THE GENETICAL SOCIETY

ABSTRACTS of Papers presented at the HUNDRED AND EIGHTY-SIXTH MEETING of the Society held on 21st, 22nd and 23rd MARCH 1978 at the UNIVERSITY OF NEWCASTLE-UPON-TYNE.

INTERACTION OF [PSI] FACTOR AND DYE RESISTANCE DETERMINANTS IN YEAST

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The efficiency of several ochre nonsense suppressors in *Saccharomyces cerevisiae* is increased by a cytoplasmically inherited genetic element called [Ψ] (Cox, *Heredity, 20*, 505, 1965). There are several plausible mechanisms by which the efficiency of suppression may be increased and in order to pin-point the role of [Ψ] factor using genetic techniques, it is necessary to relate it to a process of known mechanism. A broad search for [Ψ]-related phenomena was conducted. Treatment with methanol causes an increase in the frequency of [Ψ−] revertants in [Ψ+] cultures; whether by induction or by selection is yet to be determined. [Ψ−] strains isolated from cultures treated with methanol were found to have simultaneously lost resistance to Rhodamine 6G (Gurr's) (R6G), a polycyclic dye. Tetrad analysis of the $R6G^s$ revertants demonstrated a two-factor determination of R6G resistance. One of the determinants is inherited as a Mendelian factor and the other appears to be linked to [Ψ+]. This can be explained in one of three ways:

(a) Ochre suppression of an $R6G^s$ mutation by [Ψ+].
(b) Linkage of the R6G determinant to the [Ψ] factor.
(c) Interaction of the [Ψ] gene and the chromosomal $R6G^R$ determinant.

Tetrad analysis shows that (a) is not the explanation.

U.V. IRRADIATION MUTAGENESIS OF A CYTOPLASMIC ELEMENT IN *SACCHAROMYCES CEREVISIAE*

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In the yeast *Saccharomyces cerevisiae* the action of the serine-inserting, ochre suppressor *SUQ5* depends upon a cytoplasmically inherited genetic factor [Ψ]. In a Ψ+ background suppression is observed; in a Ψ− background *SU5* is inactive (Cox, *Heredity, 20*, 505, 1965). Cytoduction experiments demonstrate that the [Ψ] factor is located in the cytoplasm.

Ψ^+ can be mutated to Ψ^- by a number of mutagens, for example ethyl methane sulphonate, nitrosoguanidine or UV irradiation. The influence of DNA repair mechanisms on UV irradiation-induced mutation of the [Ψ] factor have been studied by

I. using strains defective in excision repair (*rad 1*) or in error-prone repair (*rad 6, rev 3*) and
II. by the use of photoreactivation.

Ψ^+ to Ψ^- mutation has been compared with UV irradiation induction of the cytoplasmic *petite* mutation and chromosomal mutation in such strains.

Results indicate that [Ψ] mutagenesis is under the control of mechanisms responsible for the repair of UV irradiation-induced nuclear DNA damage and that the [Ψ] factor is a DNA molecule. The UV irradiation induction of the *petite* mutation is subject to both specific nuclear and mitochondrial genetic controls (Moustacchi, *Molec. gen. Genet., 114*, 50, 1971). The kinetics of UV induction of Ψ+ to Ψ^- mutation observed differed from the UV induction of the mitochondrial *petite* mutation in all the systems we have tried.

LOSS OF PHOTOREVERSIBILITY OF UV DAMAGE IN THE BLUE-GREEN ALGA, *GLOEOCAPSA ALPICOLA*

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Gloeocapsa alpicola, a typical blue-green alga, possesses an extremely efficient light-dependent repair mechanism for the removal of lethal and mutagenic UV damage. However, UV-irradiated cells held in the dark or grown under non-photoreactivating light ($\lambda > 550$ nm) rapidly lose their photoreversibility. Split UV dose experiments indicate that the photoreactivation mechanism remains intact, suggesting that the dark removal of UV photoproducts is responsible for the loss of photoreversibility. These results were related to biochemical evidence for dark repair.

