega, of the University of Pais Vasco in Bilbao, Spain.

One widely accepted theory attributes the spot to storms that shoot a blob of warm gas up from Saturn's lower atmosphere and through a thick upper mantle of old, smog-stained ammonia ice. As the