

## Transposons make themselves at home

Segments of DNA that move in and out of chromosomes have been found in organisms ranging from bacteria to vertebrates (SN: 4/28/84, p. 259). From species to species, these transposons are similar in their structure and mechanism of movement. But the organism in which they reside controls when a transposon expresses the information it carries, says Gerald R. Fink of the Massachusetts Institute of Technology. He has discovered several yeast genes that regulate expression of yeast transposable elements. For example, one gene, called *spt3*, is required for the expression of all 35 or so transposons of the family called Ty, which plays a role in yeast mating. These transposons are scattered throughout the yeast DNA. Mutation in the *spt3* gene has profound effects on mating and sporulation, Fink says. He concludes, "The existence of host genes which affect the expression of a Ty element suggests that the element is not autonomous. Perhaps extended residence in an organism places a transposable element under regulatory control by that organism."

## Aging at the nerve-muscle junction . . .

The trials of old age include reduced physical strength. Some of the decline seems the product of deficient communication between nerve and muscle cells, reports Dean O. Smith of the University of Wisconsin in Madison. He has determined anatomical and biochemical changes occurring at the neuromuscular junctions of rats between the time they are mature adults 10 months old (the equivalent of 40 years old in a U.S. male) and elderly rats 28 months old (the equivalent of 73 years old in a U.S. male).

The number of nerve cell endings per muscle cell increases with age, Smith reports. But that increase does not lead to more effective communication between the cells, because there is at the same time a reduction in the amount of transmitter chemical, acetylcholine, in each nerve ending. Smith believes this decrease is due to an increased leakage of acetylcholine from the ending. He finds in elderly rats a leakage rate 11 times that of mature rats. But the same amount of transmitter is released in response to a nerve impulse. "So the tendency is to run out of transmitter faster," he says.

A consequence of the greater number of nerve endings is that muscles of elderly rats contain elevated numbers of acetylcholine receptors per endplate. But Smith finds that many of these receptors are of the less effective of two known receptor types. Old rats have twice the proportion of "extrajunctional" receptors normally associated with denervated tissue.

The effects of stress and exercise on aging are also being examined at the neuromuscular junction. Smith reports that in work done with Julie Rosenheimer, stress—daily mild electrical shocks to the feet—enhances age-related changes in a rat leg muscle; while running exercise ameliorates this enhancement. In contrast, in the diaphragm muscle, stress augments the aging process and exercising the animal further increases the age-related changes.

## . . . and at nerve cell junctions in the brain

Deficits in learning, memory and the ability to pay attention are, like decreased physical strength, common problems of aging. These behavioral deficits have been attributed to deficient acetylcholine release by nerve cells within the brain. Attempts to reverse these problems by supplying a precursor of acetylcholine have been equivocal. Now Gary E. Gibson of Cornell Medical College in New York suggests that the problem may be in the distribution of calcium ions, which are required for normal nerve cell signalling.

Uptake of calcium by nerve cells decreases with age. The uptake can be stimulated with drugs called aminopyridines, Gibson

reports. He says that in rats these drugs can "totally ameliorate" the great decrease with age in a measure of attention—ability to maneuver on a tightrope—and can improve memory as measured in a maze test. One type of aminopyridine is already in medical use for Eaton-Lambert syndrome, a defect in acetylcholine release at the neuromuscular junction. This drug is now being tested at Cornell in Alzheimer's disease patients, who show exaggerated symptoms of old age. A recently reported study in The Netherlands has already given promising results. Gibson says that his animal tests show another aminopyridine to be more effective and less toxic than the drug used in these human tests. But because it has not been used therapeutically, it must undergo extensive toxicological testing before it can be employed in any clinical trial.

## Odds of grandparenthood

The inheritance of genetic markers has long been used to provide evidence of paternity. Now geneticists are suggesting that the same analyses might be extended to establish or exclude familial relationships beyond parenthood. There are cases, unfortunately frequent in some countries, for example Argentina, where small children were abducted and their parents are dead or unknown. Such children could be returned to grandparents if the relationship could be demonstrated, French geneticist Pierre Darlu told a symposium on the role of forensic sciences in the documentation of human rights abuses. Darlu and Luigi L. Cavalli-Sforza of Stanford University have calculated the potential strength of such an analysis.

