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Dear Josh,

Congratulations to you for the clear job of exposition of DNA homology and repeated sequences in your column which appeared September 21st in the 'Washington Post.'

I have some minor points of amplification. Setting up the situation that made the repeated sequences recognizable, should indeed be credited in part to Peter Walker and Anne McLaren. More credit should go to Bill Hoyer, Brian McCarthy and Ellis Bolton. Bill actually made the first observations of animal DNA reassociation. He also made early measurements showing the imprecision of reassociated DNA in a given animal. Peter did this later - ultimately in more detail - for mouse and rat. Both Bill and Peter showed that there were fractions of the DNA which bound to DNA in the agar system and other fractions which did not - or not as well.

None of them directly faced the theoretical impasse of the much too rapid rate of reassociation or, perhaps, even believed that the rate vs. complexity argument (which goes back to Marmur and Doty) was applicable.

This was the point at which I entered, with a solid background of evidence already available to me. At first I did tests to indicate that the agar had no striking effect on the DNA and showed that the fast reassociation reaction occurred in solution. It was then conceivable that agar could have been a catalyst for reassociation. At this point I proposed to my colleagues that there were repeated DNA sequences and that some of these had diverged from each other to produce the imprecise pairing.

Mike Waring arrived as a Fellow and he and I fell by accident onto the fast reassociation of the mouse satellite. We directly measured the rate and showed that it had the concentration-dependence

of a second-order reaction. That settled the issue for one example, and made the whole idea plausible. Peter was not really convinced when I told him of all this on my visit to Edinburgh in the spring of 1965. He and Ann McLaren went ahead and published their hydroxyapatite work on the mouse satellite, stating that it was a "stable" fraction, indicating that either strand separation had not occurred, or it could fold back on itself.

There is much history after this and I will just catch a couple of things. Mike Waring and I did a lot of measurements to get quantitative control of the reassociation reaction and studied the curious, though refractory, phenomenon of network formation during reassociation of high molecular weight DNA. Dave Kohne came in on the proof of the generality of occurrence of repeated sequences and much else, including getting hard control over hydroxyapatite as a tool, and the use of it to show that there was some non-repeated DNA in calf.

I hope you will enjoy these comments as they are intended: a clarification of an interesting story. This story may sometime have a broader interest. By my present hunch, we will find that almost all of the DNA of creatures above fungi originated in the events that we now describe as saltatory replications.

I have always found the personal aspects of scientific history more satisfying than the record that appears in the "literature". It is the essential rather than the formal reality. Being personally involved, I admit my attitude is somewhat ambivalent, of course. You need only ask if you would like a list of relevant references or clarification of any points.

I am sorry to have to disillusion you about the potential information content of our own DNA. My best estimate (criterion:  $25^\circ$  below  $T_m$  of native DNA) is that 20% of amphiuma is non-repetitive. The two-thirds of human which is non-repetitive (at the same criterion) amounts to only one-tenth that of amphiuma. Ah, if only amphiuma - or we, for that matter - were to make use of anything more than a tiny fraction of all of that.

With best regards,

Sincerely yours,

  
R. J. Britten