LETTER to the EDITOR

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Human Mammary Tumor Virus (HMTV) Reshapes Risk of Women Developing Breast Cancer: Re-visiting an Under considered Variable in Tumorigenesis of the Breast

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Dear Editor

We were so drawn into one manuscript recently published by Asian Pacific Journal of Cancer Prevention (APJCP) which discussed about association of human mammary tumor virus (*HMTV*) and *BRCA1/2* mutation-harboring breast malignant tissues in Iraqis women [1]. The study re-ignites awareness of one under considered causative agent to malignancy in breast, *HMTV*, which harbors approximately 90-95% homol-ogy of retroviral sequences to mouse mammary tumor virus (MMTV) [2]. Soon after the finding of type B MMTV-like particles in 60% of patients with breast cancers, humoral and cellular immune responses against MMTV were broadly reported [3]. Uniquely, as many as scholars demonstrated the presence of *HMTV/MMTV* particles, there were also an equal number of evidence of the absence of such particles which shrunk the appealing features of the virus as one of the proposed etiological variables in breast tumorigenesis. While Mant et al., found no MMTV/*HMTV* DNA in the human breast cancer cell lines and the clinical biopsies through RFLP [4], Etkind et al. detected mutant *MMTV-ENV* gene in breast tumor [5]. Cedro-Tanda et al., supported the later mentioned finding by adding that insertional mutagenesis might be the best bet on why *HMTV* presence did not automatically imply the tumorigenesis [6]. Despite the difficulty in drawing these dichotomous results into one firm conclusion, the authors dug deeper to see if there were interactions of the *HMTV*-infected breast carcinoma with *BRCA1/2* mutations, which is widely attributed to the most hereditary breast carcinoma [7]. We are not aware of this concept being done elsewhere. *BRCA1* pathogenic variants exhibit more aggressive clinicopathological profiles than that of *BRCA2*-counterpart (7). The authors show that *HMTV* was significantly associated with grade and types of breast cancers, suggesting that *HMTV* infection in defective *BRCA1* and *BRCA2* genes played is key in breast tumorigenesis. *HMTV* can fuse into hosts' epithelial breast cells which, in turn, perturb chromo-somal stability via p53 deregulation, leading to repression of BRCA at the mRNA level [8]. As a result, p53-dependent BRCA suppression leads to transformation of breast epithelial into cancer cells [8]. Findings of the presence of *HMTV* in breast carcinoma pave the way for enriching the existing platform of risk assessment which, as a matter of fact, receives less attention than that in curative intervention. We, next, questioned whether *HMTV* directly mutates BRCA1/2, thus dependency on p53 deregulation is abrogated. Should this be multiomically addressed, particularly on how the viral genome is at play with the host genome, which might result in differentially expressed genes (DEGs) signature, we could have a crystal clear idea not only on how to maneuver with cascading mechanisms post *HMTV* infection, but also how to prevent *HMTV* taking over genome control to exert its pro-tumorigenesis properties. In regard to correlation test, which was used to back the final conclusion up, we might find ourselves in quite a dif-ferent point of view from the authors. Let us highlight the correlations between the markers being ob-served. The authors show that the correlation (r) values of *HMTV-BRCA1* and *HMTV-BRCA2* are 0.443 ($p = 0.003$) and 0.58 ($p = 0.006$) and took both as significant correlations. To our perspective both values show low to moderate correlations and these are supported by the p values, both are below either 0.05 or 0.01, which indicate that the findings of low to moderate correlations of the aforementioned markers are less likely by chance [9]. This is also the case with BRCA1-*BRCA2*, *HMTV*-grade, and *HMTV*-types of breast cancer correlations that each is represented by r value of 0.398, 0.449 and 0.348, respectively, which ex-plain weak relationship for each comparison. Here, we see a p value as an indicator of how likely the r value contains error (by chance), not directly to imply the relationship among variables being assessed. r and p values have their own proportion to delineate things. On these stuff that we particularly learned the authors might have mixed up the statistical tests and based their concluding statements solely on p values. r values, on the other hand, have been overlooked. Consequently, all comparisons are shown with pseudo-significance. Our thoughts, however, are not intended to weaken the importance of studying *HMTV* as somewhat a forgotten aspect in breast cancer emergence. They are only present to emphasize the need for a much bigger sample size and more complex disciplines to come up with a strong conclusion. Only then interested scholars might confidently claim that breast carcinoma causing *HMTV* is not anymore "rumor has it" virus with huge gaps of positive and negative findings [10].

Conflicts of Interest

Both authors declare that there are no conflicts of interest and no financial association to any party related to this correspondence.

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