When all four grandparents are available, the 18 classical genetic characteristics, including blood and tissue type (HLA) markers, can give 95.5 percent certainty in excluding a random group of four putative grandparents with respect to a random child. This statistic means that among 1,000 groups of four possible grandparents, 995 would be excluded as being the grandparents of a particular child. Determination of the classical genetic characteristics costs about \$400 per person.

The power of the genetic approach can be increased by using a recently described set of 22 genetic characteristics, called DNA polymorphic systems, that are now analyzed in only a few laboratories. With this additional information, the probability of exclusion can be raised to 99.6 percent for four grandparent sets. When only the maternal or paternal grandparents are available, the probability of exclusion would be 61.7 percent for the classical genetic systems and 84.1 percent when the DNA polymorphic systems are added. In paternity cases, a 95 percent level of exclusion is considered as strong evidence.

## Fingertip control and piano tone

Can a pianist, by altering how he or she presses down on a piano key, produce two notes of equal loudness but with different tonal qualities? For decades, some scientists have contended that there is no measurable difference between the tone produced by a human hand and one produced by a mechanical striker. The tip of an umbrella will do just as well as the finger of a concert pianist, they argued, because no amount of rocking, wiggling or caressing of a piano key, after a stroke sets the hammer in motion, can modify its action upon a string. On the other side of the controversy, many musicians and critics have maintained that a piano virtuoso's "touch" is no illusion. Now, a better understanding of what constitutes a piano's sound is helping to resolve the debate and promises striking improvements in the sound of concert grand pianos.

With the right piano, a virtuoso can draw out subtle gradations of tonal quality at any level of intensity, say Asami T. Alberti and Ramon A. Alba of the Philsonic Institute in New York. The effect

occurs because the piano is a "doubly percussive instrument," they say. Not only does a hammer strike against a string, where the hammer's speed determines the loudness and basic tone color, but the impact of the piano key upon the keypad also adds "noise." This noise is conducted from the keypad to the sounding board by way of the piano case. The blend of these two sounds—the string's ring and the keypad's thud—produces the subtle tone qualities that concert pianists try to achieve.

Taking advantage of this new insight, Alberti spent five years improving the touch and tone of a Steinway concert grand piano. This involved changing a piano key's balance and responsiveness so that it more faithfully reproduced a pianist's motions. It also meant controlling all the noises that could be generated within a piano and enhancing desirable qualities.

The result is a piano that allows "the musician to express even more subtle and delicate music, especially in the quieter ranges," says Alba. The softest sounds can range from a distant, bell-like tone to a feather-light, sighing sound, while the loudest sounds can be harsh and clangorous or rich and full. A recent test involving more than 100 piano students at the Juilliard School in New York showed considerable enthusiasm for the new piano's touch and responsiveness. Alberti is now ready to apply her techniques to modify existing concert pianos or to begin building "a new generation of concert instruments."

## Life in a maddening crowd

Living in crowded quarters is associated with poor mental health. These effects are generally explained by excessive social obligations and lack of privacy. Now Michael Hughes of the Virginia Polytechnic Institute in Blacksburg provides a more detailed analysis of crowding's mental health effects. Working with Walter R. Gove of Vanderbilt University in Nashville, Tenn., Hughes uses the number of persons per room occupying a residence as a measure of crowding. He finds that the type of household and the role of a person within a household can contribute to how severely crowding exerts its negative effects.

Crowding has the greatest negative effects on the mental health of unmarried parents (primarily women) living with their children. The effect of crowding is moderated when there is another adult, for example a grandparent or cohabitant, in the household. Among married couples with children, crowding more strongly affects women than men. Among unmarried adults without children, crowding is not a significant predictor of mental health, Hughes finds, although he cautions there were few such people in his sample.

