RAISING: a high-performance method for identifying random transgene integration sites

Yusaku Wada

FASMAC Co.

Tomoo Sato

Institute of Medical Science

Hiroo Hasegawa

Nagasaki University Hospital

Takahiro Matsudaira

FASMAC Co.

Naganori Nao

Hokkaido University

Ariella Coler-Reilly

Institute of Medical Science

Tomohiko Tasaka

Affinity Science Corporation

Shunsuke Yamauchi

Nagasaki University Hospital

Tomohiro Okagawa

Affinity Science Corporation

Haruka Momose

National Institute of Infectious Diseases

Michikazu Tanio

National Institute of Infectious Diseases

Madoka Kuramitsu

National Institute of Infectious Diseases

Daisuke Sasaki

Nagasaki University Hospital

Naoko Yagishita

Institute of Medical Science

Junji Yamauchi

Institute of Medical Science

Natsumi Araya

Institute of Medical Science

Kenichiro Tanabe

St. Marianna University

Makoto Yamagishi

The University of Tokyo

Makoto Nakashima

The University of Tokyo

Shingo Nakahata

Nagasaki University Hospital

Hidekatsu Iha

Oita University

Masao Ogata

Oita University Hospital

Yoshitaka Imaizumi

Nagasaki University Hospital

Kaoru Uchimar

The University of Tokyo

Yasushi Miyazaki

Nagasaki University Hospital

Satoru Konnai

Hokkaido University

Katsunori Yanagihara

Nagasaki University Hospital

Kazuhiro Morishita

University of Miyazaki

Toshiki Watanabe

St. Marianna University

Yoshihisa Yamano

Institute of Medical Science

Masumichi Saito (✉ saitomas@ni.go.jp)

National Institute of Infectious diseases <https://orcid.org/0000-0001-7187-1186>

Article

Keywords: transgene integration sites, RAISING, biomarkers

Posted Date: May 25th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-526444/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Version of Record: A version of this preprint was published at Communications Biology on June 2nd, 2022. See the published version at <https://doi.org/10.1038/s42003-022-03467-w>.

**RAISING: a high-performance method for identifying random
transgene integration sites**

Yusaku Wada^{1,20}, Tomoo Sato^{2,3,20}, Hiroo Hasegawa^{4,5,20}, Takahiro Matsudaira^{1,20},
Naganori Nao⁶, Ariella L. G. Coler-Reilly^{2,7}, Tomohiko Tasaka⁸, Shunsuke Yamauchi⁴,
Tomohiro Okagawa⁹, Haruka Momose¹⁰, Michikazu Tanio¹⁰, Madoka Kuramitsu¹⁰,
Daisuke Sasaki⁴, Naoko Yagishita², Junji Yamauchi², Natsumi Araya², Kenichiro
Tanabe¹¹, Makoto Yamagishi¹², Makoto Nakashima¹², Shingo Nakahata¹³, Hidekatsu
Iha¹⁴, Masao Ogata¹⁵, Yoshitaka Imaizumi¹⁶, Kaoru Uchimarui¹², Yasushi Miyazaki^{16,17},
Satoru Konnai^{9,18}, Katsunori Yanagihara^{4,5}, Kazuhiro Morishita¹³, Toshiki Watanabe¹⁹,
Yoshihisa Yamano^{2,3*}, Masumichi Saito^{10*}

¹Biotechnological Research Support Division, FASMAC Co., Ltd, 243-0021 Kanagawa,
Japan

²Department of Rare Diseases Research, Institute of Medical Science, St. Marianna
University School of Medicine, 216-8512 Kanagawa, Japan

³Division of Neurology, Department of Internal Medicine, St. Marianna University
School of Medicine, 216-8511 Kanagawa, Japan

- 19 ⁴Department of Laboratory Medicine, Nagasaki University Hospital, 852-8501
20 Nagasaki, Japan
- 21 ⁵Department of Laboratory Medicine, Nagasaki University Graduate School of
22 Biomedical Sciences, 852-8501 Nagasaki, Japan
- 23 ⁶Hokudai Center for Zoonosis Control in Zambia, Research Center for Zoonosis Control,
24 Hokkaido University, Sapporo, 001-0020 Hokkaido, Japan
- 25 ⁷Department of Internal Medicine, Division of Bone and Mineral Diseases, Washington
26 University School of Medicine, St. Louis, MO, 63110 USA
- 27 ⁸Affinity Science Corporation, 141-0031 Tokyo, Japan
- 28 ⁹Department of Advanced Pharmaceutics, Faculty of Veterinary Medicine, Hokkaido
29 University, 060-0818 Hokkaido, Japan
- 30 ¹⁰Department of Safety Research on Blood and Biological Products, National Institute
31 of Infectious Diseases, 208-0011 Tokyo, Japan
- 32 ¹¹Pathophysiology and Bioregulation, St. Marianna University Graduate School of
33 Medicine, 216-8511 Kanagawa, Japan
- 34 ¹²Department of Computational Biology and Medical Sciences, Graduate School of
35 Frontier Sciences, The University of Tokyo, 108-8639 Tokyo, Japan
- 36 ¹³Division of Tumor and Cellular Biochemistry, Department of Medical Sciences,

University of Miyazaki, 889-1692 Miyazaki, Japan.

¹⁴Department of Microbiology, Faculty of Medicine, Oita University, 879-5593 Oita, Japan

¹⁵Department of Hematology, Oita University Hospital, 879-5593 Oita, Japan

¹⁶Department of Hematology, Nagasaki University Hospital, 852-8501 Nagasaki, Japan

¹⁷Atomic Bomb Disease and Hibakusha Medicine Unit, Atomic Bomb Disease Institute, Nagasaki University, 852-8102 Nagasaki, Japan

¹⁸Department of Disease Control, Faculty of Veterinary Medicine, Hokkaido University, Sapporo, 060-0818 Hokkaido, Japan

¹⁹Department of Practical Management of Medical Information, St. Marianna University Graduate School of Medicine, 216-8511 Kanagawa, Japan

²⁰These authors contributed equally: Yusaku Wada, Tomoo Sato, Hiroo Hasegawa, and Takahiro Matsudaira

*Correspondence: Masumichi Saito (saitomas@nih.go.jp) and Yoshihisa Yamano (yyamano@marianna-u.ac.jp)

Word count: 3971 (excluding abstract, online methods, references, and figure legends)

Abstract

Both natural viral infections and therapeutic interventions using viral vectors pose significant risks of malignant transformation. Monitoring for clonal expansion of infected cells is important for detecting cancer. Here we developed a novel method of tracking transgene integration sites. RAISING (Rapid Amplification of Integration Sites without Interference by Genomic DNA contamination) is a sensitive, inexpensive alternative to established methods. Its compatibility with Sanger sequencing combined with our CLOVA (Clonality Value) software is critical for those without access to expensive next-generation sequencing. To model our method, we analyzed samples from 698 patients infected with the retrovirus HTLV-1, which causes adult T-cell leukemia/lymphoma (ATL). We defined a clonality value identifying ATL patients with 100% sensitivity and 95.3% specificity, and our preliminary longitudinal analysis suggests this may also be useful for ATL risk assessment. We anticipate future studies will confirm the broad applicability of our technology, especially in the emerging gene therapy sector.

Main

Approximately 10–15% of all human cancers are associated with viral infections¹. A

subset of viruses integrate into their host genomes, and the integration often causes malignant transformation by affecting the expression of cancer driver genes²⁻⁴. This phenomenon is also a known complication of retrovirus-based therapeutics. Indeed, a subset of retroviral gene therapy-treated patients with X-linked severe combined immunodeficiency developed T-cell acute lymphoblastic leukemia due to proto-oncogene activation^{5, 6}. Although efforts are underway to limit this problem, it is still not possible to control the site of viral vector integration. Moreover, although genome editing technologies foregoing the use of viral vectors are expected to enter the gene therapy arena⁷, these too have risks associated with off-target editing and unpredictable integration^{8, 9}. Therefore, it is critical to develop a clinically applicable method of monitoring integration sites and the clonality of transgene-integrated cells to detect early signs of cancer.

Several such methods of analyzing transgene integration events using next generation sequencing (NGS) have recently been developed: namely, ligation-mediated PCR^{10, 11}, target-capture sequencing^{12, 13}, LAM-PCR (linear amplification-mediated PCR)¹⁴, nrLAM-PCR (non-restrictive linear amplification-mediated PCR)^{15, 16}, and tag-PCR¹⁷. Some of these methods have already been employed in a clinical setting to assess the safety of retroviral and lentiviral gene therapies^{14, 15}. However, NGS analysis remains

prohibitively expensive for the many researchers and physicians seeking a more practical solution, especially in countries where such resources are scarce¹⁸. In addition, there are concerns about the poor sensitivity of methods like LAM-PCR or Target-capture sequencing that utilize restriction enzymes or a sonication to fragment the DNA. Since fragmentation occurs randomly, often only a small fraction of fragments include both enough of the transgene to anneal to the primers or capture with probes and an appropriate length of host genome for further analysis, which greatly limits the sensitivity of these methods. The newer nrLAM-PCR method eliminates the restriction digest step, greatly increasing the copy number of transgene-integrated fragments. However, this method suffers from the limitations of the single-stranded linker ligation system, namely a very long 32-hour run-time with low efficiency^{15, 16}.

Previously, we developed a novel method designed to overcome the aforementioned limitations of currently available integration site analysis technologies. Known as Rapid Amplification of Integration Sites (RAIS), our protocol substituted a polyA-tailing step for the single-stranded linker ligation system, shortening the run-time from 32 hours to 4 hours and increasing the sensitivity 100-fold¹⁹. While RAIS represented a major improvement over nrLAM-PCR, uptake of the technology was still limited by the high cost of biotinylated primers and magnetic streptavidin beads. Another drawback was the

requirement for two ssDNA purification steps, which decreased sensitivity. With these issues in mind, we devised the new method described herein, known as Rapid Amplification of Integration Sites without Interference by Genomic DNA contamination (RAISING). Forgoing the use of biotinylated primers and magnetic beads, we invented a novel procedure using poly-AG-tailing and thermomodulation to yield short, uniform transgene-integrated fragments for amplification. Thus we evolved our technology to produce a highly cost-effective and sensitive method that is practical for use in routine clinical testing as well as in basic science research.

Here we not only describe the development of RAISING but also demonstrate the clinical utility of our technology using the retrovirus human T-cell leukemia virus type-1 (HTLV-1) as a model²⁰. HTLV-1 infects at least 5 – 10 million worldwide, including many in developing countries²¹. This virus can trigger an aggressive cancer, adult T-cell leukemia/lymphoma (ATL), as well as a debilitating neuroinflammatory disease, HTLV-1-associated myelopathy/tropical spastic paraparesis (HAM/TSP)²²⁻²⁴. Since ATL has an extremely high case fatality rate, it is paramount to detect the cancer and begin treatment as early as possible; those at high risk of developing ATL must be identified and closely monitored. Screening for patients with high HTLV-1 proviral load in the peripheral blood is reportedly useful but certainly not specific^{13, 25}. Studies

using NGS technology have revealed a more specific metric for ATL risk: the oligoclonality index (OCI), which quantifies the clonality of HTLV-1-infected cells, combined with the detection of somatic mutations^{11, 13, 26}. Here we use RAISING to rapidly analyze more than 700 samples from HTLV-1-infected patients and define our own metric for ATL risk assessment, demonstrating the utility of RAISING for clinically applicable integration site analysis.

Results and discussion

Development of RAISING

Here we describe the development of our novel method, RAISING, comprising six steps to achieve amplification of transgene-integrated fragments within only 3.5 hours, plus an additional step for Sanger sequencing or NGS library preparation (Fig. 1a, see also RAISING protocol in Supplementary information).

Step 1: Single-stranded DNA (ssDNA) synthesis – This step is critical for increasing the sensitivity of RAISING by synthesizing the ssDNA of transgene-integrated fragments with using a single transgene-specific primer, F1. To determine factors influencing the sensitivity, we applied RAISING to two different sources of genomic DNA as the templates for ssDNA synthesis: freshly isolated DNA and fragmented DNA

with or without RNase A treatment. As expected, we found that the sensitivity of RAISING was decreased with the fragmented and RNase A-untreated genomic DNA (Supplementary Fig. 1a). In addition, we found that the sensitivity also positively correlated with the amount of genomic DNA used in this step (Supplementary Fig. 1b). We also determined that the length of RAISING final products depended on both the quality of genomic DNA and the ssDNA synthetic time (Supplementary Fig. 1a and 1c). Although the copy number of ssDNA can be increased with the cycle number used in the synthesis (Supplementary Fig. 1d), we decided on 25 cycles to avoid nonspecific amplification (Supplementary Fig. 1e). We could detect the appropriate length of amplified DNA with high sensitivity using KOD-Plus-Neo (Figure 2a) but not OneTaq and Q5 PCR enzymes (Supplementary Fig. 1f).

Step 2: Column purification – Here we used the Monarch PCR & DNA cleanup kit to eliminate larger genomic DNA fragments (>10kb) as well as the leftover F1 primer while preserving the ssDNA as well as smaller genomic DNA. Importantly for extracting ssDNA, this kit requires a low elution volume with low dead volumes (Supplementary Fig. 2).

Step 3: PolyAG-tailing – The ssDNA and genomic DNA isolated in the previous step underwent polyAG-tailing, as opposed to the polyA-tailing employed in our older RAIS

procedure. This is the critical step where the present method diverges from our previous method. By performing polyAG-tailing in this step, synthesis of the adaptor primer 1 (ADP1) sequence, a part of the oligo-dT-adaptor primer 1 (oligo-dT-ADP1) at the 3'-end of the ssDNA and contaminated genomic DNA, is inhibited in step 4 and 5. The inhibition sequentially blocks oligo-dT-ADP1-mediated amplifications of contaminated genomic DNA as seen in amplicons with polyA-tailing (Supplementary Fig. 3a). Thus, unlike RAIS, RAISING does not require a biotinylated primer and magnetic streptavidin-beads for eliminating contaminated genomic DNA.

Step 4: Double-stranded DNA synthesis – In this step, we modulated the conditions under which oligo-dT anneals to the polyA tails to produce dsDNA (Supplementary Fig. 3b and Supplementary Table 1). In preparation for those using NGS in the final step, we elucidated which oligo-dT-ADP1 produced the most uniform amplicon lengths. We determined that NV-oligo-dT-ADP1, which includes VN (V = A or G or C, N=A or G or C or T) at the 3'-end, performed better than V-oligo-dT-ADP1 (V only) or oligo-dT-ADP1 (neither V or N). We also tested the results using Sanger sequencing and found that in this case, all three produced similar results, meaning those using Sanger sequencing can choose any of the three oligo-dT options. Next, we selected a specific temperature for the pre-denaturation step to avoid amplifying genomic DNA

contaminants. Without ever heating the reaction to the usual high temperatures (around 95°C) used for denaturation, we employed a 5 min 65°C step followed by an annealing phase using a step-down cycle from 64°C to 52°C. In this way, we were able to selectively target the ssDNA produced using the NV-oligo-dT-ADP1 primer without reaching the temperatures that would denature genomic DNA contaminants. Finally, to allow steps 3-5 to proceed sequentially in a single tube, we selected a PCR enzyme that would function efficiently among the reagents used in step 3 for polyAG-tailing. The Q5 enzyme performed the best under these conditions (Supplementary Fig. 3c). The polyAG-tailing is exchangeable to polyTG-tailing if the transgene has a polyA sequence downstream of the specific F1 primer (Supplementary Fig. 3d).

Step 5: First PCR – Here we perform the critical PCR step, introducing a transgene-specific F2 primer as the forward primer and using full length NV-oligo-dT-ADP1 as the reverse primer. It should be noted that the ssDNA produced in step 1 is no longer the template here; because the F2 primer anneals only to the copy of the transgene produced in the previous step, it can be said that "template switching" has occurred. Thus, synthesis from the F2 forward primer produces the binding site for the full length NV-oligo-dT-ADP1 reverse primer. Importantly, we designed the primers to bind at the relatively high annealing temperature of 68°C; a lower annealing

temperature would significantly increase the duration of this step, slowing the overall run-time of our method. This step, which employs both a forward and a reverse primer, is essential for ensuring the high specificity of RAISING. The method is also highly sensitive owing to the unique design that allows step 3, 4, and 5 to proceed uninterrupted in a single PCR tube.

Step 6: Second PCR – We prepared a 1:200 dilution of the first PCR reaction to avoid nonspecific amplification and used two primers (F3-NGS-F1 and ADP1-NGS-R1) that include half of the adaptor sequence corresponding to the Illumina next generation sequencing (NGS) library. Transgene integration sites can be analyzed by Sanger sequencing using the amplicons from this step.

Additional step: NGS library preparation – The amplicons in step 6 can be re-amplified with two primers that contain 8-nucleotide sequencing indexes and the remainder of the Illumina adaptor sequence.

Performance of RAISING

After each RAISING step was fully evaluated, we compared the performance of RAISING and RAISING by assessing samples containing different percentages of two HTLV-1-infected cell lines (ED and LMY2)^{27, 28}, each harboring a single integration

site (Fig. 1b-d, and Supplementary Fig. 4a-b). As expected, the amplicons from RAISING exhibited a superior (denser) pattern compared to those from RAIS (Fig. 1b). With both RAIS and RAISING, we observed consistent Sanger sequence spectra patterns, clone size differing from the expected result by less than $\pm 10\%$, and consistent between experimental replicates within $\pm 2\%$ (Fig. 1c and 1d). These results clearly indicate that while both RAIS and RAISING are effective, unbiased methods, RAISING is better suited to produce the final amplicon length amenable to subsequent NGS analysis.

To compare the limits of the sensitivity of RAISING and RAIS, each method was tested on samples where genomic DNA from the HTLV-1-infected cell line TL-Om1 was serially diluted with genomic DNA from the HTLV-1-negative Jurkat cell line¹⁹. While RAIS could not be used to amplify integrated fragments in samples with a proviral load (PVL) less than 0.16%, the limit for RAISING was PVL 0.032%, indicating RAISING achieved a five-fold higher sensitivity compared to RAIS (Fig. 2a). We also confirmed the effectiveness of cell-direct RAISING on samples of HTLV-1-infected cell lines (KK1 and SLB-1) harboring multiple integration sites (Supplementary Fig. 5a-c).

Consistent with previous results achieved using RAIS¹⁹, RAISING successfully

discriminated between non-malignant and malignant samples in both HTLV-1-infected human specimens and bovine leukemia virus (BLV)-infected cattle specimens, regardless of whether Sanger sequencing or NGS was used for analysis (Fig. 2b, 2c, and Supplementary Table 2). By simply changing the transgene-specific primer sets, we could use the same RAISING method to amplify transgene-integrated fragments from a variety of virus-infected and genome-edited samples (HTLV-1; HIV-1, human immunodeficiency virus; SIV, simian immunodeficiency virus; HBV, hepatitis B virus; AdV, adeno virus; and low-density lipoprotein receptor knock-in mice Ldlr-mLO-4 and Ldlr-mLO-5) (Fig. 2d). When analyzing monoclonally expanded cells, we were able to identify the integration site using Sanger sequencing (Fig. 2e); for the analysis of polyclonally expanded cells, we were able to detect both the integration site and the size of each clone using NGS analysis (Fig. 2f). Importantly, RAISING with NGS analysis also successfully discriminated between on- and off-targets integrating the Loxp donor sequence into an unpredictable position in the genome-edited Ldlr-knock-in mice (Fig. 2g). Taken together, these results demonstrate that RAISING is a high-performance method for characterizing multiple-transgene integration events.

Practical application of RAIS-CLOVA and RAISING-CLOVA in a clinical field

Quantifying the clonality of HTLV-1-infected cells in patients is essential for assessing their risk of developing the aggressive cancer ATL. Previously we used the EditR software for measuring genome editing efficiency^{19, 29}; however, in this study, we developed our own software, improving on the foundation laid by EditR. Our software, known as CLOVA (Clonality value), differs from EditR in that it can automatically provide a clonality value (Cv) simply by uploading Sanger sequencing data (ab1 file), entering the proviral sequence (up to 20 bp adjacent to host genome sequence in 5'-3' orientation), and selecting a desired nucleotide length for analysis (Supplementary Fig. 6a and 6b)¹⁹.

We demonstrated that visual Sanger sequence spectra could be converted to a quantitative HTLV-1 clonality value. Theoretically, the total signal peak area for 20 nucleotides of the HTLV-1 sequence and 20 nucleotides of the host genome sequence should be identical in a monoclonal sample. In other words, there is a 1:1 ratio between the host genome and HTLV-1 spectral areas, which we classify as a Cv of 1.00. With polyclonal samples, increasing the number of clones reduces the intensity of the host genome signal, and thereby the host genome spectral area, lowering this ratio and yielding $Cv < 1.00$ (Supplementary Fig. 6c). Practically, there are slight differences in intensity between different nucleotide sequences that exert a minor influence on the Cv.

For example, occasionally a sample may yield $C_v > 1.00$, which should be interpreted as $C_v = 1.00$, a monoclonal sample. We also showed that C_v accurately reflected the size of the dominant clone (first clone), as measured using NGS analysis (Supplementary Fig. 7a and 7b). As we have previously shown that multiclonal expansion of malignant cells occurs in approximately 30% of ATL patients¹⁹, we incorporated a function into CLOVA that provides nucleotide sequences for both the first and second clones. Subsequently, these sequences can be searched on BLAST homology to confirm that two integration sites have been accurately identified (Supplementary Fig. 8a and 8b, see also Table 2).

To measure the precision of RAISING-CLOVA, we performed five independent analyses on four samples from HTLV-1-infected subjects with differing C_v values (sample A, 0.88; sample B, 0.57; sample C, 0.40; sample D, 0.12), and we found the variation in C_v was less than ± 0.03 in all samples (Supplementary Fig. 9). Similarly, two different laboratories measured the clonality of the same HTLV-1-infected samples using the RAISING-CLOVA method with high interrater agreement (Supplementary Fig. 10, $n=62$). We also tested the performance of RAISING-CLOVA against RAIS-CLOVA on the same HTLV-1-infected samples: RAISING-CLOVA produced similar clonality values despite the greatly reduced cost and procedure time

(Supplementary Fig. 11, n=24). Finally, we tested whether RAISING-CLOVA could be used to measure clonality when applied directly to whole blood samples without isolating peripheral blood mononuclear cells (PBMCs). We tested RAISING-CLOVA on samples of whole blood and PBMCs from the same patients and determined that the performance was similar (Supplementary Fig. 12, n=51).

We began investigating the clinical utility of RAISING-CLOVA by assessing the suitability of Cv for discriminating between samples from patients with and without the HTLV-1-associated cancer ATL. Since HTLV-1 proviral load (PVL) has long been considered an important marker for the development of ATL^{25,30}, we directly compared the performance accuracy of Cv and PVL. We determined the Cv of specimens from asymptomatic carriers (AC, n=200), patients with HAM/TSP (n=224), and ATL patients (n=306) using RAIS-CLOVA (n=292) or RAISING-CLOVA (n=438; Supplementary Table 3)¹⁹. Of these 730 total subjects, blood samples suitable for measuring HTLV-1 proviral load (PVL) were available for 698. As reported previously, patients with HAM/TSP as well as those with ATL exhibited significantly higher PVL than ACs (Fig. 3a)^{31,32}. Within the ATL group, patients with chronic or acute subtypes exhibited significantly higher PVL than those with smoldering or lymphoma subtypes (Supplementary Fig. 13a). Upon conducting analysis of receiver operating

characteristics (ROC), we determined that PVL analysis was highly effective for discriminating between AC and ATL (area under curve, AUC 0.963) but less effective for discriminating between HAM/TSP and ATL (AUC 0.908), especially the smoldering and lymphoma subtypes (AUC 0.843, Supplementary Fig. 14a-c). On the other hand, Cv was extremely effective for discerning any type of ATL from both AC and HAM/TSP (Fig. 3b; AUC 0.996, Supplementary Fig. 14d). Within ATL subtypes, Cv of the smoldering type was significantly lower (Supplementary Fig. 13b and 13c), supporting the clonal progression model for ATL that we proposed previously³³. We also compared our results to the oligoclonality index (OCI) by Gillet NA et al¹¹, another metric for quantification of HTLV-1 clonality, and we found that Cv showed similar patterns of clonality among AC, HAM/TSP, and ATL. This suggests that Cv from RAISING-CLOVA has the potential to be used as an alternative to OCI.

In order to assess the diagnostic value of our technology, we proceeded to define cut-off values for distinguishing subjects with and without ATL using Cv and PVL (Fig. 3c). As a preliminary step, we presupposed that subjects with a PVL less than 0.5% might be classified as non-ATL without measuring Cv. We have confirmed that RAISING-CLOVA can accurately measure Cv when the PVL is at least 0.5%, but not lower (Supplementary Fig. 15). Though this may be considered a technical limitation, it

is well established that ATL risk increases with higher PVL, so it may not be useful to measure Cv when PVL is below this very low threshold. Indeed, in our study, we report no ATL patients with PVL less than 0.5%. Next, among subjects with a PVL of at least 0.5%, we determined that a Cv cut-off value of 0.48 distinguishes subjects with and without ATL with 100% sensitivity and 95.3% specificity. For comparison, $PVL \geq 4\%$ has been previously proposed as a diagnostic test²⁵, and this cut-off value would produce only 95.6% sensitivity and 62.3% specificity.

We then took the first steps towards establishing the prognostic value of Cv. We decided that subjects with Cv above the aforementioned cut-off of 0.48 would be classified as high-risk. We confirmed that even non-ATL subjects above this cut-off possessed a large dominant clone ($\geq \sim 40\%$ of the total infected cells), which is highly suggestive of malignant expansion. To find a cut-off for classifying the remaining subjects into low- and medium-risk groups, we analyzed the distribution of Cv values among subjects without ATL (Fig. 3d, n=364). We employed a common method using the derivative function with intervals of 0.05 to identify the inflection point Cv 0.25. The vast majority (81%) of non-ATL subjects in our study thus fell into the low-risk category, with $Cv < 0.25$. The dominant clones in this group were all relatively small ($< \sim 13\%$), which also suggests a low risk of malignancy. Of course, any analysis of risk

assessment using only cross-sectional data should be interpreted with caution, and it is important to validate our proposed Cv cut-off values in a future longitudinal study.

We carried out a preliminary longitudinal analysis using available retrospective samples from two HAM/TSP patients and one AC who all ultimately developed acute ATL. In this analysis, we assessed the prognostic value of our Cv cut-off values compared with established markers such as PVL, soluble IL-2 receptor (sIL-2R), and atypical lymphocytes (Fig. 3e and Table 2). We previously reported that only the carriers exhibiting an oligoclonal or monoclonal pattern with largely expanded clones (PVL > 10% before being diagnosed with ATL) subsequently progressed to ATL³⁴.

Likewise, our present analysis identified pre-leukemic cells exhibiting a monoclonal pattern in both HAM/TSP patients years before ATL onset (9 years for HAMATL001, 2 years for HAMATL003, Fig. 3e and Supplementary Fig. 16a–b). However, PVLs of these individuals were consistently lower than 10% during the period before ATL onset.

Moreover, the PVL of the AC was also lower than 10% until three months before ATL onset (ACATL004, Fig. 3e), and we found that two small clones underwent a malignant transformation and largely expanded during the 3–6 months immediately before ATL symptoms developed (Supplementary Fig. 16c and Supplementary Fig. 17). These results illustrate the low sensitivity of PVL for ATL risk assessment and the complexity

of clonal progression patterns in ATL patients. By contrast, we found that in all cases, Cv exceeded our proposed ATL cut-off value, Cv 0.48, months or even years before onset. Moreover, a noticeable trend of rising Cv was observed in all patients before any such trend could be observed for PVL or sIL-2R (Fig. 3e, Supplementary Fig. 18, and Table 2), suggesting rising Cv may be an effective early warning sign for clinicians monitoring these patients. Finally, the dramatic decrease in Cv after one of patients was treated (HAMATL001, Fig. 3e) suggests that RAISING-CLOVA may also be a useful tool for assessing the effectiveness of ATL therapeutic agents. We used NGS analysis to confirm that the sharp decrease in Cv did indeed correspond to the eradication of the dominant clone in this patient (Supplementary Fig. 19). Collectively, these results suggest it may be beneficial to monitor patients with HTLV-1 using RAISING-CLOVA to detect the earliest signs of ATL progression. Once high-risk individuals are identified, we recommend supplementing Cv analysis by pursuing mutational profiling of genes frequently mutated in ATL^{13, 26, 35}.

Thus, we performed a comprehensive HTLV-1 clonality analysis with RAISING-CLOVA and developed a method for early detection and risk assessment for progression to ATL among HTLV-1-infected patients. However, there are several limitations in this study that should be noted. Firstly, we found that approximately 2%

of our ATL specimens (n=5) carried a dominant clone with a variant of the provirus known to lack the 3' long terminal repeat where HTLV-1-specific F2 and F3 primers bind^{12, 36}. Unsurprisingly, RAISING failed to amplify the HTLV-1-integrated fragment of the dominant clone in these cases (data not shown). Therefore, it is important to keep this limitation in mind and use another method such as southern blot analysis to determine clonality in these patients^{13, 19}. Secondly, regarding the ATL risk assessment method developed herein, we only used peripheral blood samples of HTLV-1-infected individuals, which may only be accurate for predicting the leukemia subtypes of ATL. For example, in a patient who developed the lymphoma subtype (HAMATL004, Supplementary Fig. 20), we found that the Cv in peripheral blood (0.23) was much lower than that in the lymph node (0.94). Similarly, PVL in the peripheral blood was only 0.17%, indicating there was negligible migration of malignant cells from the lymph node to the peripheral blood. Therefore, these results underline the need to utilize appropriate clinical material for clonality analysis in HTLV-1-infected individuals, especially those with lymphoma or skin cancer subtypes of ATL.

In conclusion, here we introduced the RAISING method employing Sanger sequencing as a cost-effective alternative to NGS analysis for identifying multiple transgene integration sites. We demonstrated that RAISING is even faster and more

sensitive than our previously published RAIS method, and we also introduced a new CLOVA software to facilitate analysis of clonality. Here we focused on HTLV-1 as a model system, showing we could accurately quantify the clonality of infected samples, laying the foundation for the use of this method in routine clinical testing for HTLV-1-related cancers. Our success measuring the clonality of samples infected with not only HTLV-1 but also BLV, HIV-1, and SIV suggests that RAISING shows promise as a broadly applicable technology. Future studies should explore the full breadth of these applications, especially the use of RAISING to assess the safety and off-target effects of forthcoming gene therapies.

Online Methods

Collection of human and animal samples

Peripheral bloods, and biopsies (skin, lymph nodes, and bone marrow) from asymptomatic carriers, HAM/TSP, and ATL patients were harvested after obtaining informed consent at Nagasaki University Hospital, St. Marianna University School of Medicine, Oita University, University of Miyazaki, and as a collaborative project of the Joint Study on Prognostic Factors of ATL Development (JSPFAD). Regarding ATL patients, we preferentially collected the samples showing clonal band (s) in the Southern

blotting, a routine confirmatory diagnostic test for ATL in Japan^{13, 19}. This study was primarily aimed at measuring HTLV-1 clonality in peripheral bloods using our technology, RAISING. Thus, ATL patients who had or might have clonal expansion of the malignant cells only in the other tissues were excluded in this study unless there were the available biopsies. This study was approved by the research ethics committee of Oita University (198), University of Miyazaki [972(G)], Nagasaki University (16072504), The University of Tokyo (17-118), St. Marianna University School of Medicine (1646), and National Institute of Infectious Diseases (1120).

All experimental procedures were conducted following approval from the local committee for animal studies of Hokkaido University (17-0024). Collection of BLV-infected cattle specimens was approved as simple general permission procedure for the use of blood samples for assays. Verbal informed consent was obtained from all animal owners.

Cell culture

The HTLV-1-infected cell lines TL-Om1, LMY2, ED, KK1, and SLB-1; the HTLV-1-negative acute T-cell leukemia cell line Jurkat (Clone E61: ATCC TIB152); the CD4⁺ human T-cell line PM1 (3038, NIH AIDS Reagent Program); and the

cynomolgus macaque T-cell line HSC-F (JCRB1164) were cultured in RPMI 1640 medium supplemented with 10% fetal bovine serum, 100 U/mL penicillin, and 100 µg/mL streptomycin at 37°C in a 5% CO₂ atmosphere^{27, 28, 37-39}. The adenovirus-infected HEK-293 cell line (JCRB9068) was cultured in Dulbecco's modified Eagle medium supplemented with 10% fetal bovine serum at 37°C in a 5% CO₂ atmosphere⁴⁰.

***In vitro* HIV-1 and SIV infection**

HIV-1 89.6 was produced by transfection of the p89.6 plasmid into 293T cells using Lipofectamine 2000 (Thermo Fisher Scientific, Waltham, MA, USA) according to the manufacturer's protocol. The cell culture supernatant was used to transduce the virus into PM1 cells, and then the infected cells were harvested at day 7 post-infection. HSC-F cells were infected with SIVmac293 in viral solution at a multiplicity of infection (MOI) of 0.005 plaque-forming units per cell, and the infected cells were harvested at day 6 post-infection.

Genome editing

Ldlr-knock-in mice were generated using a genome-editing technology as previously

described⁴¹. The mouse embryos at the pronuclear stage were obtained using *in vitro* fertilization, and 100 ng/μL of *Cas9* mRNA, 50 ng/μL of trans-activating crRNA (tracrRNA), 25 ng/μL of two CRISPR RNAs (crRNAs), and 50 ng/μL of long single-stranded DNA (lssDNA) were simultaneously microinjected into the cytoplasm of embryos. After culturing in KSOM medium (Merck, Darmstadt, Germany) overnight, the embryos dividing into two cells were transferred into pseudo-pregnant females. The tracrRNA, crRNA, and lssDNA were synthesized by FASMAC Co., Ltd.

Preparation of genomic DNA

Genomic DNA isolated from PBMCs and biopsies of human specimens and from the TL-Om1, LMY2, ED, Jurkat, and PM1 cell lines was purified using a QIAamp DNA Blood Mini kit (Qiagen, Hilden, Germany). At the St. Marianna University School of Medicine, genomic DNA was extracted from PBMCs and WBCs using overnight proteinase K digestion followed by phenol/chloroform extraction, whereas genomic DNA of whole blood cells was purified using Quick-DNA Miniprep Kit (Zymo Research, Irvine, CA, USA). Genomic DNA isolated from PBMCs and lymph nodes of cattle specimens was purified using a Wizard Genomic DNA Purification kit (Promega, Madison, WI, USA). Genomic DNA isolated from the HSC-F cell line was purified

469 using a DNeasy Blood & Tissue Kit (Qiagen, Hilden, Germany). Genomic DNA
470 isolated from the HEK-293 cell line was purified using Isogen-LS (Nippon Gene,
471 Tokyo, Japan). Genomic DNA of KK1 and SLB-1 was extracted using NEBNext Single
472 Cell Lysis Module with Thermolabile Proteinase K and RNase A (New England
473 BioLabs, Ipswich, MA, USA).

474

475 **Proviral load (PVL) analysis**

476 Quantitative polymerase chain reaction (qPCR) for PVL of HTLV-1 was performed
477 using LC480 (NIPPON Genetics, Tokyo, Japan) with the following primer sets for
478 HTLV-1: probe, 5'- CCAGTCTACGTGTTTGGAGACTGTGTACA-3'; forward primer,
479 5'-CCCACTTCCCAGGGTTTGGA-3'; reverse primer,
480 5'-GGCCAGTAGGGCGTGA-3'. β -globin was used as an internal control and
481 amplified with the following primer sets: probe,
482 5'-AAGGTGAACGTGGATGAAGTTGGTGG-3'; forward primer,
483 5'-GTGCACCTGACTCCTGAGGAGA-3'; reverse primer,
484 5'-CCTTGATACCAACCTGCCCCAG-3'. At the St. Marianna University School of
485 Medicine, PVL was measured using qPCR as previously described⁴², and was
486 standardized using the relative ratio determined in a previous study⁴³. The qPCR for

BLV provirus was performed using Cycleave PCR Reaction Mix (Takara Bio, Otsu, Japan) and Probe/Primer Mix for BLV (Takara Bio) with a LightCycler 480 system II (Roche Diagnostics, Mannheim, Germany). Serial dilution of a BLV positive control (Takara Bio) was used to generate calibration curves to determine the copy number of the BLV *tax* gene. Each DNA sample was tested in duplicate. The concentration of DNA was estimated by measuring the ultraviolet absorbance at 260 nm using a NanoDrop 8000 spectrophotometer (Thermo Fisher Scientific). The reported values are the mean numbers of copies per 50 ng of DNA.

The cell-direct method

Components	Volume
Cell (up to 100,000 cells)	1 μ L
10X NEBNext Cell Lysis Buffer	0.5 μ L
RNase A (100 ng/ μ L)	0.5 μ L
Thermolabile Proteinase K	0.5 μ L
H ₂ O	2.5 μ L
Total	5 μL

498

499 • Incubate at 37°C for 45 min, then at 55 °C for 10 min.

500 • Use 5 µL of sample for RAISING.

501

502 **Protocol for RAISING**

503 The protocol for RAISING is separately provided in this Supplementary information.

504

505 **Sanger sequencing analysis**

506 Sanger sequencing was performed using the BigDye Terminator v3.1 Cycle Sequencing

507 Kit according to the manufacturer's instructions (Thermo Fisher Scientific), and the

508 analysis was performed on a 3730XL DNA Analyzer (Thermo Fisher Scientific).

509

510 **Development and application of CLOVA**

511 We modified EditR²⁹ to develop CLOVA, an R program-based software that

512 automatically enables analysis of the clonality value (Cv) of transgene-integrated cells,

513 by uploading an “ab.1 file,” a Sanger sequencing file containing the integration site in

514 host genome sequence, and entering a transgene sequence (up to 20 nucleotides)

515 adjacent to the host genome sequence. The analysis can be performed on a web browser

with the R Shiny package⁴⁴, but without any cumbersome command line operations. Methods to obtain the QC filtering, total peak area before filtering plot, and percent noise peak in EditR were not modified in CLOVA. CLOVA can display the Cv values and averages of signal peak area values of the transgene and host genome sequences on “Data QA: Signal and noise plot.” As the Cv values and averages of signal peak area values depend on the length of the transgene sequence, the length is alterable in the “bp-length (default value: 20)” of CLOVA corresponding to multiple transgenes. To obtain a stable Cv, we recommend examining the length of the transgene before performing the clonality analysis as we previously described for analysis of HTLV-1 clonality¹⁹. CLOVA has an additional function that can output the Sanger sequencing results of the base call (first clone) and second call (second clone) with FASTA format on the “Download FASTA/CSV” tab using sangerseqR⁴⁵. Because the complexity of Sanger sequence spectra patterns and the quality of Sanger sequencing results for the first and second clones depend on the individual clone size, we also recommend adjusting “threshold for second call (default value: 85)” for the better discrimination of the two clones.

Quantification of HTLV-1 clonality

HTLV-1 clonality was quantified as previously described, and CLOVA was used for the quantification instead of EditR in this study.

Next-generation sequencing (NGS)

The NGS library was prepared by performing tailed-PCR using an amplicon obtained in step 6 of RAISING, and the PCR products were purified using the Agencourt AMPure XP kit (Beckman Coulter, Brea, CA, USA). Then, the DNA was quantified using a Qubit dsDNA HS assay kit (Thermo Fisher Scientific) and an Agilent BioAnalyzer with High-Sensitivity DNA chips (Agilent Technologies, Santa Clara, CA, USA). NGS was performed with a MiSeq Reagent Kit v3 (600-cycle) on an Illumina MiSeq system (Illumina, Hayward, CA, USA) according to the manufacturer's instructions.

NGS data analysis

After exclusion of sequence reads that were shorter than 50 nucleotides, homology searches were performed using Magic-BLAST (<https://ncbi.github.io/magicblast/>)⁴⁶. We extracted only sequence reads that had both an appropriate viral sequence length (40, 50, 60, and 70 nucleotides for HTLV-1, BLV, HIV-1, and SIV, respectively) and high homology with the host genome sequence ($\geq 95\%$ match score). Viral integration sites

were positioned in the *Homo sapiens* (*Homo sapiens* GRCh38.p12), *Bos taurus* (*Bos taurus* ARS-UCD1.2), or *Macaca fascicularis* (*Macaca fascicularis*_5.0) reference genomes. On- and off-targets in the *Ldlr*-mLO-4 and *Ldlr*-mLO-5 knock-in mice were identified by performing homology searches with the mouse reference genome (*Mus musculus* GRCm38.p6).

Statistical analysis

Kruskal–Wallis tests followed by Dunn’s post-hoc tests were used for comparison among the six groups (AC, asymptomatic carriers; HAM/TSP, HTLV-1-associated myelopathy/tropical spastic paraparesis patients; and four subtypes of ATL) and for comparison among the four groups (four subtypes of ATL). Receiver operating characteristic (ROC) curve analysis was performed to assess the ability of the HTLV-1 proviral load and clonality value to distinguish between ATL patients and non-ATL HTLV-1-infected individuals (AC and HAM/TSP). Statistical analyses and graph construction were performed using GraphPad Prism 7 (GraphPad Software, Inc., San Diego, CA, USA).

References

1. Moore, P.S. & Chang, Y. Why do viruses cause cancer? Highlights of the first century of human tumour virology. *Nat Rev Cancer* **10**, 878-889 (2010).
2. Hu, Z. et al. Genome-wide profiling of HPV integration in cervical cancer identifies clustered genomic hot spots and a potential microhomology-mediated integration mechanism. *Nat Genet* **47**, 158-163 (2015).
3. Rosewick, N. et al. Cis-perturbation of cancer drivers by the HTLV-1/BLV proviruses is an early determinant of leukemogenesis. *Nat Commun* **8**, 15264 (2017).
4. Tang, K.W., Alaei-Mahabadi, B., Samuelsson, T., Lindh, M. & Larsson, E. The landscape of viral expression and host gene fusion and adaptation in human cancer. *Nat Commun* **4**, 2513 (2013).
5. Hacein-Bey-Abina, S. et al. Sustained correction of X-linked severe combined immunodeficiency by ex vivo gene therapy. *N Engl J Med* **346**, 1185-1193 (2002).
6. McCormack, M.P. & Rabbitts, T.H. Activation of the T-cell oncogene

588 LMO2 after gene therapy for X-linked severe combined
589 immunodeficiency. *N Engl J Med* **350**, 913-922 (2004).

590 7. Khan, S.H. Genome-Editing Technologies: Concept, Pros, and Cons of
591 Various Genome-Editing Techniques and Bioethical Concerns for
592 Clinical Application. *Mol Ther Nucleic Acids* **16**, 326-334 (2019).

593 8. Tsai, S.Q. et al. GUIDE-seq enables genome-wide profiling of
594 off-target cleavage by CRISPR-Cas nucleases. *Nat Biotechnol* **33**,
595 187-197 (2015).

596 9. Zhang, X.H., Tee, L.Y., Wang, X.G., Huang, Q.S. & Yang, S.H.
597 Off-target Effects in CRISPR/Cas9-mediated Genome Engineering.
598 *Mol Ther Nucleic Acids* **4**, e264 (2015).

599 10. Firouzi, S. et al. Development and validation of a new
600 high-throughput method to investigate the clonality of
601 HTLV-1-infected cells based on provirus integration sites. *Genome*
602 *Med* **6**, 46 (2014).

603 11. Gillet, N.A. et al. The host genomic environment of the provirus
604 determines the abundance of HTLV-1-infected T-cell clones. *Blood*
605 **117**, 3113-3122 (2011).

- 606 12. Katsuya, H. et al. The Nature of the HTLV-1 Provirus in Naturally
607 Infected Individuals Analyzed by the Viral DNA-Capture-Seq
608 Approach. *Cell Rep* **29**, 724-735 e724 (2019).
- 609 13. Nagasaka, M. et al. Mortality and risk of progression to adult T cell
610 leukemia/lymphoma in HTLV-1-associated myelopathy/tropical
611 spastic paraparesis. *Proc Natl Acad Sci U S A* **117**, 11685-11691
612 (2020).
- 613 14. Schmidt, M. et al. High-resolution insertion-site analysis by linear
614 amplification-mediated PCR (LAM-PCR). *Nat Methods* **4**, 1051-1057
615 (2007).
- 616 15. Gabriel, R. et al. Comprehensive genomic access to vector integration
617 in clinical gene therapy. *Nat Med* **15**, 1431-1436 (2009).
- 618 16. Paruzynski, A. et al. Genome-wide high-throughput integrome
619 analyses by nrLAM-PCR and next-generation sequencing. *Nat Protoc*
620 **5**, 1379-1395 (2010).
- 621 17. Hamada, M. et al. Integration Mapping of piggyBac-Mediated CD19
622 Chimeric Antigen Receptor T Cells Analyzed by Novel
623 Tagmentation-Assisted PCR. *EBioMedicine* **34**, 18-26 (2018).

- 624 18. Helmy, M., Awad, M. & Mosa, K.A. Limited resources of genome
625 sequencing in developing countries: Challenges and solutions. *Appl*
626 *Transl Genom* **9**, 15-19 (2016).
- 627 19. Saito, M. et al. A high-throughput detection method for the clonality of
628 Human T-cell leukemia virus type-1-infected cells in vivo. *Int J*
629 *Hematol* (2020).
- 630 20. Poiesz, B.J. et al. Detection and isolation of type C retrovirus particles
631 from fresh and cultured lymphocytes of a patient with cutaneous
632 T-cell lymphoma. *Proc Natl Acad Sci U S A* **77**, 7415-7419 (1980).
- 633 21. Gessain, A. & Cassar, O. Epidemiological Aspects and World
634 Distribution of HTLV-1 Infection. *Front Microbiol* **3**, 388 (2012).
- 635 22. Gessain, A. et al. Antibodies to human T-lymphotropic virus type-I in
636 patients with tropical spastic paraparesis. *Lancet* **2**, 407-410 (1985).
- 637 23. Hinuma, Y. et al. Adult T-cell leukemia: antigen in an ATL cell line
638 and detection of antibodies to the antigen in human sera. *Proc Natl*
639 *Acad Sci U S A* **78**, 6476-6480 (1981).
- 640 24. Osame, M. et al. HTLV-I associated myelopathy, a new clinical entity.
641 *Lancet* **1**, 1031-1032 (1986).

- 642 25. Iwanaga, M. et al. Human T-cell leukemia virus type I (HTLV-1)
643 proviral load and disease progression in asymptomatic HTLV-1
644 carriers: a nationwide prospective study in Japan. *Blood* **116**,
645 1211-1219 (2010).
- 646 26. Rowan, A.G. et al. Evolution of retrovirus-infected premalignant T-cell
647 clones prior to adult T-cell leukemia/lymphoma diagnosis. *Blood* **135**,
648 2023-2032 (2020).
- 649 27. Hasegawa, H. et al. Sensitivity of adult T-cell leukaemia lymphoma
650 cells to tumour necrosis factor-related apoptosis-inducing ligand. *Br J*
651 *Haematol* **128**, 253-265 (2005).
- 652 28. Maeda, M. et al. Origin of human T-lymphotrophic virus I-positive T
653 cell lines in adult T cell leukemia. Analysis of T cell receptor gene
654 rearrangement. *J Exp Med* **162**, 2169-2174 (1985).
- 655 29. Kluesner, M.G. et al. EditR: A Method to Quantify Base Editing from
656 Sanger Sequencing. *CRISPR J* **1**, 239-250 (2018).
- 657 30. Demontis, M.A., Hilburn, S. & Taylor, G.P. Human T cell
658 lymphotropic virus type 1 viral load variability and long-term trends
659 in asymptomatic carriers and in patients with human T cell

660 lymphotropic virus type 1-related diseases. *AIDS Res Hum*
661 *Retroviruses* **29**, 359-364 (2013).

662 31. Nagai, M. et al. Analysis of HTLV-I proviral load in 202 HAM/TSP
663 patients and 243 asymptomatic HTLV-I carriers: high proviral load
664 strongly predisposes to HAM/TSP. *J Neurovirol* **4**, 586-593 (1998).

665 32. Vine, A.M. et al. Polygenic control of human T lymphotropic virus type
666 I (HTLV-I) provirus load and the risk of HTLV-I-associated
667 myelopathy/tropical spastic paraparesis. *J Infect Dis* **186**, 932-939
668 (2002).

669 33. Watanabe, T. Adult T-cell leukemia: molecular basis for clonal
670 expansion and transformation of HTLV-1-infected T cells. *Blood* **129**,
671 1071-1081 (2017).

672 34. Firouzi, S. et al. Clonality of HTLV-1-infected T cells as a risk
673 indicator for development and progression of adult T-cell leukemia.
674 *Blood Adv* **1**, 1195-1205 (2017).

675 35. Marcais, A. et al. Targeted deep sequencing reveals clonal and
676 subclonal mutational signatures in Adult T-cell leukemia/lymphoma
677 and defines an unfavorable indolent subtype. *Leukemia* (2020).

678 36. Kataoka, K. et al. Integrated molecular analysis of adult T cell
679 leukemia/lymphoma. *Nat Genet* **47**, 1304-1315 (2015).

680 37. Akari, H. et al. Effects of SIVmac infection on peripheral blood
681 CD4+CD8+ T lymphocytes in cynomolgus macaques. *Clin Immunol* **91**,
682 321-329 (1999).

683 38. Kuramitsu, M. et al. Identification of TL-Om1, an adult T-cell
684 leukemia (ATL) cell line, as reference material for quantitative PCR
685 for human T-lymphotropic virus 1. *J Clin Microbiol* **53**, 587-596
686 (2015).

687 39. Lusso, P. et al. Growth of macrophage-tropic and primary human
688 immunodeficiency virus type 1 (HIV-1) isolates in a unique CD4+
689 T-cell clone (PM1): failure to downregulate CD4 and to interfere with
690 cell-line-tropic HIV-1. *J Virol* **69**, 3712-3720 (1995).

691 40. Graham, F.L., Smiley, J., Russell, W.C. & Nairn, R. Characteristics of
692 a human cell line transformed by DNA from human adenovirus type 5.
693 *J Gen Virol* **36**, 59-74 (1977).

694 41. Miyasaka, Y. et al. CLICK: one-step generation of conditional
695 knockout mice. *BMC Genomics* **19**, 318 (2018).

696 42. Yamano, Y. et al. Correlation of human T-cell lymphotropic virus type
697 1 (HTLV-1) mRNA with proviral DNA load, virus-specific CD8(+) T
698 cells, and disease severity in HTLV-1-associated myelopathy
699 (HAM/TSP). *Blood* **99**, 88-94 (2002).

700 43. Kuramitsu, M. et al. Standardization of Quantitative PCR for Human
701 T-Cell Leukemia Virus Type 1 in Japan: a Collaborative Study. *J Clin*
702 *Microbiol* **53**, 3485-3491 (2015).

703 44. Chang, W, Joe Cheng, et al. shiny: Web Application Framework for R
704 (2020). R package version 1.4.0.2.
705 <https://CRAN.R-project.org/package=shiny>.

706 45. Hill, J.T. et al. Poly peak parser: method and software for
707 identification of unknown indels using sanger sequencing of
708 polymerase chain reaction products. *Dev Dyn* **243**, 1632-1636 (2014).

709 46. Boratyn, G.M., Thierry-Mieg, J., Thierry-Mieg, D., Busby, B. &
710 Madden, T.L. Magic-BLAST, an accurate RNA-seq aligner for long
711 and short reads. *BMC Bioinformatics* **20**, 405 (2019).

712

Fig. 1

Fig. 1 | Characterization of Rapid Amplification of Integration Site (RAIS) and RAIS without Interference by Genomic DNA contamination (RAISING). **a**, Schematic representation of RAIS and RAISING. Step 1, Single-stranded DNA (ssDNA) synthesis; Step 2, Column purification of ssDNA; Step 3, polyA-tailing and polyAG-tailing of ssDNA in RAIS and RAISING, respectively; Step 4, Double-stranded DNA (dsDNA) synthesis; Step 5, DNA purification of dsDNA with magnetic streptavidin-beads in RAIS and first PCR in RAISING; Step 6, First PCR in RAIS and second PCR in RAISING; Step 7, Second PCR in RAIS and Sanger sequencing or next generation sequencing (NGS) library preparation in RAISING. **b-d**, Linear-amplification, accuracy, and consistency between RAIS and RAISING. Genomic DNA of LMY2 and ED cell lines each harboring a single HTLV-1 integration site were mixed at the indicated percentages, and these mixed samples were processed using both RAIS and RAISING. **b**, Products were visualized by electrophoresis on 2% agarose gels. **c**, Products were analyzed using Sanger sequencing, with dotted lines indicating the position of the HTLV-1 integration sites. **d**, Products were analyzed using next generation sequencing to measure clone size. Data from two independent experiments (1 and 2) are shown.

Fig. 2 | Performance of Rapid Amplification of Integration Site without Interference by Genomic DNA contamination (RAISING). All RAISING products were visualized by electrophoresis on 2% agarose gels. Dotted lines in Sanger sequencing spectra indicate the position of transgene integration sites. **a**, The sensitivity of RAISING was assessed by serially diluting TL-Om1 genomic DNA (an HTLV-1-infected cell line harboring a single copy of HTLV-1) with Jurkat genomic DNA (an HTLV-1 negative cell line). Even extremely diluted samples (resulting in PVL as low as 0.032) could be detected by increasing the number of cycles in the second PCR of RAISING (left panel). Sanger sequencing analysis of RAISING products confirmed that the same integration site was identified in every dilution (right panel). PVL, proviral load. **b-c**, Clonality analyses of infected samples using Sanger sequencing (spectra) vs. next generation sequencing (pie charts) showed similar results. **b**, HTLV-1 clonality analysis of an asymptomatic carrier (AC) and an adult T-cell leukemia/lymphoma (ATL) patient. **c**, Bovine leukemia virus (BLV) clonality analysis of an aleukemic (AL) cow and a cow with enzootic bovine leukosis (EBL). **d**, Successful amplification of various transgene-integrated fragments (HTLV-1; HIV-1, human immunodeficiency virus; SIV, simian immuno-deficiency virus; HBV, hepatitis B virus; AdV, adenovirus; and low-density lipoprotein receptor knock-in mice Ldlr-mLO-4 and Ldlr-mLO-5) with RAISING. **e**, HBV and AdV integration sites. **f**, Clonality analysis of HIV-1 and SIV-infected cells with NGS analysis. NGS read counts indicate the size of each clone. **g**, RAISING with NGS analysis was used to identify on- and off-target effects in Ldlr-mLO-4 and Ldlr-mLO-5 knock-in mice established by genome editing technology. Chr, chromosome.

Fig. 3 | Clinical utility of clonality analysis using Rapid Amplification of Integration Site without Interference by Genomic DNA contamination (RAISING) and Clonality Value (CLOVA) software. HTLV-1 proviral load (PVL, **a**) and clonality values (Cv, **b**) of peripheral blood samples from asymptomatic carriers (AC, n=200, black), HTLV-1-associated myelopathy/tropical spastic paraparesis (HAM/TSP, n= 224, blue), and adult T-cell leukemia/lymphoma (ATL, n=274, red) patients. Results include samples analyzed previously using RAIS (n=292) as well as those analyzed using the novel RAISING method (n=438). The median PVL (**a**) and Cv (**b**) in each group and subtype are shown as horizontal lines. P-values were calculated using Dunn's multiple comparisons test. ****p < 0.0001, ***p < 0.001, **p < 0.01, *p < 0.05. **c**, Combinational analysis of PVL and Cv using the same samples as above. PVL 0.5% and Cv 0.48 indicate proposed cut-off values to differentiate ATL from non-ATL. **d**, Frequencies of subjects with ATL (red) and without ATL (green) per Cv at intervals of 0.05. Dotted lines show proposed cut-off values to classify HTLV-1-infected patients into three ATL risk groups. See supplementary Fig. 7b for detailed calculations of first clone size. **e**, Longitudinal analysis of Cv and PVL in two HAM/TSP patients (HAMATL001 and HAMATL003) and one AC (ACATL004) who all developed acute ATL. Black and orange lines indicate Cv and PVL at each time point, respectively. The same proposed cut-off values as above are again shown with dotted lines.

