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DEPARTMENT OF BIOLOGICAL SCIENCES

May 10, 1965

Professor F.H.C. Crick
Laboratory of Molecular Biology
Medical Research Council
University Postgraduate Medical School
Hills Road,
Cambridge, ENGLAND

Dear Francis:

The changes we've detected are as follows:

Set 1

Gly $\xrightarrow{UV}$ Arg $\xrightarrow{spont}$ Ser, Gly, Thr (rare), Ileu (only Arg $\longrightarrow$ Gly increased by 2AP + 5-BDU)

The same Gly $\xrightarrow{UV}$ Glu $\xrightarrow{spont}$ Ala, Val, Gly (only Glu $\longrightarrow$ Gly with 2 AP + 5 BDU)

The same Gly $\xrightarrow{UV}$ Val (only once)

The Val from Glu $\xrightarrow{spont}$ Gly, Ala

The above Ala $\xrightarrow{UV}$ Glu

The above Ser $\xrightarrow{UV}$ Arg

Set 2

Gly $\xrightarrow{UV}$ Val

Val $\xrightarrow{spont}$ Gly, Ala

Set 3

Gly $\xrightarrow{UV}$ Asp, Cys

Asp $\xrightarrow{spont}$ Gly, Ala (only Asp $\longrightarrow$ Gly increased by 2 AP)

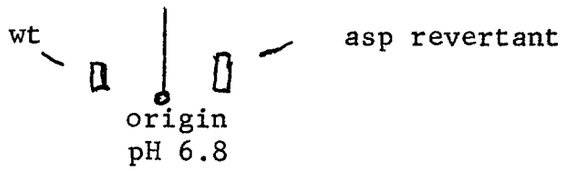
Cys $\xrightarrow{spont}$ Gly (not increased by 2 AP)

Set 4

Thr $\xrightarrow{EMS}$ Ileu

Ileu $\longrightarrow$ Thr, Ser, Asp (only Ileu $\longrightarrow$ Thr by 2 AP)

This is the Asp you doubted. The evidence that it is Asp is as follows: At pH 6.8 the Asp peptide is clearly negatively charged relative to the wt peptide.



However, in view of the disagreement with the coding data we are in the process of looking at papain fragments to be doubly sure. There is the slim possibility which we certainly haven't excluded, that there are two changes in the peptide (Ala-Gly-Val-Thr-Gly-Ala-Glu-**Asn**-Arg) Ileu ⟶ Asn and Asn ⟶ Asp.

Other changes

Tyr $\xrightarrow{\text{spont}}$ Cys

Cys $\xrightarrow{\text{spont}}$ Tyr (Increased by 2AP)

Leu $\xrightarrow{\text{spont}}$ Arg

Ser $\xrightarrow{UV}$ Leu

We have one paper in press that is pertinent, but the observations are summarized above as Set 3.

I just heard about Streisinger's result which should be conclusive--I wasn't convinced by Schweet or Rich--their data was suggestive at best. We are repeating the crosses with better outside markers. I'll let you know as soon as we have any results.*

If AGA is the Arg of Set 1, the only disagreements between our observation and the code you sent and the almost identical one Nirenberg has in press are (1) infrequent mutation of Arg ⟶ Thr ACA (Incidentally AUA almost certainly is Ileu from our replacements.)

(2) Arg x Val cross ⟶ Gly + Ser. The best explanation is that Val (GGA) mutated to Val (GGPyrimidine). The Val stock used in the cross was used as a standard lab reference stock for at least a year and I guess it could have changed, although it would seem unlikely.

(3) The presumed Ilue ⟶ Asp change discussed above. There's one other cross we haven't published.

Thr x Glu (both Set 1) ⟶ 4 recomb. analyzed, 3 Ala, 1 Gly (a revertant?)

That's it! I'll keep you posted on anything else of relevance that turns up.

With best regards,

Sincerely,

Charles Yanofsky

CY:ps

*The data we do have are as follows: