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Abstract: Questions regarding whether the recently reported particles are authentic HIV virions?

In a BBC interview (http://newsvote.bbc.co.uk/mpapps/pagetools/print/news.bbc.co.uk/2/hi/health/4642940.stm), Stephen Fuller, one of the authors of an article titled "The Mechanism of HIV-1 Core Assembly: Insights from Three-Dimensional Reconstructions of Authentic Virions" (Briggs et al., 2006) stated that the HIV particles "varied in diameter by a factor of three.…You say can you show me the structure of the HIV virus and the question is which one." The answer to this question may be even more difficult than it appears.

In their technically superb Structure article, Briggs et al wrote: "Virions were approximately spherical, with diameters between 106 and 183 nm. The mean diameter, 125 ± 14 nm, was slightly smaller than that observed previously." Gallo and Fauci, writing in Harrison's Textbook of Internal Medicine, stated that retroviruses are "usually about 100 nm in diameter (Gallo et al., 1994). In the latest definition of retroviruses, "Virions are spherical, enveloped and 80-100 nm in diameter (van Regenmortel et al., 2000). The question must be asked: "On the basis of their diameter, what percentage of the particles reported by Briggs et al as being HIV particles are in fact retroviral particles?

In their concentrate, Briggs et al must have had numerous particles. Of those they examined 75 particles. No mention is made how these particles were chosen. Lentiviruses have only one cone-shaped core. Of the 75 particles observed in the Briggs et al article, "63 contained a single core" and of these 63, 40 "contained a core with conical morphology". The question must be asked: "What is the origin and what were the other 35 particles?"

According to Briggs et al, "HIV-1 particles with minimal contamination of cellular vesicles were obtained as described previously (Welker et al, 2000)". In the Welker et al study (Welker et al., 2000), under their subtitle "Cell culture and virus preparation" the authors wrote: "MT-4 cells and C8166 cells were maintained at … supplemented with … Stocks of HIV-1 strain NL4-3 were produced by transfection of HeLa cells. MT-4 cells were initially infected with cell-free virus, and infected cultures were subsequently expanded by cocultivation." Under their subtitle "Isolation of HIV-1 cores" the authors wrote: "Virus particles were concentrated from cleared culture medium by centrifugation through a cushion of 20% (wt/wt) sucrose in phosphate-buffered saline (PBS)…". For a long time, some of the best known retrovirologists including Peter Duesberg, Robert Gallo and Howard Temin have been telling us that particles may have the morphological characteristics of retroviruses but are not viruses. At present, it is accepted that 8% of the human genome is comprised of retroviral elements (Alberts et al., 2002). Another well-known retrovirologist, George Todaro wrote: "the failure to isolate endogenous viruses from certain species may reflect the limitation of in vitro cocultivation techniques" (Todaro et al., 1976). Non-HIV infected C8166 cells release retrovirus-like particles (Dourmashkin et al., 1993). In the 1970s, Hans Gelderblom, who has intensely studied the morphology of the HIV particles, published several papers in which he reported retrovirus-like particles in HeLa cells. The MT-4 cell line is infected with HTLV-1 (Akagi et al., 1985). In a 1997 interview, when questioned about the problems related

to “HIV” purification, Montagnier responded: “I agree completely. That’s why finally we were not very ardent about using immortal cell lines”. In the “MT cell lines which have been found by the Japanese (MT2, MT4)” there “is a real soup” of retroviral particles (Tahi, 1997).
Briggs et al did not have any controls.

The questions are:
(a) How do Briggs et al know that the images they produced are those of retrovirus particles and not retrovirus-like particles?
(b) How do Briggs et al know that the images they produced are "Authentic Virions" of a unique retrovirus, “HIV”, and not of the other retroviruses in the “soup”?

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*** Cover Letter**

Dear Dr. Szweczak,

We'd be most grateful for your consideration in regard to this small contribution to the Journal.

You may recall email correspondence with Barry Page which is printed below.

Kind regards,

VF Turner

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Dear Dr. Page,

Thank you for your inquiry. We do have publication formats which enable scientists within the community to comment on work published in the journal. One option, "Matters Arising", most often takes the form of a research article. You also have the option of submitting a "Letter to the Editor" which provides a less structured format.

You are welcome to submit your comments using our on-line manuscript submission platform Editorial Manager (www.editorialmanager.com/st).

I must confess that you've made me curious. Would you care to send me a brief summary of the comments in advance?

Sincerely,

Lara Szewczak

Lara Szewczak, Ph.D.
Associate Editor, Structure

REJECTION LETTER

Feb 08, 2006

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Dear Dr. Papadopulos-Eleopulos,

Thank you for submitting this comment to Structure.

After some consideration and consultation with an expert on the structural biology of HIV, I am sorry to say that the Editors have concluded that they are unable to accept your letter for publication in Structure. We do appreciate the importance of sample preparation in any structural study, and consequently, strive to chose reviewers who are well-versed in the technical aspects of the work under consideration as well as knowledgable about the biological relevance of the study. Given the precise nature of your questions, it may be best for you to address your them to the author directly.

Kind Regards,

Lara Szewczak

Lara Szewczak, Ph.D.
Associate Editor, Structure