RETRANSFER OF F'*LAC* IN *ESCHERICHIA COLI* K12 MATING MIXTURES

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Ozeki, Stocker and Smith (*J. gen. Microbiol.*, *28*, 671-687, 1962) found that, in suitable mating conditions, *coli* could be transferred to about 50 per cent of a recipient population in 20-hour matings; this " epidemic spread " needed long periods of slow growth during which retransfer by recipients could occur.

We studied in detail the increase in the number of F'*lac* progeny during 20 hours in mating mixtures. We found that mating ability declined rapidly when F'*lac* cultures entered stationary phase. The importance of retransfer was shown qualitatively by comparison with an amber transfer-deficient mutant of F'*lac* which was unable to retransfer from a recipient cell. We estimated that retransfer by recipients occurred about once per generation (generation time 300'). This relatively low mating rate and the limited time before the cultures enter stationary phase and retransfer stops place limits on the number of recipients which receive the plasmid.

MOLECULAR RELATIONSHIPS OF *PSEUDOMONAS* PLASMIDS

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The two methods used to study the sequence relationships of plasmids are hybridisation (including heteroduplex analysis) and comparison of fragmentation patterns on electrophoresis after digestion with site specific endonucleases. We shall describe here a technique that used both endonuclease digestion and hybridisation. Plasmid DNA preparations from *Pseudomonas* strains were digested with endonuclease EcoRI and fractionated by electrophoresis through agarose. The DNA fragments were then transferred to a nitrocellulose filter, in the single-stranded form and challenged with single-stranded " probe " plasmid DNA that had been labelled with ^{32}P *in vitro*. The fragments that hybridised *in situ* were revealed by autoradiography. We find substantial homology between a number of plasmids specifying the utilisation of aromatic compounds (salycylate, naphthalene and toluene) and homology in a small region between the salicylate (SAL) and octane (OCT) utilising plasmids. The relationships of a number of R factors belonging to different incompatibility groups were also discussed.

A NOVEL CLASS OF RESTRICTION-DEFICIENT MUTANTS

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R124 is a unique R factor in compatability group F IV which confers tetracycline resistance (Tc) and carries the genes for a restriction-modification (R-M) system (Bannister,

D. and S. W. Glover, *J. gen. Microbiol.*, *61*, 63, 1970). R124/3 is a derivative plasmid which determines a R-M system of different biological specificity to R124 (S. G. Hughes, personal communication).

During experiments designed to isolate restriction-deficient (r^-) mutants of these R factors in which F-*lac*+.0 was transferred to R124 or R124/3 carrying bacteria virtually all of the colonies isolated were restriction-deficient. Restriction-deficient mutants can be isolated just as readily following transfer of these R factors to F-*lac*$^+$ carrying bacteria. Many of the restriction-deficient mutants isolated are also modification-deficient and some unexpectedly express the modifications characteristic of both R124 and R124/3.

Evidence is presented to indicate that the restriction-deficient phenotype of these R factors is not dependent on the continued presence of F-*lac*$^+$ which lead to their isolation and that other F-prime factors can interact with R124 to produce r^- mutants also at very high frequency.

Many of these r^- mutants show high "reversion" frequencies to r^+ and evidence is presented to indicate that mutation to Tc sensitivity may also arise frequently following transfer to F-*lac*$^+$ to R$^+$ bacteria.

These results are discussed in relation to what is known about the DNA of the plasmid molecules from studies conducted by Dr S. G. Hughes (personal communication).

GENETICS OF THE R-M SYSTEMS IN *HAEMOPHILUS*

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The genus *Haemophilus* is an extremely rich source of restriction endonucleases of both Type I and Type II. Altogether 22 such enzymes have been detected and partially characterised (see Roberts, R. J., *Crit. Rev. Biochem.*, 1976). About half of these enzymes have been isolated from *Haemophilus influenzae* and each of the *H. influenzae* serotypes *a*, *b*, *c*, *d*, *e* and *f* are believed to possess restriction and modification (R-M) systems.