Table. 1 Adult T-cell leukemia/lymphoma (ATL) risk assessment method.

Risk*	PVL	Cv	Non-ATL (n=424)		ATL (n=274)
			AC (n=200)	HAM/TSP (n=224)	
Low	< 0.5 %**	NA	88.5%	84.4%	0.0%
	≥ 0.5 %**	< 0.25			
Medium	≥ 0.5 %**	0.25–0.47	7.5%	11.6%	0.0%
High	≥ 0.5 %**	≥ 0.48	4.0%	4.0%	100%

Cv, clonality value; PVL, proviral load; NA, not applicable; AC, asymptomatic carrier; HAM/TSP, HTLV-1-associated myelopathy/tropical spastic paraparesis.

* This method assesses ATL risk using samples from peripheral blood but not from lymph nodes, skin, or bone marrow.

** Rapid Amplification of Integration Site without Interference by Genomic DNA contamination (RAISING)-CLOVA can reliably measure Cv when PVL is at least 0.5%, assuring the accuracy of this method.

Table. 2 Clinical profiles and HTLV-1 clonality analysis of three patients who developed adult T-cell leukemia/lymphoma (ATL).

Patient							
Collection date			Atypical			HTLV-1 integration site	Orientation of
(Months post observation)	Stage	sIL-2R (U/mL)	lymphocytes (%)	PVL (%)	Cv	Chromosome: Position	HTLV-1 provirus
HAMATL001							
2007/11/02 (0)	Asymptomatic	839	NA	3.68	0.20	Chr16: 89674607	5'_3'
2009/10/16 (23)	Asymptomatic	635	NA	2.44	0.11	ND	ND
2010/09/24 (34)	Asymptomatic	560	NA	3.66	0.23	Chr16: 89674607	5'_3'
2011/10/01 (47)	Asymptomatic	1004	NA	3.68	0.45	Chr16: 89674607	5'_3'
2012/10/05 (59)	Asymptomatic	632	NA	2.48	0.16	Chr16: 89674607	5'_3'
2013/10/04 (71)	Asymptomatic	528	NA	4.29	0.75	Chr16: 89674607	5'_3'
2014/11/06 (84)	Asymptomatic	724	4.0	6.03	0.58	Chr16: 89674607	5'_3'
2015/03/05 (88)	Asymptomatic	691	1.5	8.43	0.82	Chr16: 89674607	5'_3'
2015/11/13 (96)	Asymptomatic	835	NA	5.28	0.76	Chr16: 89674607	5'_3'
2016/03/18 (100)	Asymptomatic	1266	NA	5.11	0.88	Chr16: 89674607	5'_3'
2016/10/17 (107)	Diagnostic	20100	51.5	20.12	0.62	Chr16: 89674607	5'_3'
2017/11/20 (120)	Post treatment	1520	0.0	0.26	0.18	ND	ND
2018/12/03 (133)	Post treatment	983	0.0	1.41	0.07	ND	ND
2019/12/12 (145)	Post treatment	750	0.5	0.91	0.09	ND	ND
HAMATL003							
2016/08/01 (0)	Asymptomatic	790	2.5	9.99	0.49	Chr20: 61231839	3'_5'
2017/08/10 (12)	Asymptomatic	1020	2.5	9.21	0.37	Chr20: 61231839	3'_5'
2018/08/23 (24)	Asymptomatic	893	2.0	8.64	0.47	Chr20: 61231839	3'_5'
2018/11/15 (27)	Asymptomatic	1638	0.5	8.77	0.68	Chr20: 61231839	3'_5'
2018/12/28 (28)	Diagnostic	3965	NA	18.06	0.81	Chr20: 61231839	3'_5'
ACATL004							
2012/03/15 (0)	Asymptomatic	NA	NA	2.84	0.11	ND	ND
2013/03/07 (12)	Asymptomatic	427	0.5	4.08	0.18	ND	ND
2014/04/03 (25)	Asymptomatic	546	0.5	3.35	0.11	ND	ND
2015/04/06 (37)	Asymptomatic	376	1.5	5.21	0.11	ND	ND

2016/04/28 (49)	Asymptomatic	369	1.5	4.63	0.26	ND	ND
2017/04/06 (61)	Asymptomatic	360	1.0	3.62	0.11	ND	ND
2018/02/15 (70)	Asymptomatic	302	1.0	2.19	0.10	ND	ND
2018/05/17 (73)	Asymptomatic	426	1.0	6.15	0.22	ND	ND
2018/08/09 (76)	Asymptomatic	376	0.5	7.24	0.27	ND	ND
2018/11/01 (79)	Asymptomatic	475	0.5	9.97	0.40	ND	ND
2019/03/14 (83)	Asymptomatic	543	1.0	15.08	0.64	Chr2: 82415225 (first clone)	5'_3'
						Chr16: 51609108 (second clone)	5'_3'
2019/06/20 (86)	Diagnostic	9698	41.5	106.24	0.77	Chr2: 82415225 (first clone)	5'_3'
						Chr16: 51609108 (second clone)	5'_3'

sIL-2R, soluble interleukin-2 receptor; Cv, clonality value; PVL, proviral load; ND, not detectable; NA, not available; Chr, chromosome.

Supplementary Information

RAISING: a high-performance method for identifying random transgene integration sites

Yusaku Wada^{1,20}, Tomoo Sato^{2,3,20}, Hiroo Hasegawa^{4,5,20}, Takahiro Matsudaira^{1,20}, Naganori Nao⁶, Ariella L. G. Coler-Reilly^{2,7}, Tomohiko Tasaka⁸, Shunsuke Yamauchi⁴, Tomohiro Okagawa⁹, Haruka Momose¹⁰, Michikazu Tanio¹⁰, Madoka Kuramitsu¹⁰, Daisuke Sasaki⁴, Naoko Yagishita², Junji Yamauchi², Natsumi Araya², Kenichiro Tanabe¹¹, Makoto Yamagishi¹², Makoto Nakashima¹², Shingo Nakahata¹³, Hidekatsu Iha¹⁴, Masao Ogata¹⁵, Yoshitaka Imaizumi¹⁶, Kaoru Uchimarui¹², Yasushi Miyazaki^{16,17}, Satoru Konnai^{9,18}, Katsunori Yanagihara^{4,5}, Kazuhiro Morishita¹³, Toshiki Watanabe¹⁹, Yoshihisa Yamano^{2,3*}, Masumichi Saito^{10*}

¹Biotechnological Research Support Division, FASMAC Co., Ltd, 243-0021 Kanagawa, Japan

²Department of Rare Diseases Research, Institute of Medical Science, St. Marianna University School of Medicine, 216-8512 Kanagawa, Japan

³Division of Neurology, Department of Internal Medicine, St. Marianna University School of Medicine, 216-8511 Kanagawa, Japan

⁴Department of Laboratory Medicine, Nagasaki University Hospital, 852-8501 Nagasaki, Japan

⁵Department of Laboratory Medicine, Nagasaki University Graduate School of Biomedical Sciences, 852-8501 Nagasaki, Japan

⁶Hokudai Center for Zoonosis Control in Zambia, Research Center for Zoonosis Control, Hokkaido University, Sapporo, 001-0020 Hokkaido, Japan

⁷Department of Internal Medicine, Division of Bone and Mineral Diseases, Washington University School of Medicine, St. Louis, MO, 63110 USA

⁸Affinity Science Corporation, 141-0031 Tokyo, Japan

⁹Department of Advanced Pharmaceutics, Faculty of Veterinary Medicine, Hokkaido University, 060-0818 Hokkaido, Japan

¹⁰Department of Safety Research on Blood and Biological Products, National Institute of Infectious Diseases, 208-0011 Tokyo, Japan

¹¹Pathophysiology and Bioregulation, St. Marianna University Graduate School of Medicine, 216-8511 Kanagawa, Japan

¹²Department of Computational Biology and Medical Sciences, Graduate School of Frontier Sciences, The University of Tokyo, 108-8639 Tokyo, Japan

¹³Division of Tumor and Cellular Biochemistry, Department of Medical Sciences, University of Miyazaki, 889-1692 Miyazaki, Japan.

¹⁴Department of Microbiology, Faculty of Medicine, Oita University, 879-5593 Oita, Japan

¹⁵Department of Hematology, Oita University Hospital, 879-5593 Oita, Japan

¹⁶Department of Hematology, Nagasaki University Hospital, 852-8501 Nagasaki, Japan

¹⁷Atomic Bomb Disease and Hibakusha Medicine Unit, Atomic Bomb Disease Institute, Nagasaki University, 852-8102 Nagasaki, Japan

¹⁸Department of Disease Control, Faculty of Veterinary Medicine, Hokkaido University, Sapporo, 060-0818 Hokkaido, Japan

¹⁹Department of Practical Management of Medical Information, St. Marianna University Graduate School of Medicine, 216-8511 Kanagawa, Japan

²⁰These authors contributed equally: Yusaku Wada, Tomoo Sato, Hiroo Hasegawa, and Takahiro Matsudaira

*Correspondence: Masumichi Saito (saitomas@nih.go.jp) and Yoshihisa Yamano (yyamano@marianna-u.ac.jp)

Contents

- **Acknowledgements**
- **Author contributions**
- **Competing interest statement**
- **Data availability**
- **Code availability**
- **Protocol for RAISING**

- **Supplementary Figure legends**
- **Supplementary Table titles**
- **References**
- **Supplementary Figures**

Acknowledgements

We are grateful to Dr. Masao Matsuoka for providing the ED cell line; Dr. Masahiro Fujii for providing the SLB-1 cell line; Drs. Kousho Wakae and Masamichi Muramatsu for providing genomic DNA from the HBV-infected cell line (HepAD38); Dr. Shigeyoshi Harada for providing genomic DNA from HIV-1-infected cells (HIV-1 89.6-infected PM1 cells) and the infection method; Drs. Takushi Nomura, Hirofumi Akari, and Tetsuro Matano for providing genomic DNA from the SIV-infected cell line (SIVmac239-infected HSC-F cells) and the infection method; Mrs. Takao Tanaka and Yoshihiro Ohguchi (KAC Co., Ltd) for providing genomic DNA from knock-in mice (Ldlr-mLO-4 and Ldlr-mLO-5) and the established genome-editing method; and New England Biolabs Japan Inc. for providing OneTaq, NEBNext[®] Single Cell Lysis Module, and Thermolabile Proteinase K as samples. We also thank the patients who participated in this research as well as the faculty members of the Division of Hematology and Oncology at St. Marianna University School of Medicine (Yu Uemura and Ayako Arai), and laboratory support staff of the Institute of Medical Science at St. Marianna University School of Medicine (Katsunori Takahashi, Yasuo Kunitomo, Yumiko Hasegawa, Mikako Koike, Satoko Aratani, Chihiro Sasa, Yumi Saito, and Miho Ishikawa). This work was supported by grants from JSPS KAKENHI

(JP17H03594 and JP 16H06277 CoBiA : M.S, JP18H02733: H.H, JP19H03575: Y.Y, and JP19K07983: T.S.), AMED (JP20ek0109346 and JP20ek0109356: Y.Y), and Metabolic Skeletal Disorders Training Grant through the National Institute of Arthritis and Musculoskeletal and Skin Diseases (T32AR060719: A.L.G.CR).

Author contributions

Y.W., T.S., H.H., T.M., S.Y., H.M., M.K., D.S., and M.S performed the research; N.N, T.T., H.M, M.T, and K.T performed the data analysis; T.S., H.H., S.Y., T.O., N.Y., J.Y., N.A., M.Y., M.N., S.N., H.I., M.O., Y.I., K.U., Y.M., S.K., K.Y., K.M., T.W., and Y.Y. provided patient samples; Y.W., T.S., H.H., T.M., T.T., A.L.G.CR., Y.Y., and M.S. wrote the manuscript; and T.S., H.H., Y.Y., and M.S. supervised the study.

Competing interests statement

Yusaku Wada, Takahiro Matsudaira, and Masumichi Saito are inventors on the pending patent application (PCT/JP2020/03907) for RAISING technology. Yusaku Wada and Takahiro Matsudaira are employees of FASMAC Co., Ltd.. All other authors declare no competing interests.

Data availability

All data that support the findings of this study are available from the corresponding author upon request (saitomas@nih.go.jp).

Code availability

CLOVA is available from the following URL: http://fasmac.co.jp/rais_method_case

(Japanese website) and <http://fasmac.co.jp/en/rais> (English website).

Protocol for RAISING (Rapid Amplification of Integration Sites without Interference by Genomic DNA contamination)

In our study, all enzymatic reactions in RAISING were performed using a Veriti thermal cycler (ThermoFisher Scientific).

Primer design and DNA preparation

* Use the primer design tool Primer 3^{1,2} to obtain transgene-specific primers F1, F2, and F3, with lengths of 20–27 bases and melting temperature values of approximately 68°C. These primers are typically designed to be within 500 bp of the boundary of the transgene and the host genome, except in the case of retroviruses or virus-based vectors that have two long terminal repeats (LTRs). The F1 primer in these exceptions should be designed outside of the LTRs to avoid amplification of the viral genome or viral vector. To obtain a longer read of the transgene-integrated host genome sequence using the Illumina NGS platform, the F3 primer should be designed to be as close to the boundary as possible in all transgenes. However, we recommend designing the other F3 primer within approximately 100 bp of the boundary of the transgene and the host genome when Sanger sequencing and clonality analysis of the transgene using CLOVA will be performed instead of NGS analysis. The clonality value as well as Sanger sequence spectra with this F3 primer is more stable and reproducible than those with the F3 primer for NGS analysis.

* Genomic DNA should be purified using an appropriate method and should be treated with RNase A. We recommend checking the quality of the genomic DNA using

electrophoresis before proceeding to step 1.

Step 1: Single-stranded DNA (ssDNA) synthesis

Components	Volume
Genomic DNA (200 ng/μL)	2.5 μL
10× PCR Buffer for KOD-Plus-Neo	5 μL
2 mM dNTPs	5 μL
25 mM MgSO ₄	3 μL
10 μM F1 primer	1.5 μL
KOD-Plus-Neo (1 U/μL)	1 μL
H ₂ O	32 μL
Total	50 μL

PCR condition	Temperature	Time	Cycles
Pre-denaturation	94°C	2 min	1
Denaturation	98°C	10 s	25
Annealing ¹	50–68°C	30 s	
Extension ²	68°C	30 s to 2 min	

¹The annealing step can be avoided by designing the F1 primer with a T_m value of approximately 68°C according to the manufacturer's instructions.

²The extension time depends on the F1 primer position.

Step 2: Column purification

- Purification of ssDNA is performed using a Monarch PCR & DNA Cleanup Kit according to the manufacturer's instructions.

- The final elution volume is approximately 8.2 μL if 9.6 μL of H_2O is used for the elution.

*The ZR-96 DNA Clean & Concentrator-5 kit (ZYMO RESEARCH) can also be used for purification of ssDNA in the case of more than 96 specimens.

Step 3: PolyAG (TG)-tailing

- Use a single PCR tube for continuous reactions in steps 3–5.

*The polyAG-tailing can be replaced with polyTG-tailing if the transgene has a polyA sequence downstream of the specific F1 primer.

Components	Volume
ssDNA	8.2 μL
10 $\times$ TdT Buffer	1.1 μL
2.5 mM CoCl_2	1.1 μL
10 mM dATP	0.35 μL
TdT (20 U/ μL)	0.25 μL
Total	11 μL

- Incubate at 37°C for ≥ 20 min.

Components	Volume
PolyA-tailed ssDNA	11 μ L
10 $\times$ TdT Buffer	0.1 μ L
2.5 mM CoCl ₂	0.1 μ L
10 mM dGTP	0.35 μ L
H ₂ O	0.45 μ L
Total	12 μL

- Sequentially incubate at 37°C for ≥ 15 min and then at 75°C for 10 min.

Step 4: Double-stranded DNA synthesis

* The NV-oligo-dA-ADP1 primer must be used if polyTG-tailed ssDNA is synthesized at step 3.

Components	Volume
PolyAG-tailed ssDNA	12 μ L
5 $\times$ Q5 Reaction Buffer	12 μ L
10 mM dNTPs	1.2 μ L
10 μ M NV-oligo-dT-ADP1	3 μ L
Q5 HS-High-Fidelity DNA polymerase (2 U/ μ L)	0.6 μ L

H ₂ O	31.2 µL
Total	60 µL

PCR condition	Temperature	Time	Cycles
Pre-denaturation	65°C	5 min	1
Annealing	64°C	10 s	1
	62°C	10 s	
	60°C	10 s	
	58°C	10 s	
	56°C	10 s	
	54°C	10 s	
	52°C	10 s	
Extension ¹	72°C	30 s to 2 min	

¹The extension time depends on the F1 primer position.

Step 5: First PCR

* Step 5 should be performed immediately after step 4.

Components	Volume
Double-stranded DNA reaction mix	60 µL
25 µM F2 primer	1.2 µL
Total	61.2 µL

PCR condition	Temperature	Time	Cycles
Pre-denaturation	98°C	30 s	1
Denaturation	98°C	5–10 s	22
Annealing ¹	50–68°C	10–30 s	
Extension ²	72°C	30 s to 2 min	

¹The annealing temperature depends on the T_m value of F2 primer.

²The extension time depends on the F2 primer position.

Step 6: Second PCR

- Make a 1/200 dilution of the first PCR products.

* A consideration of PCR cycles is required based on the copy number of integrated transgenes in the genomic DNA.

Components	Volume
DNA (1/200 of first PCR reaction)	1 µL
10× PCR Buffer for KOD-Plus-Neo	5 µL
2 mM dNTPs	5 µL
25 mM MgSO ₄	3 µL
10 µM F3 primer	1.5 µL
10 µM ADP1-NGS-R1	1.5 µL
KOD-Plus-Neo (1 U/µL)	1 µL

H ₂ O	32 µL
Total	50 µL

PCR condition	Temperature	Time	Cycles
Pre-denaturation	94°C	2 min	1
Denaturation	98°C	10 s	26–32
Annealing ¹	50–68°C	30 s	
Extension ²	68°C	30 s to 2 min	

¹The annealing step can be avoided by designing the F3 primer with a T_m value of approximately 68°C according to the manufacturer's instructions.

²The extension time depends on the F3 primer position.

Reagents	Source	Identifier
KOD-Plus-Neo	TOYOBO	KOD-401
Monarch PCR & DNA Cleanup Kit	New England BioLabs	T1030
Terminal Transferase	New England BioLabs	M0315S
Deoxynucleotide (dNTP) Solution Set	New England BioLabs	N0446S
Q5 Hot Start High-Fidelity DNA Polymerase	New England BioLabs	M0493S

Additional step: NGS library preparation

- Re-amplify the amplicon in step 6 with two primers that contain a dual-indexed sequence (octoN) and the remainder of the Illumina adaptor sequence.

