LETTER

HIV-1 Tat- and Vpr-responsive MicroRNAs of Neuronal Cells

Based on Exiqon hybridization array profiling, >2-fold differential expression of 69 microRNAs was reported in both SH-SY5Y cells and primary human fetal neurons in response to HIV-1 Tat (1) or Vpr (2) in experiments with shared controls. Corrections now indicate that raw and normalized data from three profiling platforms, including two not initially described, were recently uploaded to the Gene Expression Omnibus (GSE44265 and GSE44266) for MIAME data policy compliance (3, 4).

The data suggest that the described Exiqon profiling was uniformly unsuccessful for the mainstay SH-SY5Y experiments and for several of the fetal neuron samples. Only 12 confirmed miRNAs were detected above background plus two standard deviations in all conditions of the SH-SY5Y experiment. It is unclear how reliable, quantile normalized data could be generated from background-level signal, but the processed values as provided also show no consistent changes of reported miRNAs for SH-SY5Y or fetal neurons.

Given the quality of the Exiqon data, especially for the cell line experiments advanced as the primary support, the authors are commended for providing additional, unpublished Agilent and Affymetrix data. However, the "quantile normalized" Agilent data are unnormalized raw values. Distributions of the "processed" Affymetrix data appear similarly inconsistent with normalization. MIAME compliance aside, data across the various platforms and cell types seem to challenge, *e.g.* the reported quantitative PCR finding of Tat-mediated, >400-fold miR-34a up-regulation. Experimental and analytical replication is needed, guided by an indication of which arrays contributed to Fig. 3 in both Refs. 1 and 2, correctly normalized data, and appropriate details of data processing.

Kenneth W. Witwer¹

Department of Molecular and Comparative Pathobiology, The Johns Hopkins University, Baltimore, Maryland 21205

- Chang, J. R., Mukerjee, R., Bagashev, A., Del Valle, L., Chabrashvili, T., Hawkins, B. J., He, J. J., and Sawaya, B. E. (2011) HIV-1 Tat protein promotes neuronal dysfunction through disruption of microRNAs. J. Biol. Chem. 286, 41125–41134
- Mukerjee, R., Chang, J. R., Del Valle, L., Bagashev, A., Gayed, M. M., Lyde, R. B., Hawkins, B. J., Brailoiu, E., Cohen, E., Power, C., Azizi, S. A., Gelman, B. B., and Sawaya, B. E. (2011) Deregulation of microRNAs by HIV-1 Vpr protein leads to the development of neurocognitive disorders. *J. Biol. Chem.* 286, 34976–34985
- Brazma, A., Hingamp, P., Quackenbush, J., Sherlock, G., Spellman, P., Stoeckert, C., Aach, J., Ansorge, W., Ball, C. A., Causton, H. C., Gaasterland, T., Glenisson, P., Holstege, F. C., Kim, I. F., Markowitz, V., Matese, J. C., Parkinson, H., Robinson, A., Sarkans, U., Schulze-Kremer, S., Stewart, J., Taylor, R., Vilo, J., and Vingron, M. (2001) Minimum information about a microarray experiment (MIAME)-toward standards for microarray data. *Nat. Genet.* 29, 365–371
- Witwer, K. W. (2013) Data Submission and Quality in Microarray-Based MicroRNA Profiling. Clin. Chem. 59, 392–400

DOI 10.1074/jbc.L113.541755 ¹E-mail: kwitwer1@jhmi.edu