The R-M systems from serotypes *a*, *b*, *d*, *e* and *f* have been analysed genetically (Piekarowicz, A. and S. W. Glover, *Molec. gen. Genet.*, *116*, 11, 1972; Piekarowicz, A., L. Kauc and S. W. Glover, *J. gen. Microbiol.*, *81*, 291, 1976) and the restriction endonucleases from serotypes *a*, *f* (*Hin a II*, *Hin a III* and *Hin f III*) have been partially characterised (Glover, S. W. and R. E. Drew, unpublished; Kauc, L. and A. Piekarowicz, unpublished).

All of the evidence indicates that the enzymes which form part of the *H. influenzae* R-M systems are Type I enzymes and their role appears to be similar to that of other restriction endonucleases that can be detected by *in vivo* tests.

Type II restriction endonucleases have been isolated from all of the *H. influenzae* serotypes other than serotype *a* and characterised using bacteriophage λ or other well-defined DNA molecules as substrate. These enzymes do not appear to form part of recognised R-M systems and they have little or no activity on *Haemophilus* phage DNA.

GENETICS OF R-M SYSTEMS IN *SALMONELLA*

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Salmonella typhimurium LT2 and LT7 have three R-M systems coded by chromosomal genes. Mutants with r$^-$m$^+$ and r$^-$m$^-$ phenotypes have been isolated for each of them. All three were first detected in *Escherichia coli-S. typhimurium* hybrids.

System LT was detected when phage P22 from *lac*$^+$ hybrids between *E. coli* Hfr and *S. typhimurium* LT7 *mut* (with a mutator gene) was plated on wild-type *S. typhimurium*. All mutations affecting system LT are closely linked and situated between *proA* and *proC*. System LT is present in the many *Salmonella* serotypes tested, with the exception of *S. typhi*.

System SA was first observed using hybrids with the *hsdK* genes of *E. coli:* phage L (closely related to P22) from such hybrids underwent restriction in wild-type *S. typhimurium*, independently of the presence of system LT. *hsdSA* is situated between *pyrB* and *serB* and was first thought to be the *Salmonella* allele of *hsdK* and *hsdB* in *E. coli*. System SA was found in all *S. typhimurium* strains tested, but not in other *Salmonella* serotypes.

System SB is not active on phages P22 and L and was detected with coli phage λ in *S. typhimurium* Hfr-*E. coli* F⁻ hybrids for the *thr-leu* region of the map. The *hsdSB* and *hsdSA* genes are closely linked, in the order: *pyrB-hsdSA-hsdSB-serB*. *hsdSB* is the true allele of the *E. coli* systems, as shown by the results of complementation tests between *hsdSB*, *hsdK* and *hsdB* mutants. Many alleles of *hsdSB*, each with a different specificity, are found among *Salmonella* serotypes.

PLASMID ENCODED RESTRICTION AND MODIFICATION SYSTEMS

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One of the more plausible roles suggested for restriction and modification systems is that they act as genetic barriers controlling recombination in the process of divergence and speciation during prokaryotic evolution. Within this context questions of the origin of, and relationships between plasmid and host encoded systems, as well as the fundamental question of why plasmids should carry such systems at all are of added interest. If plasmid encoded systems play a part in speciation one might expect to observe recombination between plasmid and host to generate systems of novel specificity, the grouping of determinants for restriction and modification on transposons, and the occurrence of the same restriction and modification determinants in widely diverged genera. Surveys of the distribution and enzymic mechanisms of plasmid restriction and modification systems, and of the specificities of bacterial endonucleases and DNA methylases, are beginning to provide evidence of these expected phenomena.

Evolutionary and genetic implications apart, the detailed genetic study of restriction and modification systems, particularly those where a switch of specificity is observed, offer an important approach to the study of protein nucleic acid interactions.

THE *SALGI* RESTRICTION-MODIFICATION SYSTEM

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The class II site-specific endodeoxyribonuclease *Sal*GI (≡SalI) is responsible for restriction of phages by *Streptomyces albus G* (Chater and Wilde, *J. Bacteriol., 128*, 644, 1976). After mutagenesis, about half of the restrictionless mutants isolated as phage-sensitive colonies are also defective in modification activity. A mutant has been isolated which is proficient in restriction and modification at 30°C but is unable to grow at 37°C unless it also carries a mutation causing loss of *Sal*GI. This phenotype is that predicted for a mutant temperature-sensitive for modification, and it allows positive selection of spontaneous restrictionless mutants. Most, if not all, of these are also modification-defective at 30°C.

