fibroblasts, repairability is reduced as the age of the culture increases but never falls as low as that in xeroderma cells. Despite the serious and constant defect in excision repair in xeroderma fibroblasts, these cells do not have curtailed life-span in vitro, even when no special precautions are taken to shield them from ambient light during routine manipulations.

De Serres reported on the role of repair in the production of mutations in neurospora. Several strains of neurospora have been isolated with repair deficiencies. Some of these repair-deficient strains are much more sensitive to mutagens, others are much more resistant, and a third group shows no difference from the wild type.

Hayden Coon (National Institute of Child Health and Human Development, Bethesda, Maryland) discussed the genetic heterogeneity found in patients with xeroderma pigmentosum. Different types of defects can be detected by complementarity experiments. In these studies, cell cultures from two patients are fused and the percentage of repair (measured as grain counts after the induction of unscheduled DNA synthesis) is compared in the two parent lines, fusion products, and normal controls. These studies have revealed four complementation groups for xeroderma pigmentosum, each with a different repair capacity. When cells of two complementary groups are fused, the repair capacity returns to 100 percent of normal.

Selma Silagi (New York Hospital–Cornell Medical Center) led a discussion on alterations of genome expression in differentiated cells. Silagi, studying mouse melanoma cells, has demonstrated that low concentrations of BrdU that do not appreciably alter the growth rate of the cells can markedly change genome expression. In the presence of BrdU, these cells stop producing melanin, alter their growth characteristics in culture, and have markedly reduced tumorigenicity when injected into recipient animals. Treated cells with reduced tumorigenicity have been used to immunize mice with up to 90 percent efficiency against untreated highly tumorigenic cells. The enzyme tyrosinase, detectable electrophoretically in the untreated cells, is progressively decreased in amount during growth with low concentrations of BrdU, and one of the two electrophoretic bands becomes smaller earlier than the other. These alterations are not true mutations, since the cells revert when BrdU is withdrawn. They can be manipulated in either direction by sequential additions and withdrawals of BrdU. Also, if the cells do not synthesize DNA and divide, they are not affected by the BrdU addition.

Goldstein, working with D. P. Singal (McMaster University) on clonal studies of human fibroblasts, reported a loss of some HL-A surface antigens with aging. He noted that in similar studies with mass culture techniques, these antigens usually appear to maintain stability to senescence. In comparison, fibroblasts of patients with progeria, a so-called premature aging syndrome, are negative for these antigens.

George Martin (University of Washington) discussed gene expression in diploid cells in culture with regard to a variety of possible mitotic segregation mechanisms. These mechanisms included somatic crossing-over, for which there is considerable evidence, and diploidization, a process in which cells go from two to four and back to two chromosome complements, with concomitant recombination of the original homologous pairs as measured by increase in chromosomal variants. Similar mechanisms involving haploidization resulting from multipolar mitoses, aneuploidy by mitotic nondisjunction, and recombination by translocation were also discussed. Coon noted some current work with hybrids of human and rodent cells in which the rodent chromosomes are preferentially lost. This phenomenon apparently occurs only when fresh primary rodent cultures are hybridized with cell lines of human origin. Such hybrid lines may lose the total rodent chromosome complement in addition to certain human chromosomes, resulting in a cell line monosomic for as many as eight human chromosomes.

Susumu Ohno (City of Hope National Medical Center, Duarte, California) presented a hypothesis that mutations in transfer RNA might explain the senescence phenomenon. He felt that the data on mutation rate and cell degeneration time were most compatible with mutations in this system.

James F. Danielli (Center for Theoretical Biology, Amherst, New York) expressed the view that the senescing cells in culture probably represented a complex dynamic system with a trajectory in time, rather than a continually repetitive system. Cells, he said, have many possible sets of behavior. One of these may be expressed for a time, and may initiate a period of transition to expression of a new set of characteristics, which is followed by a third set, and so forth. In this complex system, he felt, mutagenesis and mutants can be tools for studying the mechanism of aging, but this does not mean that senescence or aging is necessarily due to mutagenesis. Indeed, Danielli considers it unlikely that random mutagenesis is the primary cause of aging in mammals.

The presentations at the workshop will be published as a supplement to *International Review of Cytology*. The workshop was organized by Warren W. Nichols (Institute for Medical Research), Moorhead, Danielli, and Donald G. Murphy (National Institute of Child Health and Human Development.

WARREN W. NICHOLS
LORRAINE H. TOJI
ROBERT C. MILLER
Institute for Medical Research, Camden, New Jersey 08103

Control of Transcription

An international symposium on control of transcription was held in Calcutta, India, from 12 to 15 February 1973. This symposium was organized by the Bose Institute, Calcutta, in collaboration with the Oak Ridge National Laboratory, and was funded by the National Science Foundation and the government of India. Participants presented papers on different aspects of transcription in prokaryotes, eukaryotes, and their viruses to a group of about 100 scientists and 50 graduate students who attended the symposium as observers and took part in discussion.

