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SHORT PAPER

Postmeiotic segregation as a source of mosaics in diploid organisms

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SUMMARY

Postmeiotic segregation (PMS) of genetic variants occurs when a DNA heteroduplex formed during meiotic recombination goes undetected by repair enzymes and is transmitted unresolved to the meiotic products. PMS provides an alternative explanation for the origin of mosaics now attributed to half-chromatid mutation. In multicellular diploid eukaryotes, PMS could result in mosaic individuals with unusual migration patterns for proteins studied by gel electrophoresis. If the gonads were mosaic, complex progenies containing as many as six phenotypic classes at a single locus could be produced.

Postmeiotic segregation (PMS) is an integral feature of the recombination process and a well documented phenomenon in many lower eukaryotes where all of the meiotic products can be examined and the segregation of phenotypes in early mitotic divisions can be readily detected. The occurrence of PMS is usually signalled by aberrant segregation ratios in progeny of crosses, e.g. 5 : 3 rather than normal 4 : 4 segregations in a single eight-spore ascus of a fungus such as *Neurospora crassa* or *Ascobolus immersus* (for reviews, see Fogel *et al.* 1978; Fincham, Day & Radford, 1979 and Whitehouse, 1982). Some potential results of this phenomenon in 'higher' eucaryotes include: (*a*) individuals who are somatic mosaics for the affected gene (Chovnick, Ballantyne & Holm, 1971); (*b*) complex progenies containing more than four phenotypic classes resulting from segregation *at a single locus* (such progenies would normally indicate the involvement of more than one locus in the phenotypes expressed); and (*c*) alteration of population allele frequencies (Watt, 1972; Gutz & Leslie, 1976; Lamb & Helmi, 1982; Nagylaki, 1983*a*, *b*; Walsh, 1983). If PMS occurs regularly at one site, or if the frequency of 5+ : 3− PMS meioses is unequal to the frequency of 3+ : 5− meioses, then PMS could mimic a complex regulatory phenomenon.

These results could affect work in eucaryotic regulatory genetics and in evolutionary genetics. For example, such effects could explain the 'half-chromatid mutations' found in humans (Gartler & Francke, 1975; Lenz, 1975; Happle & Lenz, 1977; Muller *et al.* 1978; Wolff, Hameister & Roper, 1978; Fjellner, 1979; Laporte, Serville & Peant, 1979; Therman & Kuhn, 1981), mice (Bhat, 1949), and Drosophila (Muller, 1920), and some of the aberrant segregations from single-pair matings reported for an esterase locus in butterflies (Burns & Johnson, 1967). PMS can result in somatic mosaics at the *rosy* locus of repair deficient *Drosophila melanogaster* (Romans, 1980*a*, *b*; Hilliker & Chovnick, 1981; Carpenter, 1982).

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PMS is no rare event in organisms which have been carefully examined for its presence. It may be as frequent as 15% of the meioses at a single locus in *Ascobolus immersus* (Paquette & Rossignol, 1978; Rossignol, Paquette & Nicolas, 1978), 2·7% in *Saccharomyces cerevisiae* (Fogel *et al.* 1978), 0·6% in *Schizosaccharomyces pombe* (Thuriaux *et al.* 1980) and 3·2% in *Sordaria brevicollis* (Yu-Sun, Wickramaratne & Whitehouse, 1977). Moreover, rates may vary in both gene- and allele-specific fashion; different alleles at one locus may even vary in the ratio of 3:5 and 5:3 PMS octads observed (Paquette & Rossignol, 1978; Rossignol, Paquette & Nicolas, 1978; Thuriaux *et al.* 1980; Yu-Sun, Wickramaratne & Whitehouse, 1977). Like intragenic recombination and gene conversion, PMS occurs in a highly specific fashion and at rates much larger than simple mutation. Consequently, PMS may prove to be important in the explanation and analysis of developmental and population genetic anomalies.

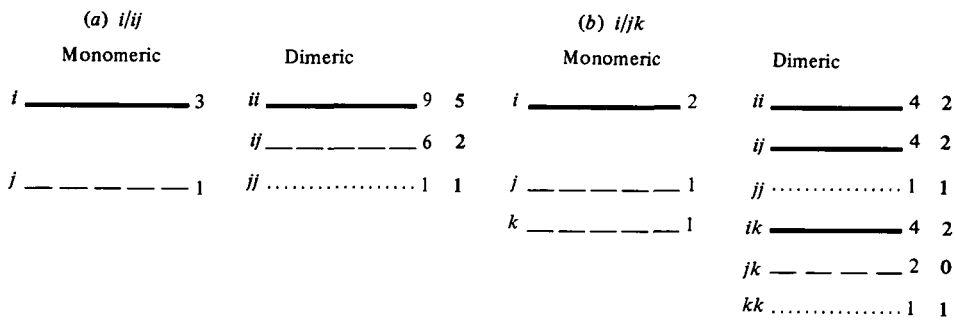

Fig. 1. Possible electrophoretic patterns of a protein from a 1:1 diploid mosaic that originated from postmeiotic segregation. (*a*) Results expected from an *i/ij* heterozygote. (*b*) Results from an *i/jk* heterozygote. Phenotypes and relative intensities are noted next to each band. For dimers, the first set of numbers is the predicted band intensities if the dimers associate and reassociate during the homogenization procedure; the second set of numbers is the predicted band intensities if the dimers do not reassociate during the homogenization procedure. Observed band intensities may differ from the predicted band intensities and will depend on variables such as the specific activity of the different isozymes, the tissue(s) producing the gene product, the relative activities and expression of the different alleles in the tissue(s), and the degree of mosaicism of the tissue(s).

