with CAS membership, the numbers were 9, 8, and 7 among the past three CCPCCs, which means that the share of CAS members, elite in the Chinese scientific community, in CCPCC has decreased.

Cong Cao
Columbia University,
New York, NY 10027, USA

Science regrets the omission of Lu Yongxiang from the list of previous members of the central committee. However, the slight reduction in the number of academicians on the central committee is more than offset by a rising number of scientists on the committee who are not CAS members but who hold leading positions in China's scientific community. There also are more senior engineers than before in the party's political bureau.—**Eds.**

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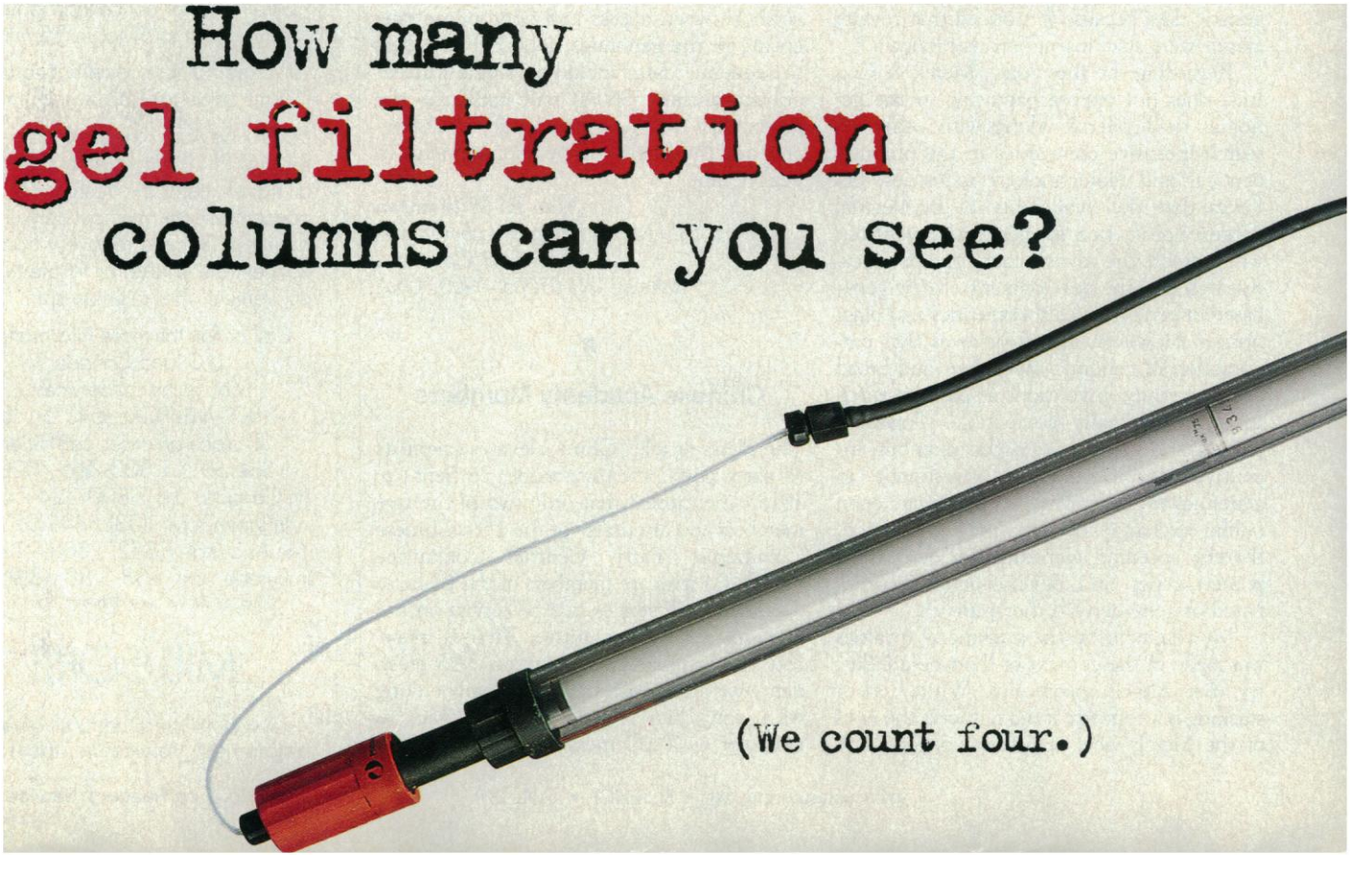
Different Subtypes of HIV-1 and Cutaneous Dendritic Cells

