BETA LACTOGLOBULINS AND THE AMINO ACID CODE

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Studies with the beta-lactoglobulins of cow's milk have shown the existence of three types of this protein A, B and AB (1, 2) in which aspartic - valine and glycine - alanine behave as alleles of a simple Mendelian factor without dominance, resulting in 2asp - 2val (A) asp - val - gly - ala (AB) and 2gly - 2ala (B) lactoglobulins. The apparent absence of crossing-over between asp - val and gly - ala (1, 2) suggests that in proceeding from gly - ala to asp - val, the two necessary base changes in the codes (3, 4) may perhaps be in nearest neighbor sequences. In terms of the genetic information, a depiction of one of the possibilities is as follows:

	Lactoglobulin B	Lactoglobulin A
	Gly Ala	Asp Val
Messenger RNA	G U G C U G	G U A U U G
Strand 1, DNA	C A C G A C	C A T A A C
Strand 2, DNA	G T G C T G	G T A T T G

Figure 1

A further assumption may be made that the base changes do not involve a decrease in messenger U, in view of the fact that this circumstance, with the exception of ileu to thr, (13) fits all the reported mutational single - amino - acid changes in DNA (5 - 12).

These assumptions, by restricting the order of the possible base sequences in the gly/asp and ala/val coding triplets may aid in postulations regarding the base sequences in the triplets for the other amino acids. Of the eight possible combinations of the gly - ala codes (4) only the four containing adjoining G and C lead to asp - val when the two adjoining letters GC or GG are simultaneously changed to AU or AA. These assumptions lead to UGG/UGA or GUG/GUA for gly/asp and CGU/UGU or CUG/UUG for ala/val. Of these, only the combination of GUG/GUA and CUG/UUG conforms with the interrelationship that results from $aspNH_2$ to lys(9,13) assuming that this mutation is from a single-base substitution.

Those not arising from HNO_2 mutants of tobacco mosaic virus may be derived on a complementary basis from corresponding changes in either DNA strand followed by messenger formation or by replication and messenger formation.

If fig. 1 is changed to list, for example, UGG for glycine, the resultant interconnected base sequences in table I lead to both AUA and UAA for lysine. Similar difficulties arise if other changes are made in fig. 1, CACCGA to CATTGA eliminates valine and CCAAGC to CCGGGC results in unknown messenger codes.

The code letter changes in table I include 16 of the 19 changes listed by Speyer *et al.*(4); those omitted in table I are asp to ser, (lack of agreement), thr to met (lack of agreement) and tyr to phe (agreement but no way of locating A in the code for tyr). The spontaneous $aspNH_2$ to arg change reported by Wittmann (13) does not fit the table. It should be emphasized that the approach is formal and the table is based entirely on the concept of a simultaneous change in two sequential bases on the DNA strand, inferred from the constancy of composition of the three beta-lactoglobulins of cow's milk.

References

(1) Aschaffenburg, R. and Drewry, J., Nature, 180,376 (1957)
(2) Gordon, W. G. Basch, J. J. and Kalan, E. B., J. Biol. Chem. 236,2900 (1961)
(3) Nirenberg, M. W. and Matthaei, J. H., Proc. Nat. Acad. Sci., 47,1588 (1961)

TABLE I

Amino Acid	Code	Supporting evidence	Base Change	References
Phe	UUU	Direct		3
Val	UUG	Beta-lactoglobulin	C to U	2
Ala	CUG	Beta-lactoglobulin		2
$GluNH_2$	UCG	$GluNH_2$ to Val	C to U	11,13,14
Ileu	UUA	Ileu to Val	A to G	13
Thr	UCA	Thr to Ileu	C to U	13
Ser	UCU	Thr to Ser	(A to U)	14
Pro	UCC	Pro to Ser	C to U	13
Leu	UUC	Pro to Leu	C to U	13
$AspNH_2$	CUA	$AspNH_2$ to Ala	A to G	13,14
Gly	GUG	Beta-lactoglobulin	A to G	2
		Asp to Gly	A to G	13
		Gly to Asp	G to A	10
Asp	GUA	Beta-lactoglobulin		2
Glu	AUG	Glu to Gly	A to G	6,13,15
		Gly to Glu	G to A	12
Arg	GUC	Arg to Gly	(C to G)	7
		Gly to Arg	(G to C)	12
Lys	AUA	Lys to Asp	A to G	8,15
		Glu to Lys	G to A	5,7
		$AspNH_2$ to Lys	(C to A)	9,13

References (cont'd.)

(4) Speyer, J. F., Lengyel, P., Basilio, C. and Ochoa, S., Proc. Nat. Acad. Sci., 48,....(1962) (in the press)
(5) Hunt, J. A. and Ingram, V. M., Nature, 184,640 (1959)
(6) Hill, R. C., and Schwartz, H. C., Nature, 184,641 (1959)
(7) Hunt, J. A. and Ingram, V. M., Nature, 184,870 (1959)
(8) Murayama, M., Fed. Proc., 19,78 (1960)
(9) Baglioni, C., and Ingram, V. M., Biochim. and Biophys. Acta, 48,253 (1961)
(10) Baglioni, C., J. Biol. Chem., 237,69 (1962)
(11) Weisberger, A. S., Presented at American Cancer Soc. Meeting, Phoenix, Ariz., March 11, 1962
(12) Helinski, D. R. and Yanofsky, C., Presented at Princeton Biochemistry Seminar, Dec. 7, 1961
(13) Wittmann, H. G., Naturwissenschaft., 48,729 (1961)
(14) Tsugita, A., Protein, Nucleic Acid, Enzyme (Tokyo) 6,385 (1961), cited by Speyer *et al.* (6)
(15) Tsugita, A., cited in (4)