



**BioUpdate
Foundation**

Do Complementary DNA Strands Code for Complementary Peptides?

Regular readers of this blog will have realised that there is a certain kind of science which fascinates me. It is science which is irrational, inexplicable or contradicts conventional wisdom, but also has good evidence to support it. What I think attracts me to it is how it challenges our objectivity when assessing scientific theories.

One might expect that evidence based science which challenged our fundamental beliefs would have a big impact. All too often, however, it simply disappears, and one has no way of knowing was it wrong, was it just a chance observation under special circumstance, or is peer review not that objective after all?

This month's blog concerns something which I came across in the 1980's. At the time I had joined a company on the basis of my experience in protein sequencing but I was tasked with the role of developing a peptide synthesiser. When I explained to the Managing Director that I had no experience in that area, he did not see a problem; "Putting peptides together amino acid by amino acid is simply the reverse of taking them apart amino acid by amino acid", he told me!

Naturally, I developed an interest in peptide synthesis and synthetic peptides, and monitoring the literature I came across a paper by a group at the University of Texas (K.L. Bost, E.M. Smith & J.E. Blalock PNAS 82 1372-1375, 1985). They studied a 24 residue ACTH peptide, and from the protein sequence derived the mRNA sequence. From a RNA sequence complementary to the mRNA sequence they could determine the protein sequence which the complementary RNA would code for, and they had this peptide synthesised. As it was a "complementary" reverse sequence they called it HTCA. They found what they described as a specific and high affinity binding between HTCA and ACTH. They showed a similar binding between γ -endorphin and its complementary peptide.

Their experiments seem to have been triggered by an observation that codons for hydrophilic and hydrophobic amino acids on one strand are complemented by codons for hydrophilic and hydrophobic amino acids on the other strand. They were of the opinion, however, that the binding could not result from simple hydrophobic interaction between the two peptides and that shape must play a role. One peptide being a kind of "internal image" of the other.

What is curious on rereading this article is that when discussing codons they do not use the term DNA. When discussing complementary sequences they only discuss them in terms of RNA. It is, however, an inescapable conclusion that a peptide coded for on one strand of DNA can have a binding affinity for a peptide coded on the opposite DNA strand. Perhaps it was a statement too far for the editors. The authors discussed their results in terms of evolution of hormones and their receptors, but if these observations are true, and they have passed peer review, then it implies something very fundamental that we have missed. Although the observation is limited to small

peptide sequences, and the more complex folding of larger proteins may well complicate the matter, it would be extraordinarily remarkable if the protein coded for on one DNA strand had a folded shape based affinity for the protein coded for the complementary strand. It would still be quite extraordinary if there was simply a chemistry based interaction – it would imply that we have missed not only something very fundamental in the relationship between DNA codons and the amino acids they code for, but also something fundamental between one amino acid and its “partner” coded for by the complementary codon.

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