Double digests of various phage DNA's with *Sal*GI and either *Hinc*II (recognition site 5′-GTPyPuAC-3′) or *Taq*I (recognition site 5′-TCGA-3′) show that the *Sal*GI recognition site is a subset of both kinds of site and is therefore 5′-GTCGAC-3′, a conclusion confirmed by direct chemical determination of the site by J. R. Arrand, P. Myers and R. J. Roberts (*J. Molec. Biol.* submitted). *In vivo* modification of *Sal*GI sites protects them (not not other *Hinc*II sites) against *Hinc*II or *Taq*I cleavage *in vitro*, suggesting that the modification enzyme is highly specific in site recognition and that modification occurs within the central four base pairs of the site.

POPULATION STRUCTURE IN SOME SCANDINAVIAN ISOLATES

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In Finland the small Lapp populations, scattered over an enormous area, have received considerable geneflow from the surrounding majority populations (Swedes, Finns), but have retained many common hereditary characteristics, for example the high frequencies of the

genes for blood group A2, Fy^a, Inv^1, PGM_1^2, acid phosphatase P^c, ADA^2 and low frequencies for B, M, cde, se (ABH non-secretor) and Gc^2 group specific components. Of clinical traits the rates of obesity, varicose veins, diabetes mellitus, rheumatoid arthritis, and high blood pressure are low, but flat foot and congenital dislocation of the hip are high. But there is genetic heterogeneity among the Lapp groups, particularly the Skolts, who are the easternmost Lapps in Finland, and this may be explained by social and geographical isolation, and by genetic drift.

In the population of the Åland Islands, relatively isolated until recent times in the northern Baltic Sea, we have attempted to estimate the distribution of grandparental gene frequencies, and these, together with demographic, anthropometric and clinical observations on the present population, together with estimations of kinship from migration and genetic data, have confirmed the isolated character of the outer archipelago populations.

In some localities the population structure has resulted in characteristic frequencies in clinical conditions. In the parish of Kökar, autosomal recessive tapetoretinal degeneration has a high frequency and so do autosomal dominant traits such as von Willebrand's disease and familial benign chronic pemphigus. Atopic hypersensitivities are very common but not colour-blindness, myopia, or juvenile diabetes, while the twinning rate is one of the highest noted amongst Whites. In some rural areas in Finland ophthalmogenetic studies have shown high frequencies of some rare eye diseases. Autosomal recessive cornea plana congenita round the lower reaches of the River Kemijoki in southern Lapland provides more cases than the total number reported elsewhere in the world. More than 70 per cent of the carriers of X-chromosomal recessive retinoschisis come from the province of Satakunta in south-western Finland, which has only 5 per cent of the total Finnish population, while in the parish of Salla in north-eastern Finnish Lapland, with about 8200 inhabitants, about 90 per cent of all Finnish cases of X-chromosomal choroideremia were born.

PROBABILITIES ON PEDIGREES AND GENOTYPES OF ANCESTORS

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The probability of observing a given set of phenotypes for some of the members of a large and complex pedigree may be required for any of several reasons. Such probabilities may be used to answer genetic counselling problems, to infer the mode of inheritance of a characteristic, or to infer genealogical relationships between individuals on the basis of phenotypic information. These probabilities also enable us to infer the most likely genotypes of the ancestors of a population, and the ancestral origins of certain alleles.

A general method is outlined for the computation of these probabilities on pedigrees of, in theory, arbitrary size and complexity, and the capability of the algorithm is demonstrated with reference to the problem of inferring the most likely joint sets of genotypes for the founders of the Tristan da Cunha population.

PARSING A GENEALOGY

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A population for which genealogical information is available may be *connected* (each person being related to every other) or *disconnected.* If a connected genealogy can be divided by the breaking of a single relationship (or *bridge*), or the removal of a single individual (or *cutpoint*), it is of interest because finding the division will facilitate drawing the genealogy and otherwise exploring its properties.