Supplementary Figure legends

Supplementary Fig. 1. Examination of step 1 in Rapid Amplification of Integration Sites without Interference by Genomic DNA contamination (RAISING). **a.** RAISING was conducted using two genomic DNA samples, freshly isolated genomic DNA and fragmented genomic DNA, with or without RNase A treatment. RAISING products were visualized using electrophoresis on 0.6% (Left panel) and 2% (Right panel) agarose gels. **b.** RAISING was performed using a different amount of genomic DNA in Fig. 2a. RAISING products were visualized using electrophoresis on 2% agarose gels. **c.** Examination of extension time for single-stranded DNA (ssDNA) synthesis in step 1 of RAISING. Schematic representation of the estimated final PCR product sizes according to the ssDNA synthetic time using KOD-Plus-Neo (Left panel). RAISING was performed using TL-Om1 (HTLV-1-infected cell line) genomic DNA, and the products were visualized using electrophoresis on 2% agarose gels (Right panel). **d.** The ssDNA synthesis in step 1 of RAISING was performed with the indicated cycle numbers using TL-Om1 genomic DNA. The relative amount of ssDNA was measured using qPCR with primers for the HTLV-1 3' long terminal repeat. Data are shown as mean $\pm$ SD of three independent qPCRs. **e.** The ssDNA synthesis in step 1 of RAISING was examined with the indicated cycle numbers using an HTLV-1-specific F1 primer and TL-Om1 genomic DNA. The arrows indicate non-specific amplifications. Genomic DNA and non-specific products were visualized using electrophoresis on 0.6% agarose gels. **f.**

Step 1 of RAISING was performed using the same genomic DNAs as shown in Fig. 2a and two PCR enzymes: OneTaq and Q5. RAISING products were visualized using electrophoresis on 2% agarose gels.

Supplementary Fig. 2. Examination of step 2 in Rapid Amplification of Integration Sites without Interference by Genomic DNA contamination (RAISING). The Dead volume of DNA purification columns in Monarch PCR and DNA cleanup kit was examined in step 2 of RAISING. The average dead volume was obtained using 15 individual columns.

Supplementary Fig. 3. Examination of steps 3–5 in Rapid Amplification of Integration Sites without Interference by Genomic DNA contamination (RAISING). **a.** The effect of polyAG-tailing was examined in steps 3–5 of RAISING. The red box shows the lane including non-specific amplifications. **b.** Oligo-dT-ADP1 primers, NV-oligo-dT-ADP1 that includes VN (V = A or G or C, N = A or G or C or T), V-oligo-dT-ADP1, and oligo-dT-ADP1 that included or did not include V at each 3'-end, respectively, were examined in step 4 and 5 of RAISING using genomic DNA of SLB-1 (HTLV-1-infected cell line) harboring multiple HTLV-1 integration sites. Visualization of PCR products (Left panel). Sanger sequencing analysis of HTLV-1 integration sites (Right panel). **c.** Four PCR enzymes (KOD-Dash, PrimeSTAR-GXL, OneTaq, and Q5) were examined in step 4 and 5 of RAISING. TdT, terminal transferase. **d.** Comparison of PolyAG-tailing with NV-oligo-dT-ADP1 and PolyTG-tailing with NV-oligo-dA-ADP1 in steps 3–5 of RAISING. RAISING was performed using TL-Om1 (HTLV-1-infected cell line) genomic DNA. Data from two independent

experiments (1 and 2) are shown. Visualization of PCR products (Left panel). Sanger sequencing analysis of HTLV-1 integration sites (Right panel). All PCR products were visualized using electrophoresis on 2% agarose gels.

Supplementary Fig. 4. Amplification of HTLV-1 integration sites in HTLV-1-infected cell lines with Rapid Amplification of Integration Sites without Interference by Genomic DNA contamination (RAISING). **a.** Genomic DNAs of LMY2 and ED harboring each single copy of HTLV-1 were used for RAISING. PCR products were visualized using electrophoresis on 2% agarose gels. **b.** HTLV-1 integration sites in LMY2 and ED were analyzed using Sanger sequencing.

Supplementary Fig. 5. Accuracy and utility of Rapid Amplification of Integration Sites without Interference by Genomic DNA contamination (RAISING). **a.** Genomic DNAs of KK1 and SLB-1 (HTLV-1 infected cell lines) harboring multiple HTLV-1 integration sites was extracted with a cell-direct method at the indicated cell number, and the genomic DNAs were sequentially used for RAISING. PCR products were visualized using electrophoresis on 2% agarose gels. **b.** HTLV-1 integration sites in KK1 and SLB-1 were analyzed using Sanger sequencing and next-generation sequencing (NGS). **c.** NGS analysis was conducted to evaluate the accuracy of RAISING in **a** and **b**. The correlation coefficient was determined by calculating the frequency of each HTLV-1 integration site in each NGS dataset.

Supplementary Fig. 6. Characterization of CLOVA, a software developed to analyze the clonality value of HTLV-1-infected cells. **a.** A representative result of Sanger

sequence spectra of HTLV-1-infected cells in an adult T-cell leukemia/lymphoma (ATL) patient and the CLOVA image. **b.** A representative result of HTLV-1-infected cells in an asymptomatic carrier and the CLOVA image. **c.** Comparison of Sanger sequence spectra patterns and clonality values analyzed using CLOVA.

Supplementary Fig. 7. Comparison of clonality values and the first clone sizes in HTLV-1-infected samples. Clonality values and the clone sizes in HTLV-1-infected samples ($n = 28$) were analyzed using Rapid Amplification of Integration Sites without Interference by Genomic DNA contamination (RAISING) with Sanger sequencing and next-generation sequencing, respectively. **a.** Samples 1, 16, and 28 are shown as examples for the analysis of clonality values and the first clone sizes. Pie charts indicate the variety and size of HTLV-1-infected clones. The first clone is shown with dark blue color in each pie chart. **b.** Positive correlation of clonality values and the first clone sizes. The correlation coefficient was determined using Microsoft Excel for Mac 2011 (ver.14.7.1) (95% confidence intervals of slope and intercept are 95.65 to 118.42 and -14.67 to -2.41 , respectively).

Supplementary Fig. 8. Identification of HTLV-1 integration sites in the first and second clones using CLOVA. **a.** Example of Sanger sequence spectra showing presence of the first and second clones in an adult T-cell leukemia/lymphoma (ATL) patient. An image of the first and second clones in CLOVA is shown. **b.** Results of a BLAST homology search for the first and second clones in **a.** The red arrows and scheme of HTLV-1 indicate the direction of nucleotide number on chromosomes and HTLV-1

provirus, respectively. The numbers under red arrows show the chromosomal nucleotide number of each HTLV-1 integration site.

Supplementary Fig. 9. Accuracy and consistency of Rapid Amplification of Integration Sites without Interference by Genomic DNA contamination (RAISING)-CLOVA. Variation of HTLV-1 clonality values among five Sanger sequence reactions. RAISING-CLOVA was performed with four samples harboring different HTLV-1 clonality values.

Supplementary Fig. 10. Comparison of HTLV-1 clonality values in two different laboratories. Rapid Amplification of Integration Sites without Interference by Genomic DNA contamination (RAISING) was performed at the National Institute of Infectious Diseases (NIID) and FASMAC, Co., Ltd. (FASMAC) using the same HTLV-1-infected specimens ($n = 62$), and HTLV-1 clonality values were determined using CLOVA. Comparison of the clonality values and correlation coefficient are shown (95% confidence intervals of slope and intercept are 0.97 to 1.04 and -0.02 to 0.01 , respectively).

Supplementary Fig. 11. Comparison of HTLV-1 clonality values in Rapid Amplification of Integration Site (RAIS)-CLOVA and Rapid Amplification of Integration Sites without Interference by Genomic DNA contamination (RAISING)-CLOVA. RAIS-CLOVA and RAISING-CLOVA were performed using the same HTLV-1-infected specimens ($n = 24$). Comparison of the clonality values and

correlation coefficient are shown (95% confidence intervals of slope and intercept are 0.91 to 0.99 and 0.01 to 0.07, respectively).

Supplementary Fig. 12. Comparison of HTLV-1 clonality values between whole blood cells (WBCs) and peripheral blood mononuclear cells (PBMCs). Rapid Amplification of Integration Sites without Interference by Genomic DNA contamination (RAISING)-CLOVA was performed using samples of WBCs and PBMCs from the same patients (n = 53). Comparison of the clonality values and correlation coefficient are shown (95% confidence intervals of slope and intercept are 0.86 to 1.08 and -0.01 to 0.07, respectively).

Supplementary Fig. 13. Comparison of HTLV-1 proviral loads and clonality values among ATL subtypes. HTLV-1 proviral load (**a**) and clonality value (**b**) derived from peripheral blood of ATL patients (n = 274) were compared among ATL subtypes. **c.** HTLV-1 clonality value of the skin (black circle), bone marrow (green circle), lymph node (blue circle), and peripheral blood (red open circle) were compared among ATL subtypes. Horizontal bars indicate the median values. Statistical analysis was performed using the Kruskal–Wallis test followed by Dunn’s post-hoc test: ****p < 0.0001, ***p < 0.001, **p < 0.01, *p < 0.05.

Supplementary Fig. 14. Receiver operating characteristic (ROC) curve analysis with HTLV-1 proviral loads and clonality values among asymptomatic carriers (AC) and HTLV-1-associated myelopathy/tropical spastic paraparesis (HAM/TSP) and ATL patients. We evaluated the ability of the HTLV-1 proviral load to discriminate between

(a) AC and ATL, (b) HAM/TSP and ATL, and (c) HAM/TSP and ATL (smoldering and lymphoma subtypes). d. Ability of HTLV-1 clonality value to discriminate ATL from both AC and HAM/TSP. AUC, area under the ROC curve; 95% CI, 95% confidence interval.

Supplementary Fig. 15. Examination of the minimum HTLV-1 proviral load (PVL) to measure a reliable clonality value with Rapid Amplification of Integration Sites without Interference by Genomic DNA contamination (RAISING)-CLOVA. **a.** RAISING-CLOVA was performed using genomic DNA of two HTLV-1-infected specimens (Samples #1 and #2) serially diluted with genomic DNA of peripheral blood mononuclear cells (HTLV-1-negative cells). PCR products were visualized using electrophoresis on 2% agarose gels. **b.** Analysis of the clonality values and identification of the minimum PVL in **a**. The dotted line indicates the minimum PVL 0.5% for HTLV-1 clonality analysis with RAISING-CLOVA.

Supplementary Fig. 16. Longitudinal analysis of HTLV-1 clonality in two HAM/TSP patients (HAMATL001 and HAMATL003) and a carrier (ACATL004) who developed the acute type of ATL. Rapid Amplification of Integration Sites without Interference by Genomic DNA contamination (RAISING) with Sanger sequencing analysis was performed. Each Sanger sequence spectra pattern with sampling date are shown.

Supplementary Fig. 17. Clonal changes of HTLV-1-infected cells in an asymptomatic carrier (ACATL004) who developed the acute type of ATL. **a.** Rapid Amplification of Integration Sites without Interference by Genomic DNA contamination (RAISING)

with next-generation sequencing was performed using five specimens collected on the indicated dates. The variety and size of HTLV-1-infected clones are shown in each pie chart with different colors. **b.** Clone size of ATL first and second clones in **a.**

Supplementary Fig. 18. Longitudinal analysis of clonality value (Cv) and soluble interleukin-2 receptor (sIL-2R) in two HAM/TSP patients (HAMATL001 and HAMATL003) and one asymptomatic carrier (AC; ACATL004) who developed the acute type of ATL. Black and pink lines indicate the Cv and sIL-2R at each time point, respectively. The same cut-off values indicated in Fig. 3e are shown with dotted lines.

Supplementary Fig. 19. Clonal changes of HTLV-1-infected cells in a HAMATL001 patient before and after treatment. **a.** Rapid Amplification of Integration Sites without Interference by Genomic DNA contamination (RAISING) with next-generation sequencing was performed using four specimens collected on the indicated dates. The variety and size of HTLV-1-infected clones are shown in each pie chart with different colors. The same clone among the top 10 clones in different specimens are shown with the same color **b.** Clone size of ATL first clone in **a.**

Supplementary Fig. 20. HTLV-1 clonality in a HAM/TSP patient (HAMATL004) who developed the lymphoma type of ATL. HTLV-1 clonality of HAMATL004 was analyzed with Rapid Amplification of Integration Sites without Interference by Genomic DNA contamination (RAISING)-CLOVA using specimens obtained from the lymph node and peripheral blood mononuclear cells (PBMCs). **a.** Sanger sequence

spectra patterns of HTLV-1 clonality in the lymph node and PBMCs. **b.** The HTLV-1 clonality values of lymph node and PBMCs in HAMATL004.

Supplementary Table titles

Supplementary Table 1. Primers used for Rapid Amplification of Integration Sites without Interference by Genomic DNA contamination (RAISING).

Supplementary Table 2. Identification of multiple transgene integration sites using Rapid Amplification of Integration Sites without Interference by Genomic DNA contamination (RAISING) with Sanger sequencing and next-generation sequencing (NGS) analysis.

Supplementary Table 3. Clinical profile of asymptomatic carriers (ACs), HTLV-1-associated myelopathy/tropical spastic paraparesis (HAM/TSP) patients and adult T-cell leukemia/lymphoma (ATL) patients.

References

1. Koressaar, T. & Remm, M. Enhancements and modifications of primer design program Primer3. *Bioinformatics* **23**, 1289-1291 (2007).
2. Untergasser, A. et al. Primer3—new capabilities and interfaces. *Nucleic Acids Res* **40**, e115 (2012).

Supplementary Fig. 1

Supplementary Fig. 2

Supplementary Fig. 3

Supplementary Fig. 4

a

b

Supplementary Fig. 5

Supplementary Fig. 6

Supplementary Fig. 7

a

b

Supplementary Fig. 9

Supplementary Fig. 10

Supplementary Fig. 11

Supplementary Fig. 12

Supplementary Fig. 13

a

b

c

Supplementary Fig. 14

Supplementary Fig. 15

a

b

Supplementary Fig. 16

Supplementary Fig. 17

a

b

Supplementary Fig. 18

Supplementary Fig. 19

a

b

Supplementary Fig. 20

Supplementary Table 1. Primers used for Rapid Amplification of Integration Sites without Interference by Genomic DNA contamination.

Transgene	Forward primer Name	Forward primer sequene (5'-3')
HTLV-1	HTLV-F1	CAAGGCCTACCACCCCTCAT
	HTLV-F2	CCTGACCCTGCTTGCTCAAC
	HTLV-F3-NGS-F1	ACACTCTTTCCCTACACGACGCTCTTCCGATCTGCCAGCGACAGCCCATYCTAT
	HTLV-F3-Sanger-F1	ACACTCTTTCCCTACACGACGCTCTTCCGATCTAAAGTTCCACCCCTTTCCCTTT
BLV	BLV-F1	ATGAATGGCTCTCCCGCCTTTTT
	BLV-F2	CTATCCGGCAGCGGTCAAGTAAG
	BLV-F3-NGS-F1	ACACTCTTTCCCTACACGACGCTCTTCCGATCTACCCGCGTTYGYTTCCTGTCTT
HIV-1	HIV-F1	CCTGGCTGGAAGCACAAGAGGAG
	HIV-F2	GGGACTTTCCAGGGAGGTGTGG
	HIV-F3-NGS-F1	ACACTCTTTCCCTACACGACGCTCTTCCGATCTGCCCGTCTGTTGTGTGACTCTGG
SIV	SIV-F1	TCAGTGAGGCCAAAAGTTCCCTA
	SIV-F2	GAGCCTGGGTGTTCCCTGCTAGA
	SIV-F3-NGS-F1	ACACTCTTTCCCTACACGACGCTCTTCCGATCTCGCCTGGTCAACTCGGTACTCAA
HBV	HBV-F1	GCCAGGTCTGTCCAAGTGTG
	HBV-F2	TCTGTGCCAAGTGTGCTGACG
	HBV-F3-NGS-F1	ACACTCTTTCCCTACACGACGCTCTTCCGATCTACTGGCTGGGGCTTGGTCAT
ADV	ADV-F1	CTGAAATGTGTGGCGTGGCTTA
	ADV-F2	CTGCGGGGTGGTGTGATGATGA
	ADV-F3-NGS-F1	ACACTCTTTCCCTACACGACGCTCTTCCGATCTCTGGGCGTGGTGCCTAAAAATGT
Ldlr-LoxP	Ldlr-LoxP-F1	GAAAGGGGGTTGAATGGTGTGG
	Ldlr-LoxP-F2	TGAGGGGTGGTCTAGCCTGATGG
	Ldlr-LoxP-F3-NGS-F1	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTGGGCACACTGAAGAGGACAAAGT
Common	NGS-F2	AATGATACGGCGACCACCGAGATCTACACNNNNNNNNACACTCTTTCCCTACACGACGC

Transgene	Reverse primer Name	Reverse primer sequene (5'-3')
Common	NV-oligo-dT-ADP1	ACAGCAGGTCAGTCAAGCAGTATTTTTTTTTTTTTTTTTTTTTT
	V-oligo-dT-ADP1	ACAGCAGGTCAGTCAAGCAGTATTTTTTTTTTTTTTTTTTTTTT
	Oligo-dT-ADP1	ACAGCAGGTCAGTCAAGCAGTATTTTTTTTTTTTTTTTTTTTTT
	ADP1-NGS-R1	gtgactggagttcagacgtgtgtcttccgatctACAGCAGGTCAGTCAAGCAGTA
	NGS-R2	CAAGCAGAAGACGGCATAACGAGATNNNNNNNNGTGACTGGAGTTACAGCGTGTG
	Sanger sequencing primer	ACACTCTTTCCCTACACGAC

*Indexes in NGS-F2 and NGS-R2 are shown in red, N.

