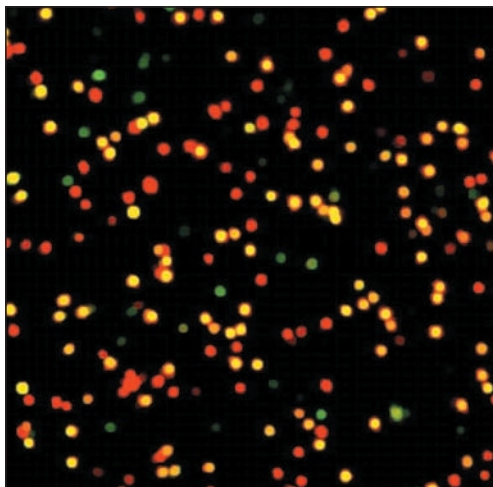


## Inexpensive CD4 counting for the developing world

A massive effort is underway to increase access to anti-retroviral treatment for HIV-positive patients in developing countries. However, essential laboratory tests such as the measurement of CD4 T lymphocytes in the peripheral blood remain expensive to carry out. Now, new research has taken aim at this obstacle with the development of a simple and inexpensive means to count CD4 lymphocytes.<sup>1</sup>



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**A digital image of whole blood from a 5-month-old boy.**<sup>2</sup> Tagged CD4 T cells are displayed in yellow; CD8 T cells, in red; and monocytes, in green. The infant's absolute CD4 count, as obtained with the low-cost prototype microchip method, was 2098 cells/ $\mu$ L; his CD4 proportion of T cells, 0.39.

In a patient with HIV infection, CD4 counts help determine the stage of infection, guide drug choices and indicate the patient's response to treatment and disease progression.<sup>2</sup> In developed countries, CD4 counts for these purposes are usually determined every 3–6 months.

Flow cytometry is the standard method to reckon CD4 cell counts. In the technique, lasers excite fluorescent markers attached to cell surfaces, which

allows a single type of cell to be counted in a mixture of many. The equipment, however, is expensive: US\$30 000–\$150 000 per machine. Add to this the costs of molecular reagents for each cell count and a technician to run the machine, and flow cytometry becomes unaffordable in the developing world.<sup>2</sup>

An inexpensive way to count CD4 cells is essential; of the people infected with HIV, over 35 million reside in developing countries. Products of previous attempts to develop other assays to measure CD4 fractions have remained technically complex or been too inaccurate for widespread use.

### A microchip for counting

William Rodriguez and his colleagues recently developed a microchip-based detection system, called an electronic taste chip,<sup>3</sup> that can detect chemicals and proteins in solution. Each chip contains microspheres in a small chamber through which fluid passes<sup>3</sup> — whole blood, for example. The microspheres are coated with monoclonal antibodies that attach to the surface proteins of lymphocytes such as CD4 as they pass through the chamber. The chip array rests atop a fluorescent microscope connected to a charge-coupled device (CCD). The CD4 cells tagged with microspheres can be distinguished via this CCD camera and counted by computer software.

**Table 1: Validity of prototype microchip assay for counts of CD4 T lymphocytes in blood**

Cells/ $\mu$ L	Sensitivity	Specificity
< 250	0.86	0.81
< 350	0.97	0.83
< 500	0.96	0.85

To test the system, the authors enrolled 67 HIV-positive people in Botswana: 61 adults and 6 children. CD4 counts measured by both the microchip system and standard flow cytometry ranged from 35 to 1087 cells/ $\mu$ L. The microchip assay showed a bias of  $-50$  cells/ $\mu$ L (95% confidence interval  $-81$  to  $-20$  cells/ $\mu$ L); its sensitivities and specificities at various CD4 cell counts are listed in Table 1.

The microchip assay has the advantages of providing results quickly (within 15 minutes) and requires only small volumes of blood (16.5  $\mu$ L). The authors suggest that the system could be pushed to operate with as little as 5  $\mu$ L of blood, which can be obtained by fingerstick. Moreover, they estimate that the manufactured machine could cost under \$5000, a small fraction of the price of other assay systems. They have patented the technology and are working to develop a hand-held version.

However, it is important to point out that the microchip-based CD4 cell counter is a prototype<sup>2</sup> and requires further research in larger studies. Its actual costs are as yet unknown. Nevertheless, care of HIV-positive patients in the developing world requires a cheaper alternative for counting CD4 cells, and this microchip is a promising choice. — *David Secko, Vancouver*

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