In the opening meeting, Alexander Hollaender of the Oak Ridge National Laboratory and the University of Tennessee described the genesis and objectives of this symposium. The scientific sessions started with the presentation of electron microscopic pictures of genes active in transcription by Barbara Hamkalo (Oak Ridge National Laboratory). In bacteria, active structural genes could be identified by gradients of attached polyribosomes because transcription and translation are tightly coupled in these cells. Active ribosomal RNA genes were distinguishable from structural genes by the absence of attached ribosomes. Active loci synthesizing

ribosomal RNA in amphibian oocytes and HeLa cells presented one interesting feature. Neighboring ribosomal precursor RNA genes in a cluster were separated by segments of DNA that apparently are not transcribed.

Richard Losick (Harvard University) discussed the changes in RNA polymerase in sporulating *Bacillus subtilis*. Along with an early change in template specificity and a subsequent replacement of one β-subunit of the RNA polymerase, an additional sigma-like protein appears which may direct the transcription of sporulating genes. Henry Paulus (Harvard Medical School) described a similar sporulating system, that of *Bacillus brevis*, where the antibiotic tyrothricin and other small molecules like cyclic 3′,5′-guanosine monophosphate, adenosine triphosphate, deoxyadenosine triphosphate, and nicotinamide adenine dinucleotide might be involved in control of transcription. A. M. Chakraborty (General Electric Research and Development Center) described the expression of plasmid genes in *Pseudomonas* capable of breaking down hydrocarbons and indicated that these bacteria may be useful in sewage treatment and in keeping the oceans free of oil sludge. U. N. Singh (Tata Institute of Fundamental Research, Bombay) presented a theoretical analysis of stringent coupling between transcription, translation, and degradation of messenger RNA (mRNA) in an inducible system. Andrew Travers (Medical Research Council Laboratory of Molecular Biology, England) discussed open and closed conformations of promoters in *Escherichia coli*. Interaction with other protein effectors like the protein synthesis elongation factors Tu and Ts may regulate the conformation of RNA polymerase itself and control the initiation specificity of the enzyme with respect to different promoters.

On the subject of bacteriophage, E. K. F. Bautz (University of Heidelberg, West Germany) compared RNA initiation by T3 RNA polymerase, which consists of one subunit only, and by host RNA polymerase. Umadas Maitra (Albert Einstein College of Medicine) showed that T3 specific RNA polymerase initiates RNA chains exclusively with guanosine triphosphate and can terminate RNA chains faithfully without any additional factors in vitro. Audrey Stevens (Oak Ridge National Laboratory) indicated that some small proteins coded by T4 bacteriophage might be involved in late production of T4 mRNA. Salil K. Niyogi (Oak Ridge National Laboratory) discussed the use of specific dinucleoside monophosphates in the elucidation of RNA initiation sequences during in vitro transcription of T4 DNA. Mituru Takanami (Kyoto University, Japan) discussed the physical mapping of transcribed regions of coliphage fd by cleaving its RF-DNA (replicate form of DNA) with restriction enzymes. Maharani Chakravorty (Banaras Hindu University, Varanasi) implicated the *sie* and m_3 genes of phage P22 in the control of transcription in host *Salmonella typhimurium*. R. K. Poddar (Saha Institute of Nuclear Physics, Calcutta) described some changes in induced enzyme synthesis in *E. coli* infected with ϕX 174 phage.

A number of speakers dealt with the bacteriophage lambda, which is the most well studied system with respect to control of transcription. Waclaw Szybalski (University of Wisconsin) elaborated on the multielement structure of the sites of initiation of transcription in lambda phage and on its positive and negative controlling elements. The transcriptional controls operating during development of lambda phage are strongly interlocked and coupled to DNA replication. Sushil Kumar (Indian Agricultural Research Institute, New Delhi) implicated two *E. coli* functions *tra*L and *tra*R in the control of the leftward and rightward transcription of lambda DNA. Sudhamoy Ghosh (Bose Institute) described a DNA-binding protein factor (factor D) that could improve the initiation fidelity of lambda DNA transcription. Sankar Adhya (National Cancer Institute) discussed the possible role of the gene *N* product of lambda as antiterminator of the phage versus host RNA transcription by counteracting the effect of the bacterial rho factor.

Joe Sambrook (Cold Spring Harbor Laboratory) discussed the control of transcription of SV40 DNA. Most cell lines transformed by SV40 contained three types of virus-specific RNA's which might be involved in maintaining the transformed character. Amiya K. Banerjee (Roche Institute of Molecular Biology) described the transcription of the reovirus that contains double-stranded RNA as its genome. A. S. Bhagwat (Bhabha Atomic Research Centre, Bombay) described the isolation of two protein fractions that may act as repressors for specific RNA synthesis during growth of *Neurospora crassa*.