## Health effects at a toxic waste site

More than a decade ago, a now-bankrupt chemical treatment company mishandled a large volume of chemical wastes on a 5-acre site within 400 feet of a densely populated, residential neighborhood in Lowell, Mass. Three years ago, the state government finished removing hundreds of barrels, many of them leaking, from the site but left behind the contaminated soil. A new study, directed by David M. Ozonoff of the Boston University School of Public Health, now reveals that residents of the "target" area show a higher incidence of respiratory ailments than people living in a "control" area farther away. However, the results also show that the target population did not experience an unusual degree of reproductive problems or of cancer.

Ozonoff concedes that target-area residents may have had better recall of symptoms than those in the control area. Nevertheless, he says, "It is not possible at this time to say that the waste site is or is not the cause of these findings, but the results are consistent with such an effect. . . . Speedy abatement of any remaining exposures from the site is indicated."

## RNA twist in cancer therapy

When researchers talk about "the mismatched inducer," they're not discussing a mystery novel or summer movie. They're referring to Ampligen (poly [I]-poly [C<sub>12</sub>U]), a potential anticancer drug that stimulates the body to make interferon by mimicking viral infection. In its first clinical trials, seven of 12 cancer patients treated with Ampligen "have shown some level of antitumor response," reports William A. Carter of Hahnemann University in Philadelphia, who helped develop the drug. Hahnemann spokeswoman Phyllis Fisher cautions that these "Phase I" clinical trials were designed to test Ampligen for side effects and do not establish its therapeutic value.

By enhancing the body's immunological defenses, the drug may help the body "control and eliminate residual tumor cells," according to Ampligen's coinventor Paul O.P. Ts'o of Johns Hopkins University in Baltimore. The key to Ampligen's success as a "biological response modifier" is its charade: It's a synthetic double stranded (ds) RNA. RNA is usually single stranded in cells, but certain viruses make dsRNA during part of their infection cycle. Thus when cells recognize dsRNA, they "interpret" it as a viral invasion and mount an immune response, which includes interferon production, says James J. Greene of Catholic University of America in Washington, D.C., who collaborates with Ts'o. Interferon shouldn't get all the credit for Ampligen's apparent anticancer properties, Greene notes. "Double stranded RNA will also inhibit cell division and that mechanism of action is not mediated through interferon," he says. "Its spectrum of action may overlap interferon's, but it definitely has its own special activity."

## High lead doses inhibit male hormone

Researchers concerned about the effects of workplace contaminants on male reproduction usually focus on fertility, but the damage may be more subtle, reports Larry Ewing of Johns Hopkins School of Public Health in Baltimore. He found that male rats exposed to high doses of lead in their drinking water were able to impregnate females, but showed a sharp drop in production of testosterone, a hormone crucial to differentiation of embryonic reproductive organs and important in adult sexual behavior. Low doses of lead—below levels that induce symptoms of lead poisoning in humans—do not trigger the hormone drop. Still, the results hint that current tests for toxic effects on the reproductive system may not be sensitive enough, Ewing says.

## Food and drug capsules

- Diabetic patients given large daily doses of the sugar substitute aspartame, equivalent to levels consumed in 14 cans of diet soda, reported fewer side effects than subjects given an inert placebo in a study at the University of Illinois in Chicago. "More than twice as many adverse reactions were reported by those on placebo," Jeanine K. Nehrling told a meeting of the American Diabetes Association (ADA) this week. Nehrling and David L. Horwitz studied 62 diabetics for 18 weeks, including insulin dependent and non-insulin dependent patients, in their quest to help confirm or refute anecdotal reports that aspartame is associated with headaches, dizziness and mood changes (SN: 8/27/83 p. 134). ADA officials concur with the researchers that the sweetener is a useful sugar alternative for diabetics, "provided it is not used in excessive amounts."

- Claims by more than 400 Britons against the Indianapolis-based Eli Lilly Co. regarding its anti-arthritis drug Oralflex have been dismissed by an Indiana circuit court. Though 61 deaths have been linked to use of the drug in Britain (SN: 12/3/83, p. 361), the judge ruled the suits should have been brought there where access to evidence and expertise in applying the relevant British law would be better.