Max Essex and his group (L. E. Soto-Ramirez *et al.*, Reports, 1 Mar. 1996, p. 1291) describe observations that suggested that human immunodeficiency virus–type 1 (HIV-1) strains from genetic subtype E were more replication-competent than subtype B strains in Langerhans' cells (LCs), which are dendritic cells (DCs) isolated from epidermal tissues. Studies in humans and in the simian immunodeficiency virus (SIV)–infected macaque model suggest that these cells may be involved in the transmission of HIV-1 across the vaginal epithelium (*1*). Thus, Soto-Ramirez *et al.* propose that their observations could account for the rapid spread of subtype E strains by heterosexual intercourse in Thailand (*2*). This proposal received much attention in the news media and public health organizations and gave rise to speculation about a new wave of heterosexual, subtype E HIV-1 infections in America and Europe as a result of sex tourism in southeast Asia. The concept of subtype-dependent variations in transmissibility of HIV-1 would also have important implications for the design of HIV-1 vaccines. Consequently, in two independent studies (*3*, *4*), we investigated these conclusions, but were unable to confirm them.

Studies by Dittmar *et al.* described the infection of mature, granulocyte-macrophage colony-stimulating factor-cultured LC suspensions with 26 HIV-1 isolates of subtype A, B, C, D, E, and F (*3*). In general, activated peripheral blood mononuclear cells (PBMCs) replicated virus more efficiently than the LCs, irrespective of the viral subtype and phenotype. Furthermore, the heterosexually transmitted isolates tested did not exhibit a specific tropism for LCs when compared to homosexually transmitted isolates, again irrespective of the genetic subtype. The presence of both CXCR4 and CCR5 mRNA in the LCs, and the fact that the usage of CXCR4 and CCR5 was independent of virus subtype for all the primary isolates used in this study (*3*), suggest that the selective transmission of non–syncytium-inducing (NSI) viruses cannot be attributed solely to the selective expression of certain co-receptors on LCs. In a separate study, cutaneous DCs (comprising LCs and dermal DCs) were isolated from skin organ cultures and purified by cell sorting. With the use of these DCs, Pope *et al.* observed that, although there was considerable strain-dependent variation in replication efficiency (the viruses usually replicated better in activated PBMCs), there was no evidence for the preferential replication of subtype E HIV-1 isolates in the DC cultures, as compared with the subtype B isolates (20 E and 30 B subtype viruses were tested) (*4*). HIV-1 replication in DC-T cell cocultures was also independent of whether the viruses were characterized as T cell–tropic/SI or macrophage-tropic/ NSI.



Neither purified DCs nor resting T cells could alone support HIV-1 replication, but a small proportion (3 to 5%) of T cells in such a DC-enriched population (and vice versa) was sufficient to create a very permissive environment for the replication of HIV-1 isolates from subtypes E and B (*4*).

These studies have demonstrated that there are no discernible differences between the ability of different HIV-1 subtypes to replicate in skin-derived DCs. Although there are minor differences in methodology between each of these studies and that of the report by Soto-Ramirez *et al.*, the observations of that group cannot be reproduced in similar experimental systems. We detected strain-dependent variation in the replication of HIV-1 in DC cultures, but we were unable to detect subtype-dependent variation (*3*, *4*). In vitro systems that attempt to mimic the complex processes of HIV-1 transmission in vivo are oversimplistic, so great care must be taken before drawing sweeping conclusions from studies of this nature. However, in vivo studies of HIV-1 transmission in chimpanzees after vaginal/cervical inoculation do not support the premise that subtype B strains cannot be transmitted efficiently by this route (*5*).

There are several alternative reasons for the apparent segregation of subtype E strains among heterosexual cohorts, and subtype B strains among injecting-drug users and homosexual cohorts (*6*), and related studies should be consulted for other explanations of the epidemiology of the Thai HIV-1 epidemic (*6*–*9*). But the general notion that subtype B strains of HIV-1 are poorly transmissible through heterosexual contact is inconsistent with the characteristics of the HIV-1 epidemic in the Caribbean and South America (*6*, *7*, *9*, *10*), as noted recently by Fultz (*5*). We conclude that the study by Soto-Ramirez *et al.* does not explain important features of the HIV-1 epidemic and should not be relied on for decisions that affect public health policy or the design of HIV-1 vaccines.

M. Pope
Rockefeller University, 1230 York Avenue, New York, NY 10021, USA
E-mail: popem@rockvax.rockefeller.edu
D. D. Ho
J. P. Moore
Aaron Diamond AIDS Research Center, Rockefeller University, 455 First Avenue, New York, NY 10016, USA
J. Weber
Imperial College School of Medicine, St. Mary's Hospital, London W2 1PG, United Kingdom
M. T. Dittmar
R. A. Weiss
Chester Beatty Laboratories, Institute of Cancer Research, 2 London SW3 6JB, United Kingdom

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Response: Although HIV-1 B viruses have been present in Asia and Africa for some time, none of the major heterosexual epidemics in those regions have been attributed to HIV-1 B. Conversely, epidemics that have occurred primarily in males in the United States and Europe have usually been

the result of infection by HIV-1 B. The latter has been linked primarily to receptive rectal intercourse among homosexual men and injection drug use. We postulated in our report that prevailing strains of HIV-1 B in the United States and Europe might have reduced capacity for transmission by vaginal intercourse.

Most researchers would agree that LCs represent the most logical target for cervico-vaginal entry and exit of HIV-1. We postulated that most isolates of HIV-1 subtypes such as E and C, which have been linked to the major heterosexual epidemics, might grow more efficiently in LCs. The data we published support this hypothesis, which has at times been misconstrued to mean that no subtype B could ever be adapted to heterosexual transmission.

Pope *et al.* cite two recent papers that they interpret as not supporting our hypothesis. The data in the paper by Dittmar *et al.* (*1*) seem compatible with our hypothesis. We believe that the other paper cited (*2*) has several internal inconsistencies and is not relevant to our hypothesis. These two papers, cited by Pope *et al.* to make their point, are in major disagreement with each other. One shows that direct replication of HIV-1 occurs in LCs (*1*); the other states that such replication cannot occur (*2*).

A third paper, not cited by Pope *et al.*, defines two separate pathways by which LCs may be infected (*3*). The first, described earlier by Pope *et al.* (*4*), requires fusion between LCs and T4 cells (LC/T conjugates) for productive HIV infection to occur. Entry for this first pathway is based on the capture of the virus and is independent of the known receptors and co-receptors (*3*). Without evidence for LC/T conjugates in vaginal mucosa, it is unclear how this capture pathway could be involved in the selective production of HIV-1 for heterosexual transmission, as has been described (*5*).

The second pathway for infection of LCs is productive infection involving LCs alone (*3*). This is more relevant to our results and to our hypothesis. This pathway appears to be dependent on cytokines and to be mediated through CD4 and chemokine receptors (*3*). It is this second pathway that best fits the results of Dittmar *et al.* (*1*), which describe productive replication in LC in the absence of LC/T conjugate formation (*1*). Others have also described this productive infection pathway (*6*).

Dittmar *et al.* examined 26 HIV-1s from six subtypes, HIV-1 A to F. On the basis of their data (*1*, table 1), we believe there is a statistical difference (*7*) in that the 17 HIV-1 non-Bs grew better in LCs than did the nine HIV-1 Bs. Also, of the six HIVs found to grow better in LCs than in peripheral blood mononuclear cells, five were of non-B subtypes. Is this result not compatible with our data and our hypothesis?

Pope *et al.* also state that the selective transmission of NSI viruses cannot be attributed to selective expression of certain co-receptors on LCs. However, recent observations of Blauvelt *et al.* show that tissue LCs, unlike cells in culture, show selective surface expression of CD4 and CCR5, but not CXCR4 (*8*). Whether this can fully explain the selective release of NSI viruses remains to be determined. However, the selective release of NSI viruses cannot be readily explained by the T cell conjugate capture pathway presented by Pope *et al.* (*2*, *4*). Also, differences in receptor binding affinity need not be the only explanation for differences in cell tropism. Different cell types express different amounts of DNA binding proteins that interact with different enhancers and promoters in the long terminal repeat region of HIV-1. We recently showed that both the regulatory gene sequences and the transactivator genes of HIV-1s are conserved within HIV-1 B subtypes, but that there is significant independent evolution in the case of HIV-1 Es and Cs (*9*).

Recent results from South Africa also suggest that the long-term presence of HIV-1 B did not result in a heterosexual epidemic, while the more recent introduction of HIV-1 C is causing a serious heterosexual epidemic (*10*). Others have recently found that HIV-1 As, associated with heterosexual epidemics in other regions of Africa, also grow better in LCs (*11*).

In summary, independent observations by several groups support our hypothesis that LC tropism may help explain the association between certain HIV subtypes and the major heterosexual epidemics. It is important to recognize that receptor-mediated productive infection of LCs and the ability of LCs to capture virus are mediated through separate pathways. We propose that the "productive pathway" is more relevant for heterosexual transmission.

M. Essex, B. Renjifo, V. Peña-Cruz, M. F. McLane, R. Marlink, T. H. Lee, *Harvard AIDS Institute, 651 Huntington Avenue, Boston, MA 02115, USA;* **K. Mayer,** *Research Department, Fenway Community Health Center, Boston, MA 02115, USA and Division of Infectious Diseases, Department of Medicine, Memorial Hospital of Rhode Island, Pawtucket, RI 02860, USA, and Brown University School of Medicine, Providence, RI 02912, USA;* **P. Auewarakul, R. Sutthent, C. Wasi,** *Siriraj Hospital, Mahidol University, Faculty of Medicine, Bangkoknoi, Bangkok 0700, Thailand;* **P. Vithayasai, V. Vithayasai, C. Apichartpiyakul,** *Department of Microbiology, Faculty of Medicine, Chiang-Mai University, Chiang-Mai 50002, Thailand;* **L. Soto-Ramirez,** *Departmento de Infectologia, Instituto Nacional de la Nutricion, Tlalpan, Mexico, D.F. 14000*

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Color Vision, Genetics, and Computers?

In their thought-provoking report "Visual pigment gene structure and the severity of color vision deficits" (1 Nov. 1996, p. 801), J. Neitz *et al.* used genetics to study the relative preservation of "trichromatic" vision in deuteranomalous individuals—color-blind men who lack the gene for the middle-wavelength cone pigment.

Color vision in some deuteranomalous individuals can approach that of normal people. Neitz *et al.* found that the degree of preservation of trichromatic vision was inversely correlated with the similarity of the individual's long-wavelength pigments. In other words, the brains of deuteranomalous individuals with relatively preserved trichromatic vision presumably use the short-wavelength pigment and two slightly split long-wavelength pigments to produce color vision—a task that is accomplished in normal people with the use of short-, middle-, and long-wavelength pigments.

Software could be developed for computers (or other monitors) that would take advantage of the brain function of deuteranomalous individuals to give them a fuller range and vividness of color vision. Furthermore, even for non-color-blind individuals (especially women, who have twice as many pigment genes as do most men), one can imagine that genetic and psychophysical testing might be useful in conjunction with such software to individualize color monitor displays.

Eric L. Altschuler
School of Medicine, University of California at San Diego, La Jolla, CA 92093–0606, USA
E-mail: elaltsch@sdcc3.ucsd.edu
Martin Lades
Lawrence Livermore National Laboratory, Livermore, CA 94551, USA

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LKLF and FasL Expression: Correction and Clarification

In the report "LKLF: A transcriptional regulator of single-positive T cell quiescence and