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Retraction: Identification of calcium-modulating cyclophilin ligand as a human host restriction to HIV-1 release overcome by Vpu

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Retraction: Identification of calcium-modulating cyclophilin ligand as a human host restriction to HIV-1 release overcome by Vpu

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We reported that calcium-modulating cyclophilin ligand (CAML) was the Vpu-responsive restriction factor in human cells that was responsible for retention of HIV-1 particles at the plasma membrane. Tetherin (also known as BST-2 or CD317) was identified as the Vpu-responsive host restriction factor in human cells just before our report (*Nature* **451**, 425–430, 2008). We are confident that CAML interacts with Vpu and that expression of human CAML in Cos-7 cells limits particle release by an unclear mechanism. However, a direct head-to-head comparison of tetherin and CAML in our laboratory (S.A., L.D. and P.S.) has led to serious questions regarding the major conclusions of our report. Specifically, knockdown of CAML in HeLa cells does not relieve the restriction to particle release, and overexpression of CAML in normally permissive 293T or HT1080 cells does not induce a restriction to particle output that is separable from its tendency to exert toxic effects on cells. Parallel experiments show that tetherin knockdown relieves the restriction to particle release and that tetherin expression in permissive 293T cells or HT1080 cells renders them restrictive and responsive to Vpu. Furthermore, CAML knockdown did not prevent the restriction of particle release in 293T cells expressing tetherin, indicating that CAML is not required for tetherin's effects on particle release. Together, these data contradict our previous conclusions that CAML is a human host restriction factor that acts at the level of particle release and is counteracted by Vpu.

F. Kirchhoff (University of Ulm) and P. Cannon (University of Southern California) have provided us with data in which they were unable to reproduce the restrictive effects of CAML in human cells. We have heard from investigators in additional laboratories that tetherin, not CAML, restricts particle release in their hands. The Correspondence in this issue from Kühl *et al.* (*Nat. Med.* **16**, 155–157, 2010) adds to this consensus and is completely consistent with what we have found in comparing CAML and tetherin head-to-head. Thus, our own present findings, along with those from other laboratories, contradict major findings from our previous report, and we (S.A., L.D. and P.S., along with R.J.B.) feel that the paper should be retracted.

V.V., E. H.-N., R.M.S. and J.R. declined to sign the retraction (see *Nat. Med.* **16**, 157, 2010). They maintain that the original observations of the report from 2008 are correct and reproducible, including the enhanced release of Vpu-deficient particles from CAML-depleted lymphocytic cell lines. The Varthakavi laboratory continues to study a CAML-specific effect on HIV-1 Gag trafficking and release and is testing the hypothesis that CAML inhibits HIV particle release at a different step than does tetherin. Y.S., who worked in V.V.'s laboratory, was unavailable to comment on the retraction.