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Dear Peter:

There seem to be three distinct questions about the nomenclature proposal that need to be agreed upon: the scientific question, of how the inserted sequences are to be operationally defined; the lexical question, of which names will be clearest and easiest to use; and the political question, of who is to do the naming.

The scientific question, raised by several "purists", is whether one can define a gene as a nucleic acid sequence coding for a protein product, and alleles as related or homologous sequences: the classical geneticist would define genes by complementation tests, and alleles by segregation tests. Given that nucleic acid technology is now so much more powerful than classical genetics, both for viral genes and even more so, for cellular genes, it seems clear that classical definitions can no longer be regarded as necessary or sole criteria. However one will have to be careful about how the sequences are defined. The revised Coffin-Varnus manuscript covers the most important points, in particular that virus-related sequences such as the rat 30S sequences in KiSV and the xenotropic MuLV sequences in SFFV should not be included as cellular inserts, and that independently expressed sequences should be distinguished (e.g. erb-a, erb-b). One problem which is not explicitly discussed is how distantly related sequences from distinct species (e.g., fps and fes) should be treated; I would favor keeping them distinct. Future problems which may arise include how one is to define and refer to spacer and/or intervening sequences in cellular genes; or rearrangements; or gene families; or sequences directly isolated from the cellular genome by cloning, rather than as inserts into a viral genome: probably one should postpone consideration of these questions until the occasion arises.

As far as the names themselves are concerned, the Coffin-Varnus proposal still seems preferable to either the Duesberg or the Robinson proposals. The Duesberg proposal, to name the onc genes by the initials of the prototype virus, is likely to lead to confusion between virus and sequence, since it depends solely on the difference between upper and lower cases to distinguish the two (e.g., AEV/aev); this would certainly lead to confusion in conversation and probably even in print. I think it is better to give different names to virus and gene. The Robinson proposal strikes me as too cumbersome for practical use, and the

use of numbers rather than names makes it impossible to remember. Overall the use of three letter names, derived from but not the same as the name of the prototype virus, seems the most sensible solution, provided that the names are generally agreed upon. The name of the prototype virus, in this context, could include the name of the person who first isolated or studied the virus (e.g., Fujinami), the name of a disease (e.g., sarcoma, leukemia, erythroblastosis), or the name of a host species (e.g., rat), depending purely on accepted practice and historical precedent. It might be useful in the final report to indicate exactly how the names were derived, wherever this is not obvious.

The objection that pathogenic or transforming specificity should not be used as the sole basis for nomenclature is a reasonable one. Graf however continues to justify the names erb, myb, and mac on the basis of differences in target-cell specificity. There are two possible solutions to this problem. The simplest is to reiterate as clearly as possible that the names are based on the names of the prototype virus (which may for historical reasons include some reference to disease); the change from mac to myc should be sufficient to make this clear. The other would be to change the names to something else; however since the new names would probably also contain some reference to disease it would not really represent a significant improvement.

Finally, as regards the political question of who is to be responsible for questions of nomenclature, it would probably be a good idea to set up a standing sub-committee to consider future questions of this sort. Presumably there are a limited number of cellular transforming genes, but it is unlikely that all of them have yet been isolated as inserts into viral genomes and so questions of priority and criteria for nomenclature will continue to arise.

I hope these comments are of some use.

Best regards,

Yours,



G. Steven Martin

GSM:tta-o