Techniques will be described for finding bridges and cutpoints and for solving the more complex problem of parsing a genealogy into blocks when single bridges and cutpoints do not exist.

MIGRATION AND GENETIC DIVERSITY IN AN ISLAND POPULATION

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This paper examines genetic diversity on Karkar Island, Papua, New Guinea, and its relationship to patterns of migration within and between the two linguistic groups (Waskia and Takia) on the island. Exchange between linguistic groups is found to be small—less than 3 per cent of married individuals living in one linguistic group were born in the other. There is evidence of a secular trend in movement with significantly greater proportions of younger married individuals living outside their village group of birth. The migration patterns are examined by principal co-ordinate analysis of kinship coefficients derived from three sets of migration probabilities—ages 15-29, 30-44, 45 and over. For all three age groups the linguistic division is preserved and there is broad agreement between relatedness and the geographical arrangement of the village groups.

The 22 polymorphic genetic systems examined show considerable diversity, most of which is within or between village groups in the same linguistic division. The greater level of diversity between Takia groups is consistent with their greater isolation from one another. Genetic distances between village groups show good agreement with geographical distances and there is no overlap between Waskia and Takia. The present-day genetic structure of Karkar Island can be interpreted as being largely the result of the interplay of migration and drift processes. The paper considers the use of analyses of this kind in establishing the magnitude and role of evolutionary forces operating on the genetic structure of human populations and the problems of unravelling rigorously and in detail the historical development of this structure.

GENETICS AND SOCIAL CLASS IN AN URBAN COMMUNITY

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Various genetic polymorphisms were examined in blood samples collected at NBTS donor sessions in Nottingham and Edwinstowe. Each blood donor was questioned about his occupation and place of residence as well as his or her parental occupations. From these data it has been possible to compute genotypic frequencies for each socio-economic class amongst the donor sample. It has also been possible to see if any changes might be occurring between parental and offspring socio-economic grouping with respect to changing gene frequencies.

The problems involved in analysing these data are briefly discussed. Finally, the possible uses of such data are outlined with particular reference to disease patterns within a community.

SOME POLYMORPHISMS IN BURMA

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Samples from Burmese, Chins, Nagas, Kachins, Shans, Kayahs and Mawkins were tested for a variety of polymorphisms. In particular the frequency of haemoglobin variants ($Hb_{\beta}E$) is higher amongst the Burmese of the plains than amongst the hill tribes, while transferrin variants (Tf^{D}) are common amongst the Shans. The origin of the Mawkins has been a mystery for many years but they have some features in common with the Malays.

A CHROMOSOMAL DIFFERENCE BETWEEN BORNEAN AND SUMATRAN ORANGUTANS

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Wild populations of orangutan (*Pongo pygmaeus*) exist in the islands of Sumatra and Borneo which became geographically isolated some 8000 years ago. Blood samples were obtained from 27 orangutans, 8 of Bornean origin, 17 of Sumatran origin and 2 hybrid animals which have resulted from matings of captive animals from the two populations. All Bornean animals were found to be homozygous for a subtelocentric type of chromosome 2 (centromeric index = 10·2), but in the Sumatran animals this chromosome type was carried by one animal in the heterozygous condition. This specimen was bred in captivity and there is a possibility that it is of hybrid origin. The homologue to this chromosome in the carrier, as well as that carried by other 16 Sumatran animals in the homozygous condition, corresponded to a more metacentric chromosome (C.I. = 18·9). The two hybrid animals studied were carriers of both types of chromosome 2. Chromosome banding (Q-, R- and G-) showed differences in the short arm and subcentromeric region of the two types of chromosome 3, and each chromosome can be derived from the other by a single pericentric inversion.

The frequency of each chromosome type differs significantly between the two populations, suggesting that each of them has become fixed following selection or genetic drift and a high degree of inbreeding. We propose that each chromosome type should be designated as " Bornean " and " Sumatran " chromosome 2 in *Pongo pygmaeus*. The homologous chromosomes to chromosome 2 of the orangutan in other hominoids and man can be more simply derived by a single pericentric inversion from the " Bornean " rather than from the " Sumatran " chromosome 2, thus suggesting that the " Bornean " chromosome could be the ancestral chromosome 2 in *Pongo pygmaeus* from which the " Sumatran " chromosome has derived. The possibility of producing hybrid animals by mating captive orangutans from Sumatra and Borneo is discussed in view of the fact that the offspring of such matings would produce offspring heterozygous for one pericentric inversion, and therefore potentially less fertile than chromosomally normal animals.