The control of transcription in eukaryotes presents much more complex problems because of the structural

and functional complexity of chromosomes. W. J. Rutter (University of California at San Francisco) compared the properties of multiple RNA polymerases 1, 2, and 3 from different eukaryotic organisms and their organelles. Pierre Chambon (Institut de Chimie Biologique, Strasbourg) described the characterization of RNA products synthesized on circular SV40 DNA by A and B RNA polymerases of rat liver, calf thymus, and *E. coli*. The most interesting point was that, while *E. coli* holoenzyme transcribes SV40 DNA asymmetrically, the animal enzymes do it symmetrically, apparently indicating that the animal enzymes lacked the sigma-like discriminatory factor. P. H. W. Butterworth (University College, London) discussed the importance of selecting suitable DNA templates whose integrity affects the activity of different RNA polymerases. The only report of a sigma-like factor from any eukaryotic system was made by B. B. Biswas (Bose Institute), who studied multiple RNA polymerases and two protein factors from plant cell nuclei. He also presented evidence that an indoleacetic acid acceptor protein from the same source can modulate RNA synthesis in vitro in a completely homologous system. R. K. Mandal (Bose Institute) indicated that the low transcriptional activity of avian erythrocyte nuclei might be due to the absence of factors of RNA polymerase although the enzymes and templates were there. G. P. Talwar (All India Institute of Medical Sciences, New Delhi) discussed the expression of the phosvitin-synthesizing gene in chickens by the action of estradiol, which favors clonal proliferation and also effects transcription of the competent genes.

The transport of mRNA in eukaryotes presents a special problem in that their sites of synthesis and function are separated. E. M. Lukanidin (Academy of Sciences, Moscow) dealt with the regulation of precursor mRNA biosynthesis and transport. He implicated special protein particles (termed informofers) in the processing and transfer of mRNA across the nuclear membrane. Mary Edmonds (University of Pittsburgh) discussed the isolation and characterization of poly A sequences covalently linked to polysomal mRNA and heterogeneous nuclear RNA, thus indicating their precursor-product relation.

Reverse transcription, that is, RNA-dependent DNA synthesis, was the topic of discussion by three speakers. Robert C. Gallo (National Cancer In-

stitute) described the RNA-directed DNA polymerase in human leukemic cells. M. R. Das (Tata Institute of Fundamental Research, Bombay) discussed the same enzyme in viruslike particles in the milk of women with breast cancer. Inder M. Verma (Massachusetts Institute of Technology) described the use of reverse transcriptase to synthesize DNA complementary to mRNA's. This may be a useful step in producing specific eukaryotic genes.

A symposium on transcription would not, perhaps, be complete without a discussion of the role of transcription in DNA replication. Sankar Mitra (Oak Ridge National Laboratory) dwelt on the transcriptional control of M13 phage DNA synthesis. R. B. Wickner (Albert Einstein College of Medicine) described two enzyme systems in *E. coli* which are required for conversion of fd DNA to the replicative form, in addition to DNA polymerase 2. One of these systems might involve RNA polymerase. The same was not true for ϕX 174 DNA. W. Szybalski (University of Wisconsin) discussed a primer RNA 81 nucleotides in length which plays a role in the initiation of phage lambda DNA replication.

R. K. MANDAL

Bose Institue,
Calcutta 700009, India

Forthcoming Events

January

14–18. **Biology and Chemistry of Eucaryotic Cell Surfaces** Conf., 6th, Intern. Union of Biochemistry, Miami, Fla. (Miami Winter Symposia, P.O. Box 906, Biscayne Annex, Miami 33152)

14–18. International Soc. of **Magnetic Resonance,** 5th, Bombay, India. (D. Fiat, Weizmann Inst. of Science, Rehovot, Israel)

14–25. International Assoc. of **Meteorology and Atmospheric Physics,** Melbourne, Australia. (G. B. Tucker, Commonwealth Meteorology Research Centre, P.O. Box 5089AA, Melbourne 3001)

15–17. American Soc. for **Surgery of the Hand,** Dallas, Tex. (J. A. Boswick, Jr., 4200 E. Ninth Ave., Denver, Colo. 80220)

15–19. American **Mathematical** Soc., San Francisco, Calif. (E. Pitcher, Dept. of Mathematics, Lehigh Univ., Bethlehem, Pa. 18015)

15–19. National Soc. of **Professional Engineers,** Biloxi, Miss. (P. H. Robbins, NSPE, 2029 K St., NW, Washington, D.C. 20006)

17–18. Symposium on **Blood,** 22nd, Detroit, Mich. (E. F. Mammen, Dept. of Physiology, Wayne State Univ., School