Biology

Eukaryotes, prokaryotes: Who's first?

In plants and animals, the vast majority of DNA is never translated into protein. These stretches of silent DNA, called introns, may be a clue in evolution's mystery of first appearances: Are intron-laden eukaryotes (higher organisms) the most ancient living things? Or does that honor go to the less elaborate prokaryotes (bacteria), in which what you see in DNA more closely resembles what you get in protein?

Periannan Senapathy of the National Institutes of Health in Bethesda, Md., reports that a statistical analysis shows eukaryotes to be the older of the two. Senapathy says eukaryotic DNA is similar to a randomly generated series of DNA subunits – and, he hypothesizes, to the randomly organized bits of genetic material in the "primordial soup."

According to the report, which appears in the April PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES (No. 8), there are generally no more than 200 consecutive coding bits (codons) of DNA in random sequences before a bit that would read as a "stop" message during copying. "In the first primitive cells," Senapathy says, "the main selective pressure must have been to generate long coding sequences from short" ones, to make longer proteins. To avoid the interfering "stop" codons, Senapathy says, primordial eukaryotes evolved a splicing mechanism. The stretches whose information is deleted by the splicing machinery are the introns. Prokaryotes, with sequences of coding bits that often far exceed the limits in random DNA, may have evolved from eukaryotes, losing both introns and the splicing mechanism used to circumvent them.

It is the resemblance between eukaryotic gene structure and the hypothetically random structure of such sequences in the "primordial soup" that makes Senapathy argue for the precedence of primordial eukaryotes. But, says biologist Lynn Margulis of Boston University, "There are strong arguments against random pieces of DNA in the primordial soup. [Senapathy's study shows] probably bona fide phenomena that I see much more as a consequence of how eukaryotic cells are put together, and how they function. To go from there to primitiveness, or earliness in a geological sense – it just isn't warranted by the data."

Leaner pork via biotechnology?

Pigs with reduced fat and an increased growth rate have been raised by scientists in University Park, Pa. They injected pigs daily with growth hormone isolated from pig pituitaries. A month's treatment increased the pigs' growth rate by 14 percent and decreased carcass fat by 30 percent. Terry Etherton of Pennsylvania State University says the hormone, called somatotropin, increased feed efficiency – the weight gained per volume of feed consumed – more than 20 percent, a development that could save pork producers $2 billion to $4 billion annually. His laboratory is currently testing somatotropin produced less expensively by genetically engineered microbes.

The corresponding growth hormone for cows, which increases their milk production, has been at the center of a heated debate (SN: 4/5/86, p. 213). Use of the microbially produced bovine growth hormone appears to be commercially feasible, but some argue that increased milk production is not economically desirable in the United States. Etherton says the use of pig somatotropin is not commercially feasible, because farmers would have to make daily injections for the five to six months it takes the pig to reach market weight.

"The critical question to be resolved is the mechanism of delivery," he says. Various laboratories are trying to develop systems that release such substances as hormones and drugs at a fixed rate. Etherton says, "It would be beneficial to have a delivery system whereby a farmer would inject a pig only once every 30 days."

Biomedicine

Cancer genes: Whence malignant power?

Within the chromosomes of any normal cell are DNA sequences almost identical to those associated with various cancers. Scientists have two major hypotheses to explain why these sequences sometimes initiate malignancies. One is that the sequences become overactive, creating abnormally high levels of crucial growth-controlling proteins. The other is that a minor difference – a single nucleotide change, or "point mutation" – in the DNA sequence turns a normal gene into a potent cell-transforming agent. But some scientists now argue, against the prevailing models, that a major restructuring of a gene must occur to trigger cancer.

"A cell doesn't contain 'cancer genes.' Only after considerable structural change does a cellular sequence become a cancer gene," says Peter H. Duesberg of the University of California at Berkeley. "The point mutation is just a tune-up."

In the April PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES (No. 8), Duesberg and Klaus Cichutek report that reversing the single nucleotide changes in cancer-causing DNA segments known as *ras* genes, which were then packaged in viruses, did not prevent them from transforming cells.

Duesberg and Cichutek propose that a DNA region "upstream" of the *ras* gene is actually a crucial part of the normal cellular gene that corresponds to *ras*. The *ras* gene is composed of four coding regions called exons, numbered 1 to 4, separated by noncoding regions called introns. The Berkeley scientists now propose that there is a fifth exon, which they call exon −1, whose outer boundary has not yet been identified. This newly proposed exon, either by encoding a currently unknown protein segment or by containing regulatory functions, is essential to normal cell growth, they say. It is the truncation of this region, either by a cancer-causing virus encasing a segment of normal DNA or by molecular biologists isolating the *ras* gene, that confers malignant power.

Other scientists working on *ras* genes are skeptical, or even incensed, by Duesberg's proposal. One says the data supporting the role of point mutations in cancer-gene activation are so strong that no further explanation is needed. Another says determinations of DNA sequence now under way are likely to prove Duesberg wrong. Meanwhile, Cichutek and Duesberg plan to locate the other end of exon −1 and see whether it can prevent the other exons from triggering cancer.

Historical roots of hypertension

Blacks in America, and those in Africa with a westernized lifestyle, are about twice as likely as Caucasians to develop high blood pressure. Researchers have hypothesized that the predisposition in westernized blacks may reflect an interaction between a modern high-salt diet and genes that adapted to a historical scarcity of salt. In the April 5 LANCET, Thomas Wilson of Bowling Green (Ohio) State University bolsters the hypothesis by correlating blood pressure differences among West African tribes with historical accounts of salt availability.

"In Senegal and Gambia, where salt was always available, blood pressures are low," the historian says, pointing to epidemiologic studies on blood pressures in the Mandinka and Serer tribes in those countries. Present-day blood pressures are much higher in the Yoruba, a Nigerian tribe historically situated inland from sources of sea salt, and south of Saharan salt mines. Salt was so scarce in those regions that it was sometimes traded pound-for-pound for gold, and accounts by 19th-century European travelers refer to an "unbelievable" lack of salt.

"Because a large proportion of the population in West Africa have descended from a salt-deprived line," Wilson says, "the increase in salt consumption in West Africa is a serious public health hazard."