Analysis	Homo sapiens				Homo sapiens				Canis				Canis				Homo sapiens				Homo sapiens				Macaca fascicularis				Homo sapiens				Mus musculus				Mus musculus			
	Homo sapiens				Homo sapiens				Canis				Canis				Homo sapiens				Homo sapiens				Macaca fascicularis				Homo sapiens				Mus musculus				Mus musculus			
	Chromosome	Position	NSD read count	Chromosome	Position	NSD read count	Chromosome	Position	NSD read count	Chromosome	Position	NSD read count	Chromosome	Position	NSD read count	Chromosome	Position	NSD read count	Chromosome	Position	NSD read count	Chromosome	Position	NSD read count	Chromosome	Position	NSD read count	Chromosome	Position	NSD read count	Chromosome	Position	NSD read count							
1	1	193899	2085	1	1702542	131	1	665139	9800	1	1506271	31	1	1001507	2	1	1015815	2	1	1007915	4	19	326547	ND	19	326547	ND	19	326547	ND	19	326547	ND							
2	1	193899	2085	1	1702542	131	1	665139	9800	1	1506271	31	1	1001507	2	1	1015815	2	1	1007915	4	19	326547	ND	19	326547	ND	19	326547	ND	19	326547	ND							
3	1	193899	2085	1	1702542	131	1	665139	9800	1	1506271	31	1	1001507	2	1	1015815	2	1	1007915	4	19	326547	ND	19	326547	ND	19	326547	ND	19	326547	ND							
4	1	193899	2085	1	1702542	131	1	665139	9800	1	1506271	31	1	1001507	2	1	1015815	2	1	1007915	4	19	326547	ND	19	326547	ND	19	326547	ND	19	326547	ND							
5	1	193899	2085	1	1702542	131	1	665139	9800	1	1506271	31	1	1001507	2	1	1015815	2	1	1007915	4	19	326547	ND	19	326547	ND	19	326547	ND	19	326547	ND							
6	1	193899	2085	1	1702542	131	1	665139	9800	1	1506271	31	1	1001507	2	1	1015815	2	1	1007915	4	19	326547	ND	19	326547	ND	19	326547	ND	19	326547	ND							
7	1	193899	2085	1	1702542	131	1	665139	9800	1	1506271	31	1	1001507	2	1	1015815	2	1	1007915	4	19	326547	ND	19	326547	ND	19	326547	ND	19	326547	ND							
8	1	193899	2085	1	1702542	131	1	665139	9800	1	1506271	31	1	1001507	2	1	1015815	2	1	1007915	4	19	326547	ND	19	326547	ND	19	326547	ND	19	326547	ND							
9	1	193899	2085	1	1702542	131	1	665139	9800	1	1506271	31	1	1001507	2	1	1015815	2	1	1007915	4	19	326547	ND	19	326547	ND	19	326547	ND	19	326547	ND							
10	1	193899	2085	1	1702542	131	1	665139	9800	1	1506271	31	1	1001507	2	1	1015815	2	1	1007915	4	19	326547	ND	19	326547	ND	19	326547	ND	19	326547	ND							
11	1	193899	2085	1	1702542	131	1	665139	9800	1	1506271	31	1	1001507	2	1	1015815	2	1	1007915	4	19	326547	ND	19	326547	ND	19	326547	ND	19	326547	ND							
12	1	193899	2085	1	1702542	131	1	665139	9800	1	1506271	31	1	1001507	2	1	1015815	2	1	1007915	4	19	326547	ND	19	326547	ND	19	326547	ND	19	326547	ND							
13	1	193899	2085	1	1702542	131	1	665139	9800	1	1506271	31	1	1001507	2	1	1015815	2	1	1007915	4	19	326547	ND	19	326547														

[illegible]

[illegible]

[illegible]

[illegible]

[illegible]

[illegible]

2164	6	44653295	1	7	15373663	1	4	55323750	1
2165	6	44653278	1	7	15259030	1	4	55324274	1
2166	6	44653262	1	7	15259494	1	4	55337990	1
2167	6	44653247	1	7	15259428	1	4	55353865	2
2168	6	44653234	1	7	15259400	1	4	55406020	1
2169	6	44376724	1	7	15229042	1	4	55426439	1
2170	6	42196452	1	7	15211480	1	4	55442511	1
2171	6	41011834	1	7	15209465	1	4	55467624	1
2172	6	41011739	1	7	15190146	1	4	55466734	1
2173	6	40629373	1	7	151777163	1	4	55689781	4
2174	6	40629352	1	7	15140544	1	4	55689511	1
2175	6	39765347	1	7	149726559	1	4	57082251	1
2176	6	39765346	1	7	149620238	1	4	57172386	1
2177	6	38676297	1	7	149620196	1	4	57572369	1
2178	6	38637775	1	7	149299116	1	4	57611249	1
2179	6	35696387	1	7	149182850	1	4	61074856	3
2180	6	35696380	1	7	149097980	1	4	61217768	1
2181	6	35347720	1	7	148471652	1	4	61534622	1
2182	6	35091478	1	7	147933719	1	4	63032846	1
2183	6	35091474	1	7	146116021	1	4	63266523	1
2184	6	34267937	1	7	145374317	1	4	63733063	1
2185	6	32679014	1	7	145274316	1	4	63889118	3
2186	6	32264531	1	7	144916554	1	4	63913234	1
2187	6	31941124	1	7	14441132	1	4	64438223	1
2188	6	30539417	1	7	142665643	1	4	64623277	1
2189	6	30546688	1	7	141003853	1	4	64646178	1
2190	6	2892416	1	7	141040841	1	4	65060127	1
2191	6	27227446	1	7	140801655	1	4	6506445	1
2192	6	26894278	1	7	140801647	1	4	65134238	1
2193	6	25873327	1	7	140592034	1	4	65333660	1
2194	6	24622980	1	7	140592030	1	4	65263259	2
2195	6	24393027	1	7	140592023	1	4	65421110	1
2196	6	23727219	1	7	140592018	1	4	65577946	2
2197	6	23676771	1	7	140592012	1	4	66030399	1
2198	6	23676768	1	7	140111846	1	4	67154201	1
2199	6	23676767	1	7	139972188	1	4	67234198	1
2200	6	23676764	1	7	139621812	1	4	67723516	1
2201	6	23676767	1	7	13941795	1	4	67830680	1
2202	6	23676760	1	7	138713871	1	4	67968118	1
2203	6	23676742	1	7	138273441	1	4	68759441	1
2204	6	23676727	1	7	137211432	1	4	69145538	1
2205	6	23676708	1	7	135912633	1	4	71963707	1
2206	6	23676697	1	7	135912630	1	4	72701325	1
2207	6	23676647	1	7	135912629	1	4	72760226	2
2208	6	22438738	1	7	135654018	1	4	72792653	1
2209	6	22438677	1	7	134202863	1	4	73519711	1
2210	6	20489151	1	7	133714865	1	4	7373832	1
2211	6	19984485	1	7	132513751	1	4	74889	1
2212	6	19744932	1	7	132329164	1	4	75324778	1
2213	6	19541438	1	7	131533802	1	4	76366990	1
2214	6	17937137	1	7	131553791	1	4	76549711	1
2215	6	160030413	1	7	131553742	1	4	76874517	1
2216	6	16077626	1	7	13153737	1	4	76826639	1
2217	6	16775581	1	7	1313380	1	4	76268373	2
2218	6	16726985	1	7	13126364	1	4	84212266	2
2219	6	16660778	1	7	129269302	1	4	84326209	1
2220	6	16660775	1	7	128931756	1	4	84601090	2
2221	6	166607728	1	7	128420814	1	4	8565271	1
2222	6	166607683	1	7	127632324	1	4	85712384	1
2223	6	16636246	1	7	12695300	1	4	86200965	1
2224	6	16626374	1	7	126368697	1	4	86220352	1
2225	6	16603337	1	7	126205654	1	4	86252156	1
2226	6	165234215	1	7	123881567	1	4	86305991	3
2227	6	16243430	1	7	120614134	1	4	86307793	1
2228	6	161873504	1	7	120614123	1	4	86330470	2
2229	6	16036367	1	7	120141034	1	4	86365998	1
2230	6	159661627	1	7	117935444	1	4	86362687	1
2231	6	159116686	1	7	115790765	1	4	86365368	1
2232	6	158140070	1	7	115790763	1	4	86657796	1
2233	6	15779623	1	7	115636264	1	4	86679657	1
2234	6	152714238	1	7	1125532	1	4	86782821	2
2235	6	154120579	1	7	112159568	1	4	86789943	1
2236	6	154189567	1	7	112159560	1	4	86787055	1
2237	6	153162207	1	7	112159585	1	4	86784918	1
2238	6	149793362	1	7	112159544	1	4	86785349	1
2239	6	149493035	1	7	112159531	1	4	86787407	1
2240	6	149493015	1	7	109205951	1	4	86747572	1
2241	6	149059085	1	7	108901534	1	4	86822845	1
2242	6	149059085	1	7	108942623	1	4	86826298	1
2243	6	149059054	1	7	108920326	1	4	86829221	1
2244	6	147874444	1	7	107491998	1	4	86824793	1
2245	6	143576784	1	7	106796394	1	4	90664432	1
2246	6	141709638	1	7	106370840	1	4	90644222	1
2247	6	137546984	1	7	105769652	1	4	94359515	2
2248	6	137578622	1	7	105690380	1	4	94369383	1
2249	6	134276726	1	7	105646526	1	4	94854065	1
2250	6	134276715	1	7	105635251	1	4	94971982	1
2251	6	134276678	1	7	10555683	1	4	96277243	1
2252	6	134266079	1	7	105518342	1	4	96461909	1
2253	6	133885673	1	7	105436005	1	5	100009103	2
2254	6	132789966	1	7	105311334	1	5	100369983	1
2255	6	131137584	1	7	10412183	1	5	10068123	1
2256	6	1271429723	1	7	104059973	1	5	101532291	1
2257	6	125710270	1	7	104059973	1	5	101860076	1
2258	6	125710218	1	7	10405980	1	5	102141957	1
2259	6	125710273	1	7	103113901	1	5	102584642	1
2260	6	125214944	1	7	102546068	1	5	102513267	1
2261	6	124607359	1	7	102265054	1	5	102583181	1
2262	6	12470047	1	7	101796644	1	5	104074239	1
2263	6	122608815	1	7	10148026	1	5	10424207	1
2264	6	122807770	1	7	101423211	1	5	104862608	1
2265	6	122539175	1	7	101296320	1	5	105179381	1
2266	6	120919063	1	7	101190336	1	5	105654118	1
2267	6	119404504	1	7	101151848	1	5	107338685	1
2268	6	118836529	1	7	101142694	1	5	107433593	2
2269	6	11460981	1	7	100822996	1	5	108007135	1
2270	6	11409050	1	7	100772195	1	5	108894919	1
2271	6	111762623	1	7	100339226	1	5	108922642	1
2272	6	109697180	1	7	100224624	1	5	109099661	2
2273	6	108369666	1	7	100135295	1	5	110477703	1
2274	6	105318612	1	7	100076977	1	5	111926428	1
2275	6	108112511	1	7	100076968	1	5	111524213	1
2276	6	107745056	1	8	6778142	71	5	111524467	2
2277	6	103625700	1	8	4185784	67	5	111951028	1
2278	6	103625696	1	8	3643705	23	5	113003368	1
2279	6	1021939	1	8	4853680	12	5	113119988	3
2280	7	117054444	2447	8	2108989	6	5	114368172	1
2281	7	112159514	2144	8	7373089	7	5	114586829	1
2282	7	54255136	1241	8	9144634	6	5	114911111	1
2283	7	149493221	781	8	51864735	5	5	114704941	1
2284	7	27722256	751	8	3802055	5	5	114654384	1
2285	7	56371267	719	8	23584947	5	5	117024462	1
2286	7	14902399	683	8	2761721	4	5	117959916	1
2287	7	100205988	618	8	142779028	4	5	118006067	1
2288	7	8911810	652	8	13441718	4	5	118904655	1
2289	7	15294988	652	8	94581041	3	5	120783885	2
2290	7	59232140	499	8	4853984	3	5	121794226	1
2291	7	81502723	493	8	1767468	3	5	121220508	2
2292	7	131553811	456	8	132976176	3	5	121233232	1
2293	7	6852477	456	8	127914650	3	5	121282272	1
2294	7	96098986	453	8	103064451	3	5	121352000	1
2295	7	100789616	441	8	102886429	3	5	121434603	1
2296	7	11701070	415	8	101793206	3	5	121861130	1
2297	7	1728179	401	8	6762447	2	5	12187978	1
2298	7	6519943	387	8	9741109	2	5	123215234	1
2299	7	145243106	377	8	80217985	2	5	12511467	1
2300	7	121385443	346	8	80104949	2	5	12595452	1
2301	7	6789186	340	8	7963082	2	5	129169342	1
2302	7								

[illegible]

3249	9	3684500	1	12	5740480	2	5	5636403	2
3250	9	3684407	1	12	5727254	2	7	5637506	1
3251	9	3682032	1	12	4575687	1	7	5638748	1
3252	9	3542917	1	12	4033897	2	7	5640042	1
3253	9	33420186	1	12	3262255	2	7	5640087	1
3254	9	33102687	1	12	30128408	2	7	5640141	1
3255	9	33102644	1	12	16055015	1	7	56796134	1
3256	9	33102632	1	12	123421759	2	7	5753267	3
3257	9	33102594	1	12	123421753	2	7	58344919	1
3258	9	33102567	1	12	123421752	2	7	58369243	1
3259	9	33102566	1	12	123421751	1	7	58371134	1
3260	9	33011093	1	12	123332678	2	7	58375670	2
3261	9	33169334	1	12	118211480	2	7	58399207	1
3262	9	31862930	1	12	109110475	1	7	58399972	1
3263	9	29421287	1	12	109110463	2	7	58399988	1
3264	9	29421257	1	12	99162360	1	7	58798932	1
3265	9	29178731	1	12	9879010	1	7	61122218	1
3266	9	29178730	1	12	9877804	1	7	62778863	1
3267	9	27683934	1	12	9875921	1	7	62794983	1
3268	9	27683933	1	12	9871666	1	7	62801832	1
3269	9	27683932	1	12	96583788	1	7	62842520	2
3270	9	25771623	12	96307727	1	7	62856121	1	
3271	9	25666127	12	95817833	1	7	62975025	1	
3272	9	25436034	1	92428135	1	7	62980304	1	
3273	9	25436916	1	92020374	1	7	62983700	1	
3274	9	25436926	1	92025469	1	7	62984401	1	
3275	9	25436858	1	92000738	1	7	6330644	1	
3276	9	25436855	1	92005134	1	7	63402329	1	
3277	9	25436838	1	8888596	1	7	65009125	1	
3278	9	25436838	1	8780779	1	7	65058487	1	
3279	9	25369995	1	8780779	1	7	65100880	1	
3280	9	2486233	1	86515623	1	7	65184120	1	
3281	9	23660335	1	83328788	1	7	65600052	1	
3282	9	23667780	1	79387752	1	7	65622237	1	
3283	9	2233119	1	79254674	1	7	65655709	2	
3284	9	2233116	1	7505481	1	7	65744818	2	
3285	9	2233360	1	74577624	1	7	65781831	1	
3286	9	21727439	1	74361178	1	7	65865588	1	
3287	9	21727385	1	74361166	1	7	65867897	1	
3288	9	20758173	1	72038229	1	7	66435556	1	
3289	9	20582753	1	71118874	1	7	680091	1	
3290	9	19707024	1	69559881	1	7	69476050	1	
3291	9	19150076	1	69559881	1	7	69501127	1	
3292	9	1897452	1	6949037	1	7	69514376	1	
3293	9	18665700	1	69455606	1	7	69522863	1	
3294	9	17679610	1	68842180	1	7	69542320	1	
3295	9	1739181	1	68817009	1	7	69553061	1	
3296	9	16652558	1	67455050	1	7	70150130	1	
3297	9	16652715	1						

3444	10	12203708	201	13	98006831	58	8	10066376	1
3445	10	12203710	198	13	98018931	59	10	10136892	1
3446	10	41801156	188	13	98027524	34	10	101402430	34
3447	10	41847843	183	13	97287387	27	8	10140938	1
3448	10	40400778	174	13	98026853	15	8	101417338	1
3449	10	3998686	174	13	98036833	15	10	101425178	1
3450	10	98471058	164	13	98026821	15	8	101428195	1
3451	10	70162815	164	13	98026827	15	8	101442774	1
3452	10	103335408	164	13	98036842	14	8	101447680	1
3453	10	122873224	151	13	98036825	14	10	101667417	4
3454	10	14102308	150	13	98036838	10	8	101958442	1
3455	10	10034837	142	13	98036841	9	8	101964173	1
3456	10	3997231	141	13	98036838	10	8	102083931	1
3457	10	4066763	131	13	98037512	6	8	102098379	1
3458	10	5411961	138	13	98036863	6	8	102101937	1
3459	10	28796796	128	13	98036862	6	8	102281658	1
3460	10	9799477	128	13	98036861	6	8	10231460	1
3461	10	93164578	121	13	98036848	6	8	103462174	1
3462	10	69020871	118	13	98036828	6	8	103480590	1
3463	10	15003232	116	13	33519122	6	8	103662291	1
3464	10	133689652	112	13	109424327	6	8	105613716	3
3465	10	41846665	103	13	98036846	5	8	10641121	1
3466	10	89742843	100	13	44658986	5	8	107907401	1
3467	10	97346881	97	13	105627769	5	8	109582741	1
3468	10	103842843	90	13	98037537	4	8	110287268	3
3469	10	54474743	89	13	98037523	4	8	110424334	1
3470	10	38014740	88	13	98037460	4	8	11133327	2
3471	10	33093030	85	13	98036911	4	8	11133446	1
3472	10	42067580	74	13	98036870	4	8	116752678	1
3473	10	29336636	73	13	98036863	4	8	116752628	1
3474	10	35714089	70	13	98036865	4	8	11680616	1
3475	10	2890776	63	13	98036847	4	8	116888691	1
3476	10	13259982	61	13	98036835	4	8	11700099	1
3477	10	84071827	58	13	98036826	4	8	118124388	1
3478	10	78462752	58	13	43817479	4	8	11821628	1
3479	10	3893448	56	13	109424330	4	8	1182284	1
3480	10	130400020	56	13	109424330	4	8	11861021	1
3481	10	7483117	55	13	109424326	4	8	11916262	1
3482	10	110334508	44	13	109424323	4	8	119379791	1
3483	10	39986979	42	13	98037517	3	8	119413407	1
3484	10	14696937	42	13	98036909	3	8	120441	1
3485	10	16434165	39	13	98036872	3	8	12112289	1
3486	10	116166227	38	13	98036881	3	8	121696435	3
3487	10	59030645	26	13	98036859	3	8	124289254	1
3488	10								

