CF-1 11/18/98

Avram Goldstein, M.D.
Professor Emeritus of Pharmacology, Stanford University
735 Dolores, Stanford, CA 94305-8427
650-324-9251 (FAX 650-328-8412)
e-mail: avram.goldstein@stanford.edu

[For mailing: Use street address only, not department or university]

November 7, 1998

Joshua:

All I can tell you about my 1952 letter to you -- 46 years ago!!! -- is that it obviously refers to the mutator strain of E. Coli that I eventually reported in J Bacteriol 70:588,1955. It has been a long journey from bacteria to neuropeptides and drug addiction!

About my views on medical school teaching, which were implemented in the Stanford curriculum:

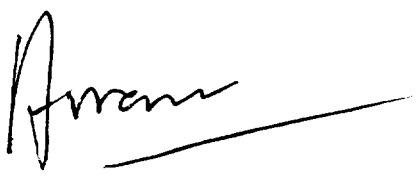
J Med Education 31:365(1956); 33:193(1958) and especially J Med Education 36:686(1961) ("The basic medical sciences in the Stanford Plan").

You ask when I met you and Esther prior to that 1952 letter. Since I was working on bacteria and antibiotic resistance then, maybe a Gordon Conference? I don't recall it.

Finally, yes, Alex is dead serious about his foundation, which has been transformed into an actual Institute for the study of the genetics and neurobiology of addiction.

By the way, the article from PNAS that you sent him (by Bond et al, including Mary Jeanne and others) has an extremely misleading title, and in a strange way mixes two SNPs that they find. The most common SNP (A118G, which produces N40D) affects a glycosylation site on the N-terminal extracellular tail of the mu opioid receptor. It increases the affinity and potency of beta-endorphin by a factor of about 3. But it shows no difference in prevalence between heroin addicts and non-addicts.

On the other hand, C17T, which produces A6V in the same N-terminal domain, does differ between heroin addicts and non-addicts, but the statistical significance, although $P<0.05$ (I compute $P=0.036$ by Fisher's exact method) must still be considered marginal. In any case, all the data on binding and signal transduction concern the other SNP, not this one. Moreover, the actual discovery of these two SNPs is not original; they were reported previously by Berrettini et al (ref 12) and also by Bergen et al (ref 13).

In summary, the work is good but prematurely published inasmuch as the SNP with a physiologic consequence (slightly tighter binding and slightly greater potency of beta-endorphin) does not have a different frequency in heroin addicts, whereas the paper tells us nothing about binding or signal transduction for the SNP that is more common among heroin addicts.

With best wishes,