PARENTAL AGE AND BIRTH ORDER IN CHROMOSOME ANEUPLOIDY

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Studies of aetiological factors underlying rare chromosome abnormalities have generally relied on simple tests of significance, which do not permit evaluation of the sizes or interrelationships of the effects. A multiple regression technique, using the live full-born sibs of propositi as controls, has been developed. (Carothers *et al.*, *Ann. Hum. Genet.*, *41*, 277-287) which achieves this end. Applied to data from the Cytogenetic Registry of this Unit on several types of chromosome aneuploidy, the technique distinguishes the effects of three highly correlated variables—paternal age, maternal age and birth order—and reveals quite clearly that for the data on 47,XXY's it is maternal age (as has long been suspected), rather than paternal age or birth order, that is most closely associated with an increased risk, and that the increased risk is evident from all sources of ascertainment. Results have also been derived for 47,XXX's and 47,XYY's and it is hoped to extend the studies to other categories, such as 45,X's, mosaics, chromosomal mutants and Down's Syndrome.

THE STRUCTURAL GENE FOR PURINE HYDROXYLASE II OF *ASPERGILLUS NIDULANS* IS ADJACENT TO ITS COGNATE REGULATORY GENE

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Mutations lacking purine hydroxylase II (Scazzocchio, Holl and Foguelman, *Eur. J. Biochem., 36,* 428-445, 1973) belong to two tightly linked complementation groups. Mutations at *hxn*S result in loss of purine hydroxylase II activity and show variable levels of purine hydroxylase II CRM. The pattern of reversion of *hxn*S-5 determines *hxn*S as the structural gene for purine hydroxylase II. Mutations at *hxn*R result in non-inducibility for purine hydroxylase II, uniform loss of CRM and failure to grow on 6-hydroxynicotinic acid as nitrogen source, presumably through non-inducibility of 6-hydroxynicotinic dehydrogenase. *hxn*R-2 reverts to the wild type phenotype, while *hxn*-10 fails to revert and to complement with mutations at either group. The latter mutant is probably a deletion overlapping both genes. This cluster is tightly linked to *apl*A^c mutations, constitutive for purine hydroxylase II (*loc. cit.*). We have not yet determined whether *apl*A^c and *hxn*R mutations are allelic.

MUTATIONS OF PURINE HYDROXYLASE I RESULTING IN ALTERED SPECIFICITY

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*hx*A is the structural gene for purine hydroxylase I (xanthine dehydrogenase) in *Aspergillus nidulans.* Mutations lacking all enzyme activity and CRM, others lacking enzyme activity but retaining full CRM, cold sensitive mutations presumably defective in dimer formation, and mutations resulting in altered substrate and inhibitor specificity map at this locus. Among the more interesting mutations are *hx*A-101 and *hx*A-102 resulting in what is virtually a new enzyme. In contrast to the wild type the mutant enzyme hydroxylates 2-hydroxypurine at position 6 rather than 8, fails to hydroxylate xanthine, shows a drastically lower Vmax for hypoxanthine and accepts allopurinol as a substrate. These differences have been used to construct a simple model of the geometry of the active site-substrate interactions. The different relative positions of an " orientating site " and a catalytic site account for the observed differences between the wild type and mutant enzymes.