3870	11	42019442	1	15	45006777	1	9	4208189	1
3871	11	42488885	1	15	44603885	1	9	42378727	2
3872	11	3887409	1	15	44570911	1	9	4348456	2
3873	11	3817409	1	15	43905852	1	9	44014480	2
3874	11	37532070	1	15	43611505	1	9	44110888	1
3875	11	37516880	1	15	43343430	1	9	4406890	1
3876	11	35666661	1	15	42947472	1	9	44056235	1
3877	11	32542498	1	15	42697379	1	9	44059293	1
3878	11	32542451	1	15	42414894	1	9	44047454	1
3879	11	31657988	1	15	42220087	1	9	44015552	1
3880	11	31405478	1	15	42128895	1	9	43941037	1
3881	11	31398489	1	15	41883950	1	9	438472579	1
3882	11	3087361	1	15	41768261	1	9	43809820	1
3883	11	27686333	1	15	37295395	1	9	43751420	1
3884	11	27686303	1	15	35356520	1	9	43684487	1
3885	11	2677809	1	15	3417842	1	9	43600046	2
3886	11	2346518	1	15	2968124	1	9	4350808	1
3887	11	2328140	1	15	2962380	1	9	43500146	2
3888	11	21688950	1	15	2960358	1	9	43092277	1
3889	11	21688811	1	15	2815677	1	9	43079752	1
3890	11	21688889	1	15	2814794	1	9	43068082	1
3891	11	21688685	1	15	22952527	1	9	41444039	1
3892	11	21688682	1	15	22952513	1	9	41452003	1
3893	11	20664042	1	15	1872005	1	9	41686833	1
3894	11	20664001	1	15	10113527	1	9	41688488	1
3895	11	20663205	1	15	100591033	1	9	41708336	1
3896	11	20663638	1	16	9562738	151	9	41748038	1
3897	11	20663931	1	16	8512266	43	9	41751285	1
3898	11	20663926	1	16	28037187	19	9	41783586	2
3899	11	18555415	1	16	58894089	17	9	41807184	1
3900	11	17757373	1	16	4900566	17	9	42020488	1
3901	11	17271184	1	16	3558910	14	9	42025230	1
3902	11	14419281	1	16	8796457	13	9	42060990	2
3903	11	14418280	1	16	80142188	11	9	42146381	1
3904	11	133341912	1	16	9133383	8	9	42364486	2
3905	11	133174071	1	16	4523372	8	9	42431753	1
3906	11	1260207168	1	16	80842717	6	9	42473209	2
3907	11	128834891	1	16	68054822	6	9	42478946	1
3908	11	127559547	1	16	71819004	4	9	42388881	1
3909	11	127559514	1	16	5957015	4	9	43018440	1
3910	11	127559500	1	16	53266389	4	9	43018859	1
3911	11	127559448	1	16	88120594	3	9	43313748	1
3912	11	127559446	1	16	8142794	3	9	43483232	1
3913	11	126342059	1	16	58086517	3	9	43470890	1
3914	11	126329028	1	16	57963348	3	9	43562444	1
3915	11	123394730	1	16					

[illegible]

[illegible]

[illegible]

[illegible]

6349	X	10072530	1			15	10047188	1		
6350	X	10004684	1			15	10008188	3		
6351	Y	20778026	906			15	110081464	1		
6352	Y	7297516	561			15	110043532	1		
6353	Y	17356008	453			15	110044875	1		
6354	Y	56674955	438			15	110044586	1		
6355	Y	10033811	273			15	110044677	1		
6356	Y	56675407	212			15	110053244	2		
6357	Y	1329862	168			15	110051013	3		
6358	Y	56673684	163			15	110718871	1		
6359	Y	23665268	155			15	112700461	4		
6360	Y	20437673	144			15	11330703	2		
6361	Y	13811320	144			15	11339144	1		
6362	Y	20505251	142			15	11435943	1		
6363	Y	8469116	160			15	11681010	1		
6364	Y	10105365	116			15	11691715	1		
6365	Y	8660174	115			15	11714625	1		
6366	Y	23448418	101			15	12225786	1		
6367	Y	17471817	75			15	13123899	1		
6368	Y	7773628	65			15	13178803	1		
6369	Y	56674750	47			15	13508106	1		
6370	Y	105021	40			15	13750310	1		
6371	Y	56673725	36			15	1380581	1		
6372	Y	20740206	21			15	1382004	1		
6373	Y	21242188	15			15	1388199	3		
6374	Y	2333168	2			15	13882531	1		
6375	Y	2419384	10			15	1390205	1		
6376	Y	1242570	7			15	13930336	2		
6377	Y	56673835	5			15	1395840	1		
6378	Y	10547490	1			15	1406931	1		
6379	Y	10247124	5			15	1416460	1		
6380	Y	5669487	3			15	1420161	2		
6381	Y	24109624	3			15	1420246	1		
6382	Y	5669247	1			15	1424971	1		
6383	Y	56674952	2			15	1469176	1		
6384	Y	1760280	1			15	1467738	1		
6385	Y	11185448	2			15	14890501	1		
6386	Y	8468173	1			15	1481188	2		
6387	Y	7773408	63			15	1482771	2		
6388	Y	7297609	1			15	16000824	1		
6389	Y	7297973	1			15	16009462	1		
6390	Y	7297558	1			15	16105167	3		
6391	Y	7297541	1			15	16155302	1		
6392	Y	7394355	1			15	16169932	1		
6393	Y	56642604	1			15	16194177	2		
6394	Y	56637894	1			15	16364372	1		
6395	Y	56637853	1			15	16370869	1		
6396	Y	56737222	1			15	16408431	1		
6397	Y	56736239	1			15	16411031	1		
6398	Y	56680171	1			15	16421246	1		
6399	Y	56675441	1			15	1643547658	2		

[illegible]

[illegible]

6870	6870	15	51452402	1
6871	6871	15	51452279	1
6872	6872	15	51456886	1
6873	6873	15	51456886	1
6874	6874	15	51457127	4
6875	6875	15	51487380	1
6876	6876	15	51488444	2
6877	6877	15	51543625	1
6878	6878	15	51601687	1
6879	6879	15	51623936	2
6880	6880	15	51671767	3
6881	6881	15	51674721	1
6882	6882	15	51683235	1
6883	6883	15	51682631	1
6884	6884	15	51692598	1
6885	6885	15	51691620	1
6886	6886	15	52057594	1
6887	6887	15	52063793	1
6888	6888	15	52489698	1
6889	6889	15	53271130	1
6890	6890	15	53554345	1
6891	6891	15	53667022	2
6892	6892	15	53658645	1
6893	6893	15	53750806	1
6894	6894	15	53748834	1
6895	6895	15	53865704	1
6896	6896	15	53879783	4
6897	6897	15	53907176	1
6898	6898	15	53953701	3
6899	6899	15	53955665	2
7000	7000	15	53959658	1
7001	7001	15	53963933	3
7002	7002	15	53969941	1
7003	7003	15	53973224	1
7004	7004	15	53978019	1
7005	7005	15	53975246	1
7006	7006	15	53975615	4
7007	7007	15	53980336	1
7008	7008	15	53981633	1
7009	7009	15	53984789	2
7010	7010	15	53988238	1
7011	7011	15	54027338	1
7012	7012	15	54071300	5
7013	7013	15	54074302	3
7014	7014	15	54102229	2
7015	7015	15	54114098	1
7016	7016	15	54115949	1
7017	7017	15	54122731	1
7018	7018	15	54371183	1
7019	7019	15	5448487	2
7020	7020	15	54487591	2
7021	7021	15	5451415	1
7022	7022	15	5451321	1
7023	7023	15	54849882	1
7024	7024	15	54869620	1
7025	7025	15	54869620	2
7026	7026	15	54862281	1
7027	7027	15	54905448	2
7028	7028	15	54905628	1
7029	7029	15	54971582	2
7030	7030	15	55012010	2
7031	7031	15	55011962	1
7032	7032	15	55014462	1
7033	7033	15	55014698	2
7034	7034	15	55019876	2
7035	7035	15	55020010	1
7036	7036	15	55170256	1
7037	7037	15	55812147	1
7038	7038	15	55819190	1
7039	7039	15	55986900	1
7040	7040	15	56010960	1
7041	7041	15	56159591	1
7042	7042	15	56200182	1
7043	7043	15	56248338	5
7044	7044	15	56253786	1
7045	7045	15	56255403	1
7046	7046	15	56254020	1
7047	7047	15	56270732	1
7048	7048	15	56288999	1
7049	7049	15	56532789	3
7050	7050	15	56602624	3
7051	7051	15	56812575	1
7052	7052	15	56813844	1
7053	7053	15	56819615	1
7054	7054	15	56820464	1
7055	7055			

[illegible]

[illegible]

[illegible]

[illegible]

[illegible]

[illegible]

[illegible]

[illegible]

[illegible]

[illegible]

[illegible]

[illegible]

[illegible]

Supplementary Table 3. Clinical profile of asymptomatic carriers (ACs), HTLV-1-associated myelopathy/tropical spastic paraparesis (HAM/TSP) patients, and adult T-cell leukemia/lymphoma (ATL) patients.

No.	Sample name	Symptom	Subtype (ATL)	Tissue	PVL	Amplification method	Cv	Other information
1	AC1	-	-	PBMCs	3.60	RAISING	0.17	-
2	AC2	-	-	PBMCs	5.27	RAISING	0.15	-
3	AC3	-	-	PBMCs	0.27	RAISING	0.13	-
4	AC4	-	-	PBMCs	11.34	RAISING	0.20	-
5	AC5	-	-	PBMCs	12.73	RAISING	0.86	-
6	AC6	-	-	PBMCs	8.69	RAISING	0.21	-
7	AC7	-	-	PBMCs	8.01	RAISING	0.28	-
8	AC8	-	-	PBMCs	10.02	RAISING	0.63	-
9	AC9	-	-	PBMCs	5.03	RAISING	0.24	-
10	AC10	-	-	PBMCs	11.11	RAISING	0.12	-
11	AC11	-	-	PBMCs	5.64	RAISING	0.21	-
12	AC12	-	-	WBCs	3.89	RAISING	0.56	-
13	AC13	-	-	PBMCs	17.99	RAISING	0.42	-
14	AC14	-	-	PBMCs	21.99	RAISING	0.60	Same subject as ATL308
15	AC15	-	-	PBMCs	2.82	RAISING	0.15	-
16	AC16	-	-	PBMCs	1.62	RAISING	0.19	-
17	AC17	-	-	PBMCs	2.88	RAISING	0.25	-
18	AC18	-	-	PBMCs	1.53	RAISING	0.24	-
19	AC19	-	-	PBMCs	19.76	RAISING	0.18	-
20	AC20	-	-	PBMCs	4.67	RAISING	0.15	-
21	AC21	-	-	PBMCs	20.05	RAISING	0.49	-
22	AC22	-	-	PBMCs	3.88	RAISING	0.32	-
23	AC23	-	-	PBMCs	9.03	RAISING	0.12	-
24	AC24	-	-	PBMCs	0.60	RAISING	0.23	-
25	AC25	-	-	PBMCs	2.19	RAISING	0.38	-
26	AC26	-	-	PBMCs	1.04	RAISING	0.31	-
27	AC27	-	-	PBMCs	0.16	RAISING	0.22	-
28	AC28	-	-	PBMCs	2.34	RAISING	0.09	-
29	AC29	-	-	PBMCs	0.11	RAISING	0.18	-
30	AC30	-	-	PBMCs	1.41	RAISING	0.11	-
31	AC31	-	-	PBMCs	18.03	RAISING	0.36	-
32	AC32	-	-	PBMCs	2.17	RAISING	0.44	-
33	AC33	-	-	PBMCs	0.11	RAISING	0.31	-
34	AC34	-	-	PBMCs	0.15	RAISING	0.08	-
35	AC35	-	-	PBMCs	0.28	RAISING	0.15	-
36	AC36	-	-	PBMCs	0.67	RAISING	0.08	-
37	AC37	-	-	PBMCs	1.44	RAISING	0.16	-
38	AC38	-	-	PBMCs	1.54	RAISING	0.16	-
39	AC39	-	-	PBMCs	0.04	RAISING	0.36	-
40	AC40	-	-	PBMCs	1.01	RAISING	0.08	-
41	AC41	-	-	PBMCs	0.57	RAISING	0.16	-
42	AC42	-	-	PBMCs	0.14	RAISING	0.31	-
43	AC43	-	-	PBMCs	0.16	RAISING	0.08	-
44	AC44	-	-	PBMCs	0.16	RAISING	0.16	-
45	AC45	-	-	PBMCs	2.83	RAISING	0.14	-
46	AC46	-	-	PBMCs	0.48	RAISING	0.12	-
47	AC47	-	-	PBMCs	0.54	RAISING	0.24	-
48	AC48	-	-	PBMCs	1.32	RAISING	0.12	-
49	AC49	-	-	PBMCs	0.43	RAISING	0.23	-
50	AC50	-	-	PBMCs	5.24	RAISING	0.11	-
51	AC51	-	-	PBMCs	0.09	RAISING	0.24	-
52	AC52	-	-	PBMCs	3.90	RAISING	0.17	-
53	AC53	-	-	PBMCs	1.39	RAISING	0.09	-
54	AC54	-	-	PBMCs	5.03	RAISING	0.12	-
55	AC55	-	-	PBMCs	1.76	RAISING	0.11	-
56	AC56	-	-	PBMCs	0.41	RAISING	0.29	-
57	AC57	-	-	PBMCs	3.56	RAISING	0.70	-
58	AC58	-	-	PBMCs	4.08	RAISING	0.43	-
59	AC59	-	-	PBMCs	0.13	RAISING	0.16	-
60	AC60	-	-	WBCs	2.82	RAISING	0.21	-
61	AC61	-	-	WBCs	0.37	RAISING	0.17	-
62	AC62	-	-	WBCs	10.67	RAISING	0.70	-
63	AC63	-	-	PBMCs	2.81	RAISING	0.10	-
64	AC64	-	-	PBMCs	0.24	RAISING	0.20	-
65	AC65	-	-	PBMCs	4.81	RAISING	0.42	-
66	AC66	-	-	PBMCs	1.48	RAISING	0.10	-
67	AC67	-	-	WBCs	9.28	RAISING	0.08	-
68	AC68	-	-	PBMCs	0.20	RAISING	0.13	-
69	AC69	-	-	PBMCs	3.13	RAISING	0.21	-
70	AC70	-	-	WBCs	0.18	RAISING	0.20	-
71	AC71	-	-	PBMCs	0.17	RAISING	0.20	-
72	AC72	-	-	WBCs	0.28	RAISING	0.30	-
73	AC73	-	-	PBMCs	2.57	RAISING	0.13	-
74	AC74	-	-	PBMCs	0.57	RAISING	0.26	-
75	AC75	-	-	PBMCs	1.21	RAISING	0.14	-
76	AC76	-	-	WBCs	3.30	RAISING	0.09	-
77	AC77	-	-	PBMCs	12.80	RAISING	0.13	-
78	AC78	-	-	PBMCs	3.28	RAISING	0.09	-
79	AC79	-	-	PBMCs	0.47	RAISING	0.14	-
80	AC80	-	-	PBMCs	1.56	RAISING	0.10	-
81	AC81	-	-	PBMCs	0.98	RAISING	0.17	-
82	AC82	-	-	PBMCs	0.28	RAISING	0.11	-
83	AC83	-	-	PBMCs	2.62	RAISING	0.10	-
84	AC84	-	-	PBMCs	0.13	RAISING	0.48	-
85	AC85	-	-	WBCs	0.57	RAISING	0.10	-
86	AC86	-	-	PBMCs	1.55	RAISING	0.11	-
87	AC87	-	-	PBMCs	0.50	RAISING	0.24	-
88	AC88	-	-	PBMCs	1.59	RAISING	0.09	-
89	AC89	-	-	PBMCs	1.25	RAISING	0.27	-
90	AC90	-	-	PBMCs	2.04	RAISING	0.14	-
91	AC91	-	-	PBMCs	0.28	RAISING	0.12	-
92	AC92	-	-	WBCs	0.15	RAISING	0.40	-
93	AC93	-	-	PBMCs	0.99	RAISING	0.12	-
94	AC94	-	-	PBMCs	0.47	RAISING	0.10	-
95	AC95	-	-	WBCs	0.31	RAISING	0.26	-
96	AC96	-	-	WBCs	0.17	RAISING	0.44	-
97	AC97	-	-	WBCs	0.43	RAISING	0.20	-
98	AC98	-	-	PBMCs	1.09	RAISING	0.12	-
99	AC99	-	-	WBCs	1.67	RAISING	0.32	-
100	AC100	-	-	WBCs	0.11	RAISING	0.17	-
101	AC101	-	-	PBMCs	0.52	RAISING	0.15	-
102	AC102	-	-	PBMCs	2.04	RAISING	0.14	-
103	AC103	-	-	WBCs	0.92	RAISING	0.20	-
104	AC104	-	-	WBCs	1.79	RAISING	0.19	-
105	AC105	-	-	WBCs	0.04	RAISING	0.51	-
106	AC106	-	-	PBMCs	1.41	RAISING	0.07	-
107	AC107	-	-	WBCs	2.75	RAISING	0.18	-
108	AC108	-	-	PBMCs	5.88	RAISING	0.10	-
109	AC109	-	-	PBMCs	6.14	RAISING	0.07	-
110	AC110	-	-	WBCs	0.21	RAISING	0.38	-
111	AC111	-	-	PBMCs	0.15	RAISING	0.13	-
112	AC112	-	-	PBMCs	1.89	RAISING	0.07	-
113	AC113	-	-	PBMCs	0.06	RAISING	0.37	-
114	AC114	-	-	WBCs	0.74	RAISING	0.09	-
115	AC115	-	-	WBCs	0.10	RAISING	0.32	-
116	AC116	-	-	WBCs	0.90	RAISING	0.06	-

