Reviewer's report

Title: The 3' region of Human Papillomavirus type 16 early mRNAs decrease translation

Version: 1 Date: 1 July 2005

Reviewer: Stefan Schwartz

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General

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
Vinther J. et al have investigated the cis-acting effect on mRNA and protein levels of sequences from the early region in HPV-16. The reason for this being that this sequence many times is present on the HPV-16 hybrid mRNAs encoding the viral oncoproteins that are produced from integrated genomes. The stability of these mRNAs therefore affect expression levels of the E6 and E7 viral proteins.

This is a sincere effort to investigate how various HPV-16 sequences may affect E6 and E7 mRNA levels that disserves publication.

The Authors demonstrate that a rather large sequence from the early region of HPV-16 has reduce mRNA levels when present in cis. This sequence spans 2582-4214 and therefore includes RNA instability elements in the early UTR of HPV-16 previously described by Jeon and Lambert (PNAS, 1995, 92: 1654). Surprisingly, the sequences that reduce mRNA levels in Vinthers experiments do not map to the early UTR. As a matter of fact the early UTR does not seem to affect RNA levels substantially. These results are in support of those published by Schwartz group (Zhao et al, J. Virol, 79:4270). This is discussed by Vinther. Vinther found that an upstream region affect mRNA levels and speculate that splicing elements may be responsible for the reducing mRNA levels. This sounds reasonable and further documents that various RNA processing signals taken out of their natural context may have detrimental effects on gene expression.

Vinther also monitor reporter GUS protein levels and quantitates cyto mRNA levels by real time PCR and propose that translation is inhibited. In fact, this is also mentioned in the title of the manuscript. The result on translation inhibition is the weak point of the manuscript. There is now evidence provided that translation is inhibited other than quantitations of very low levels of RNA. The authors should tone down their speculations on translation and focus on what they actually show: Observation that the certain sequences in the early region in the HPV-16 genome act in cis to reduce mRNA levels. This should be reflected in the title.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Discretionary Revisions (which the author can choose to ignore)
What next?: Accept after minor essential revisions

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: No

Declaration of competing interests:
I declare that I have no competing interests’