THE POSITIVE REGULATORY GENE, *ua*Y

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*ua*Y is a positive regulatory gene essential for the expression of at least six genes involved in purine degradation and uptake in *Aspergillus nidulans* (Scazzocchio and Gorton, Physiology and Genetics of *Aspergillus*, Smith and Pateman, editors, 255-265, 1977). We have determined that adenine deaminase and the xanthine alternative pathway (Darlington and Scazzocchio, *Biochem. Biophys. Acta, 166,* 569-71, 1968) are also under *ua*Y control. We have identified a protein coded by the *ua*Y gene and shown its binding with the phosphate backbone of DNA and specific binding to both natural and gratuitous inducers with a K_{diss} for uric acid $< 2 \times 10^{-7}$M. A very stringent effector specificity was found, uric acid and its two and eight thio-analogues being the only effective inducers. The pseudo-constitutive mutation *ocp*^{r}-5 (Scazzocchio and Gorton, *loc. cit.*) has been positioned in relation to *ua*Y alleles and a fine structure map of the gene allows a tentative location of the DNA binding site.

HETEROGENEITY OF ALLELES AT A CONTROL SITE IN *ASPERGILLUS NIDULANS*

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We have described previously *uap*-100, a *cis*-acting mutation, closely linked to the putative structural gene for the xanthine-urate permease (Arst and Scazzocchio, *Nature, 254*, 31-34, 1975). *uap*-100, and two new closely linked mutations, *uap*-302 and *uap*-310, were isolated as suppressors of *are*A-102, an *are*A mutation resulting in non-expression of the *uap*A gene. In contrast with *uap*-100, *uap*-302 and *uap*-310 are not distinguishable from *uap*+ in an *are*A+ background. The evidence available at present suggests that while *uap*-100, *uap*-302 and *uap*-310 can accommodate the modified *are*A-102 product, they do not alleviate the stringent requirement for functional *are*A and *ua*Y products.

ALLELE-SPECIFIC SUPPRESSOR MUTATIONS IN *ASPERGILLUS NIDULANS*

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Allele-specific suppressor mutations have been isolated by co-reversion of mutations in *A. nidulans* and partially characterised. At least one suppressor acts simultaneously on one allele at each of three loci, *al*X, *s*B, *alc*A specifying allantoinase, sulphate permease and alcohol dehydrogenase respectively. Several other suppressors act jointly on the *s*B and *al*X mutations. At least four of the seven suppressors studied are inherited as single gene mutations, which co-suppress their original suppressible alleles but not other alleles at the same locus.

sup-101, -105, -109, -115 mutations result also in a morphological effect. Suppressors have been assigned to at least two loci in chromosomes III and VII. Preliminary evidence places two suppressor mutations, *sup*-105 and *sup*-101 at the same locus on linkage group III. *sup*-105 only suppresses *al*X-4 whereas *al*X-4, *s*B-43 and *alc*A-125 are co-suppressed by *sup*-101, hence this suppressor locus may exhibit heterogeneity.

All the suppressible mutations are unleaky and extracts of the *alc*A-125 mutant exhibit no enzyme activity on acrylamide gels or in assays. *alx*-4 has no detectable allantoinase activity. Further work should determine whether we are dealing with missense or nonsense suppressors.

CHARACTERISATION OF SUPPRESSORS OF MITOCHRONDRIALLY INHERITED MUTATION IN *ASPERGILLUS NIDULANS*

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Previously we have characterised two nuclear suppressor loci of the cold sensitive mitochondrial mutation (*cs*-67) (*Heredity, 37*, 153, 1976). Two new suppressor loci have been identified mapping in chromosomes I and IV. A mitochondrial suppressor mutation was shown not to map in the same gene as (*cs*-67). This suppressor maps in between (*cs*-67) and (*oli*A-1), (Rowlands, R. T. and Turner, G., *Molec. gen. Genet., 126*, 201-216, 1973), assuming a circular mitochondrial map.

Suppressor mutations interact strongly, the presence in the same strain of (*cs*-67) and more than one suppressor mutation, resulting in severe impairment of growth at 37°C.

Purified mitochondrial membrane fractions isolated from (*cs*-67) show clear abnormalities in their protein profile when analysed on denaturing gradient gels. These are partially corrected by the mitochondrial suppressor. Mitochrondria from (*cs*-67) show abnormally low cytochrome a-a_3 (Turner, G., and Rowlands, R. T., *J. Bact., 126*, 389-397, 1976) and low cytochrome oxidase activity. The cytochrome a-a_3 levels are partially restored by the suppressor mutations.