Electrophoretic techniques present an attractive route for the detection of PMS in multicellular eucaryotes. Using these techniques, both somatic mosaics and allele segregation in complex progenies can be unambiguously analysed. We will illustrate the action of PMS, then, with respect to electrophoretically detectable phenotypes. We suppose a variable locus with five electrophoretically distinct alleles: *i*, *j*, *k*, *l* and *m*; this example will be used to explore the somatic and transmission consequences of PMS.

Suppose a new zygote receives one normal gamete carrying the *i* allele and one PMS gamete heteroduplex for *i* and *j*; this embryo will be a 1:1 mosaic of homozygous and heterozygous cells. If the organism is large, biopsy and electrophoresis would reveal this mosaicism directly. If the organism is small, and thus homogenized whole, the more complex electrophoretic phenotypes seen (for monomeric and dimeric proteins) are given in Fig. 1a. The *i/ij* mosaics can be detected qualitatively. For monomers, the densities of the *i* and *j* bands are compared and the *i* band will be found to be much denser than the *j* band. In a non-mosaic *i/j* heterozygote, the *i* and *j* bands would be of equal density. For dimers, the densities of the *ii* and *jj* bands are compared and the *ii* band will be found to be much denser than the *jj* band. In a non-mosaic *i/j* heterozygote, the *ii* and *jj* bands would be of equal density.

Suppose instead that the PMS gamete carries alleles j and k, then a mosaic of two different heterozygous genotypes will result. The resulting mixed-homogenate phenotypes are illustrated in Fig. 1 b. The i/jk mosaics can be detected qualitatively by extra bands in the banding pattern. With monomers, three bands will be present instead of the normally expected two. With dimers, five or possibly even six bands will be present instead of the normally expected three.

Table 1. *Segregation ratios among the progeny of a 1 : 1 gonadal mosaic that originated by postmeiotic segregation*

Genotype of mosaic parent	Gamete frequencies in mosaic parent	Genotype of non-mosaic parent										
		ii	*jj*	*ij*	*kk*	*ik*	*jk*	*kl*	*ll*	*il*	*jl*	*lm*
(A) i/ij	$3i$	$3ii$	$3ij$	$3ii$	$3ik$	$3ii$	$3ij$	$3ik$				
	$1j$	$1ij$	$1jj$	$4ij$	$1jk$	$3ik$	$3ik$	$3il$				
				$1jj$		$1ij$	$1jj$	$1jk$				
						$1jk$	$1jk$	$1jl$				
(B) i/jk	$2i$	$2ii$	$2ij$	$2ii$	$2ik$	$2ii$	$2ij$	$2ik$	$2il$	$2ii$	$2ij$	$2il$
	$1j$	$1ij$	$1jj$	$3ij$	$1jk$	$3ik$	$2ik$	$2il$	$1jl$	$2il$	$2il$	$2im$
	$1k$	$1ik$	$1jk$	$1jj$	$1kk$	$1ij$	$1jj$	$1jk$	$1kl$	$1ij$	$1jj$	$1jl$
				$1ik$		$1jk$	$2jk$	$1jl$		$1jl$	$1jl$	$1jm$
				$1jk$		$1kk$	$1kk$	$1kk$		$1ik$	$1jk$	$1kl$
								$1kl$		$1kl$	$1kl$	$1km$

Genotypes and expected frequencies of progeny are given in the body of the table. Relative frequencies apply within vertical columns and not between columns.

Normally, this somatic mosaicism will not be transmitted as such to a carrier's offspring. However, non-Mendelian phenotypic classes and segregation ratios within the progeny will result from the mosaicism of the gonads. Table 1 contains a summary of results such as might be expected if the gonads are a 1:1 mosaic. Fundamentally, an i/ij type mosaic will, as a reproductive adult, generate $3i:1j$ segregation in its gametes, leading to 3 : 1, 3 : 4 : 1, or 3 : 3 : 1 : 1, progenies depending on the genotype of the other parent (Table 1 A). The i/ij segregation may mimic a gene conversion event, or in a multipoint cross may simulate intragenic recombination (Watt, 1972). An i/ij mosaic segregates $2i:1j:1k$ gametes, producing progenies containing three, five, or even six classes of genotypes from segregation at a single locus (Table 1 B). The i/jk segregation will appear to indicate the action of a modifier gene or some other kind of multiple-locus effect; however, the characteristic 2 : 1 : 1 gametic ratio coming from the PMS-mosaic parent should be sufficient to distinguish this effect from other possible models. The most diverse progeny would result from an $i/jk \times l/m$ cross, but still not more than six segregant classes would be expected.

These unusual segregation patterns could also be seen in PMS cases affecting morphology. Affected individuals might show bilateral asymmetry in obscure to prominent characters of form or colour. Such morphological effects might be most easily detected in systems such as the wing pattern of insects.

There is one case in which apparent transmission of the somatic mosaic phenotype can occur; if the locus in question carries a 'hot spot' for the occurrence of PMS, so that PMS occurs at a high frequency in the gametes of a mosaic, and its offspring likewise are mosaic. Other extra-Mendelian effects, such as gene conversion, are known to display such hot spots (Gutz, 1971).

PMS effects such as those described above complicate the analysis of regulatory

systems in eukaryotes by suggesting that multiple loci or modifiers are involved in either regulation or expression of the system in question. These same effects could also confound population-genetic analysis of variation by suggesting that multiple, rather than single, loci are controlling the trait, and by requiring additional alleles with unusual properties to explain some of the banding patterns observed following gel electrophoresis.

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