117	AC117	-	-	WBCs	0.90	RAISING	0.20	-
118	AC118	-	-	PBMCs	0.34	RAISING	0.12	-
119	AC119	-	-	PBMCs	1.54	RAISING	0.14	-
120	AC120	-	-	WBCs	0.59	RAISING	0.17	-
121	AC121	-	-	WBCs	0.12	RAISING	0.52	-
122	AC122	-	-	PBMCs	0.66	RAISING	0.18	-
123	AC123	-	-	PBMCs	0.79	RAISING	0.10	-
124	AC124	-	-	PBMCs	1.26	RAISING	0.12	-
125	AC125	-	-	WBCs	0.33	RAISING	0.23	-
126	AC126	-	-	WBCs	1.09	RAISING	0.14	-
127	AC127	-	-	PBMCs	1.42	RAISING	0.14	-
128	AC128	-	-	WBCs	0.93	RAISING	0.18	-
129	AC129	-	-	PBMCs	1.91	RAISING	0.15	-
130	AC130	-	-	PBMCs	0.85	RAISING	0.11	-
131	AC131	-	-	PBMCs	0.94	RAISING	0.08	-
132	AC132	-	-	WBCs	0.67	RAISING	0.08	-
133	AC133	-	-	WBCs	1.11	RAISING	0.12	-
134	AC134	-	-	WBCs	0.14	RAISING	0.30	-
135	AC135	-	-	WBCs	0.86	RAISING	0.14	-
136	AC136	-	-	PBMCs	5.81	RAISING	0.12	-
137	AC137	-	-	PBMCs	3.16	RAISING	0.12	-
138	AC138	-	-	WBCs	0.71	RAISING	0.10	-
139	AC139	-	-	PBMCs	4.69	RAISING	0.16	-
140	AC140	-	-	PBMCs	2.03	RAISING	0.17	-
141	AC141	-	-	PBMCs	2.36	RAISING	0.44	-
142	AC142	-	-	PBMCs	3.58	RAISING	0.15	-
143	AC143	-	-	WBCs	0.90	RAISING	0.17	-
144	AC144	-	-	PBMCs	11.78	RAISING	0.19	-
145	AC145	-	-	PBMCs	0.85	RAISING	0.11	-
146	AC146	-	-	PBMCs	5.94	RAISING	0.51	-
147	AC147	-	-	PBMCs	0.63	RAISING	0.11	-
148	AC148	-	-	PBMCs	0.10	RAISING	0.34	-
149	AC149	-	-	PBMCs	4.68	RAISING	0.09	-
150	AC150	-	-	WBCs	3.28	RAISING	0.09	-
151	AC151	-	-	PBMCs	0.19	RAISING	0.18	-
152	AC152	-	-	PBMCs	0.93	RAISING	0.10	-
153	AC153	-	-	PBMCs	0.18	RAISING	0.19	-
154	AC154	-	-	PBMCs	1.36	RAISING	0.14	-
155	AC155	-	-	PBMCs	0.75	RAISING	0.13	-
156	AC156	-	-	PBMCs	0.79	RAISING	0.13	-
157	AC157	-	-	PBMCs	7.31	RAISING	0.09	-
158	AC158	-	-	PBMCs	1.11	RAISING	0.12	-
159	AC159	-	-	PBMCs	4.12	RAISING	0.09	-
160	AC160	-	-	PBMCs	3.13	RAISING	0.12	-
161	AC161	-	-	PBMCs	2.80	RAISING	0.10	-
162	AC162	-	-	PBMCs	11.96	RAISING	0.40	-
163	AC163	-	-	PBMCs	2.08	RAISING	0.13	-
164	AC164	-	-	PBMCs	0.27	RAISING	0.08	-
165	AC165	-	-	PBMCs	3.31	RAISING	0.11	-
166	AC166	-	-	PBMCs	3.61	RAISING	0.13	-
167	AC167	-	-	PBMCs	0.83	RAISING	0.23	-
168	AC168	-	-	PBMCs	1.80	RAISING	0.11	-
169	AC169	-	-	PBMCs	4.43	RAISING	0.11	-
170	AC170	-	-	PBMCs	1.88	RAISING	0.15	-
171	AC171	-	-	PBMCs	4.66	RAISING	0.14	-
172	AC172	-	-	PBMCs	1.72	RAISING	0.09	-
173	AC173	-	-	PBMCs	1.26	RAISING	0.14	-
174	AC174	-	-	PBMCs	0.41	RAISING	0.11	-
175	AC175	-	-	PBMCs	0.98	RAISING	0.18	-
176	AC176	-	-	PBMCs	1.37	RAISING	0.14	-
177	AC177	-	-	PBMCs	3.02	RAISING	0.06	-
178	AC178	-	-	PBMCs	0.13	RAISING	0.26	-
179	AC179	-	-	PBMCs	0.70	RAISING	0.06	-
180	AC180	-	-	PBMCs	2.80	RAISING	0.11	-
181	AC181	-	-	PBMCs	0.39	RAISING	0.48	-
182	AC182	-	-	PBMCs	1.02	RAISING	0.15	-
183	AC183	-	-	PBMCs	0.29	RAISING	0.12	-
184	AC184	-	-	PBMCs	1.63	RAISING	0.08	-
185	AC185	-	-	PBMCs	0.28	RAISING	0.12	-
186	AC186	-	-	PBMCs	0.81	RAISING	0.11	-
187	AC187	-	-	PBMCs	4.58	RAISING	0.08	-
188	AC188	-	-	PBMCs	4.93	RAISING	0.14	-
189	AC189	-	-	PBMCs	6.63	RAISING	0.11	-
190	AC190	-	-	PBMCs	1.04	RAISING	0.13	-
191	AC191	-	-	PBMCs	0.73	RAISING	0.10	-
192	AC192	-	-	PBMCs	0.73	RAISING	0.12	-
193	AC193	-	-	PBMCs	0.20	RAISING	0.16	-
194	AC194	-	-	PBMCs	0.24	RAISING	0.21	-
195	AC195	-	-	PBMCs	3.98	RAISING	0.10	-
196	AC196	-	-	PBMCs	0.55	RAISING	0.11	-
197	AC197	-	-	PBMCs	0.93	RAISING	0.10	-
198	AC198	-	-	PBMCs	0.89	RAISING	0.12	-
199	AC199	-	-	PBMCs	2.52	RAISING	0.07	-
200	AC200	-	-	PBMCs	0.29	RAISING	0.26	-
201	HAM1	HAM	-	PBMCs	9.99	RAISING	0.49	Same subject as ATL310
202	HAM2	HAM	-	PBMCs	21.57	RAISING	0.29	-
203	HAM3	HAM	-	PBMCs	5.72	RAISING	0.10	-
204	HAM4	HAM	-	PBMCs	7.57	RAISING	0.11	-
205	HAM5	HAM	-	PBMCs	8.29	RAISING	0.09	-
206	HAM6	HAM	-	PBMCs	25.50	RAISING	0.11	-
207	HAM7	HAM	-	PBMCs	13.67	RAISING	0.13	-
208	HAM8	HAM	-	PBMCs	7.61	RAISING	0.11	-
209	HAM9	HAM	-	PBMCs	13.27	RAISING	0.10	-
210	HAM10	HAM	-	PBMCs	12.70	RAISING	0.04	-
211	HAM11	HAM	-	PBMCs	17.82	RAISING	0.19	-
212	HAM12	HAM	-	PBMCs	3.99	RAISING	0.09	-
213	HAM13	HAM	-	PBMCs	7.67	RAISING	0.08	-
214	HAM14	HAM	-	PBMCs	18.87	RAISING	0.09	-
215	HAM15	HAM	-	PBMCs	10.94	RAISING	0.11	-
216	HAM16	HAM	-	PBMCs	6.11	RAISING	0.10	-
217	HAM17	HAM	-	PBMCs	8.25	RAISING	0.10	-
218	HAM18	HAM	-	PBMCs	14.33	RAISING	0.11	-
219	HAM19	HAM	-	PBMCs	10.83	RAISING	0.30	-
220	HAM20	HAM	-	PBMCs	6.84	RAISING	0.20	-
221	HAM21	HAM	-	PBMCs	9.59	RAISING	0.12	-
222	HAM22	HAM	-	PBMCs	8.52	RAISING	0.11	-
223	HAM23	HAM	-	PBMCs	5.72	RAISING	0.17	-
224	HAM24	HAM	-	PBMCs	13.45	RAISING	0.21	-
225	HAM25	HAM	-	PBMCs	10.77	RAISING	0.18	-
226	HAM26	HAM	-	WBCs	22.17	RAISING	0.81	-
227	HAM27	HAM	-	PBMCs	10.31	RAISING	0.09	-
228	HAM28	HAM	-	PBMCs	9.10	RAISING	0.14	-
229	HAM29	HAM	-	PBMCs	7.03	RAISING	0.48	-
230	HAM30	HAM	-	PBMCs	4.55	RAISING	0.48	-
231	HAM31	HAM	-	PBMCs	9.95	RAISING	0.14	-
232	HAM32	HAM	-	PBMCs	2.84	RAISING	0.11	Same subject as ATL311
233	HAM33	HAM	-	PBMCs	3.68	RAISING	0.20	Same subject as ATL309
234	HAM34	HAM	-	PBMCs	4.59	RAISING	0.36	-

235	HAM35	HAM	-	PBMCs	0.90	RAISING	0.13	-
236	HAM36	HAM	-	PBMCs	2.68	RAISING	0.32	-
237	HAM37	HAM	-	PBMCs	5.80	RAISING	0.21	-
238	HAM38	HAM	-	PBMCs	10.26	RAISING	0.42	-
239	HAM39	HAM	-	PBMCs	5.94	RAISING	0.73	-
240	HAM40	HAM	-	PBMCs	12.63	RAISING	0.18	-
241	HAM41	HAM	-	PBMCs	8.29	RAISING	0.11	-
242	HAM42	HAM	-	PBMCs	17.13	RAISING	0.22	-
243	HAM43	HAM	-	PBMCs	2.46	RAISING	0.53	-
244	HAM44	HAM	-	PBMCs	5.80	RAISING	0.21	-
245	HAM45	HAM	-	PBMCs	22.85	RAISING	0.31	-
246	HAM46	HAM	-	PBMCs	16.58	RAISING	0.08	-
247	HAM47	HAM	-	PBMCs	8.33	RAISING	0.06	-
248	HAM48	HAM	-	PBMCs	10.26	RAISING	0.21	-
249	HAM49	HAM	-	PBMCs	9.39	RAISING	0.60	-
250	HAM50	HAM	-	PBMCs	8.98	RAISING	0.15	-
251	HAM51	HAM	-	PBMCs	3.83	RAISING	0.15	-
252	HAM52	HAM	-	WBCs	2.66	RAISING	0.19	-
253	HAM53	HAM	-	WBCs	3.76	RAISING	0.15	-
254	HAM54	HAM	-	WBCs	3.48	RAISING	0.17	-
255	HAM55	HAM	-	WBCs	2.87	RAISING	0.16	-
256	HAM56	HAM	-	WBCs	9.88	RAISING	0.16	-
257	HAM57	HAM	-	WBCs	2.76	RAISING	0.16	-
258	HAM58	HAM	-	WBCs	2.91	RAISING	0.20	-
259	HAM59	HAM	-	WBCs	4.02	RAISING	0.44	-
260	HAM60	HAM	-	WBCs	1.12	RAISING	0.20	-
261	HAM61	HAM	-	WBCs	5.28	RAISING	0.07	-
262	HAM62	HAM	-	WBCs	7.89	RAISING	0.13	-
263	HAM63	HAM	-	WBCs	4.63	RAISING	0.16	-
264	HAM64	HAM	-	WBCs	4.56	RAISING	0.07	-
265	HAM65	HAM	-	WBCs	8.77	RAISING	0.13	-
266	HAM66	HAM	-	WBCs	6.19	RAISING	0.19	-
267	HAM67	HAM	-	WBCs	2.68	RAISING	0.11	-
268	HAM68	HAM	-	WBCs	7.01	RAISING	0.17	-
269	HAM69	HAM	-	WBCs	0.74	RAISING	0.26	-
270	HAM70	HAM	-	WBCs	4.60	RAISING	0.15	-
271	HAM71	HAM	-	WBCs	2.04	RAISING	0.12	-
272	HAM72	HAM	-	WBCs	3.20	RAISING	0.19	-
273	HAM73	HAM	-	WBCs	4.44	RAISING	0.11	-
274	HAM74	HAM	-	WBCs	9.17	RAISING	0.12	-
275	HAM75	HAM	-	WBCs	12.17	RAISING	0.15	-
276	HAM76	HAM	-	WBCs	8.36	RAISING	0.14	-
277	HAM77	HAM	-	WBCs	9.43	RAISING	0.07	-
278	HAM78	HAM	-	WBCs	5.23	RAISING	0.10	-
279	HAM79	HAM	-	WBCs	3.23	RAISING	0.47	-
280	HAM80	HAM	-	WBCs	5.00	RAISING	0.25	-
281	HAM81	HAM	-	WBCs	3.15	RAISING	0.16	-
282	HAM82	HAM	-	WBCs	7.43	RAISING	0.18	-
283	HAM83	HAM	-	WBCs	4.44	RAISING	0.16	-
284	HAM84	HAM	-	WBCs	0.91	RAISING	0.20	-
285	HAM85	HAM	-	WBCs	3.20	RAISING	0.26	-
286	HAM86	HAM	-	WBCs	2.69	RAISING	0.12	-
287	HAM87	HAM	-	WBCs	2.16	RAISING	0.16	-
288	HAM88	HAM	-	WBCs	6.18	RAISING	0.16	-
289	HAM89	HAM	-	WBCs	4.71	RAISING	0.09	-
290	HAM90	HAM	-	WBCs	3.98	RAISING	0.17	-
291	HAM91	HAM	-	WBCs	4.91	RAISING	0.19	-
292	HAM92	HAM	-	WBCs	1.60	RAISING	0.09	-
293	HAM93	HAM	-	WBCs	4.40	RAISING	0.08	-
294	HAM94	HAM	-	WBCs	1.29	RAISING	0.20	-
295	HAM95	HAM	-	WBCs	5.54	RAISING	0.08	-
296	HAM96	HAM	-	WBCs	7.21	RAISING	0.14	-
297	HAM97	HAM	-	WBCs	6.35	RAISING	0.08	-
298	HAM98	HAM	-	WBCs	6.00	RAISING	0.07	-
299	HAM99	HAM	-	WBCs	4.65	RAISING	0.14	-
300	HAM100	HAM	-	WBCs	3.34	RAISING	0.18	-
301	HAM101	HAM	-	WBCs	2.90	RAISING	0.22	-
302	HAM102	HAM	-	WBCs	6.78	RAISING	0.15	-
303	HAM103	HAM	-	WBCs	2.96	RAISING	0.13	-
304	HAM104	HAM	-	WBCs	1.89	RAISING	0.16	-
305	HAM105	HAM	-	WBCs	2.89	RAISING	0.15	-
306	HAM106	HAM	-	WBCs	7.98	RAISING	0.13	-
307	HAM107	HAM	-	WBCs	4.51	RAISING	0.18	-
308	HAM108	HAM	-	WBCs	3.52	RAISING	0.13	-
309	HAM109	HAM	-	WBCs	6.61	RAISING	0.11	-
310	HAM110	HAM	-	WBCs	6.76	RAISING	0.10	-
311	HAM111	HAM	-	WBCs	2.88	RAISING	0.48	-
312	HAM112	HAM	-	WBCs	3.50	RAISING	0.37	-
313	HAM113	HAM	-	WBCs	5.19	RAISING	0.08	-
314	HAM114	HAM	-	WBCs	1.02	RAISING	0.09	-
315	HAM115	HAM	-	WBCs	3.62	RAISING	0.23	-
316	HAM116	HAM	-	WBCs	2.14	RAISING	0.24	-
317	HAM117	HAM	-	WBCs	3.29	RAISING	0.16	-
318	HAM118	HAM	-	WBCs	4.61	RAISING	0.19	-
319	HAM119	HAM	-	WBCs	0.94	RAISING	0.27	-
320	HAM120	HAM	-	WBCs	2.74	RAISING	0.06	-
321	HAM121	HAM	-	WBCs	5.34	RAISING	0.18	-
322	HAM122	HAM	-	WBCs	4.31	RAISING	0.22	-
323	HAM123	HAM	-	WBCs	13.42	RAISING	0.13	-
324	HAM124	HAM	-	WBCs	4.28	RAISING	0.16	-
325	HAM125	HAM	-	WBCs	3.99	RAISING	0.12	-
326	HAM126	HAM	-	WBCs	1.69	RAISING	0.22	-
327	HAM127	HAM	-	WBCs	3.86	RAISING	0.18	-
328	HAM128	HAM	-	WBCs	2.77	RAISING	0.20	-
329	HAM129	HAM	-	WBCs	5.57	RAISING	0.08	-
330	HAM130	HAM	-	WBCs	6.48	RAISING	0.15	-
331	HAM131	HAM	-	WBCs	6.26	RAISING	0.11	-
332	HAM132	HAM	-	WBCs	2.24	RAISING	0.22	-
333	HAM133	HAM	-	WBCs	5.14	RAISING	0.09	-
334	HAM134	HAM	-	WBCs	3.00	RAISING	0.24	-
335	HAM135	HAM	-	WBCs	4.48	RAISING	0.13	-
336	HAM136	HAM	-	WBCs	2.88	RAISING	0.17	-
337	HAM137	HAM	-	WBCs	0.08	RAISING	0.39	-
338	HAM138	HAM	-	WBCs	1.05	RAISING	0.21	-
339	HAM139	HAM	-	WBCs	32.16	RAISING	0.06	-
340	HAM140	HAM	-	WBCs	2.90	RAISING	0.14	-
341	HAM141	HAM	-	WBCs	0.81	RAISING	0.10	-
342	HAM142	HAM	-	WBCs	2.57	RAISING	0.07	-
343	HAM143	HAM	-	WBCs	2.35	RAISING	0.14	-
344	HAM144	HAM	-	WBCs	2.10	RAISING	0.18	-
345	HAM145	HAM	-	WBCs	1.59	RAISING	0.11	-
346	HAM146	HAM	-	WBCs	2.58	RAISING	0.14	-
347	HAM147	HAM	-	PBMCs	0.77	RAISING	0.07	-
348	HAM148	HAM	-	PBMCs	2.74	RAISING	0.15	-
349	HAM149	HAM	-	PBMCs	0.62	RAISING	0.15	-
350	HAM150	HAM	-	PBMCs	4.30	RAISING	0.10	-
351	HAM151	HAM	-	PBMCs	2.24	RAISING	0.31	-
352	HAM152	HAM	-	PBMCs	5.71	RAISING	0.11	-

353	HAM153	HAM	-	PBMCs	1.47	RAISING	0.39	-
354	HAM154	HAM	-	PBMCs	0.13	RAISING	0.20	-
355	HAM155	HAM	-	PBMCs	10.97	RAISING	0.11	-
356	HAM156	HAM	-	PBMCs	5.50	RAISING	0.08	-
357	HAM157	HAM	-	PBMCs	11.47	RAISING	0.20	-
358	HAM158	HAM	-	PBMCs	0.22	RAISING	0.14	-
359	HAM159	HAM	-	PBMCs	0.78	RAISING	0.10	-
360	HAM160	HAM	-	PBMCs	0.11	RAISING	0.32	-
361	HAM161	HAM	-	PBMCs	2.63	RAISING	0.13	-
362	HAM162	HAM	-	PBMCs	0.16	RAISING	0.22	-
363	HAM163	HAM	-	PBMCs	7.70	RAISING	0.43	-
364	HAM164	HAM	-	PBMCs	2.62	RAISING	0.21	-
365	HAM165	HAM	-	PBMCs	5.93	RAISING	0.12	-
366	HAM166	HAM	-	PBMCs	0.45	RAISING	0.19	-
367	HAM167	HAM	-	PBMCs	9.24	RAISING	0.39	-
368	HAM168	HAM	-	PBMCs	1.80	RAISING	0.13	-
369	HAM169	HAM	-	PBMCs	6.41	RAISING	0.12	-
370	HAM170	HAM	-	PBMCs	1.06	RAISING	0.08	-
371	HAM171	HAM	-	PBMCs	12.02	RAISING	0.20	-
372	HAM172	HAM	-	PBMCs	5.54	RAISING	0.10	-
373	HAM173	HAM	-	PBMCs	3.25	RAISING	0.14	-
374	HAM174	HAM	-	PBMCs	6.97	RAISING	0.36	-
375	HAM175	HAM	-	PBMCs	14.96	RAISING	0.47	-
376	HAM176	HAM	-	PBMCs	10.10	RAISING	0.14	-
377	HAM177	HAM	-	PBMCs	3.48	RAISING	0.34	-
378	HAM178	HAM	-	PBMCs	1.71	RAISING	0.22	-
379	HAM179	HAM	-	PBMCs	5.32	RAISING	0.10	-
380	HAM180	HAM	-	PBMCs	1.48	RAISING	0.21	-
381	HAM181	HAM	-	PBMCs	4.61	RAISING	0.44	-
382	HAM182	HAM	-	PBMCs	0.87	RAISING	0.37	-
383	HAM183	HAM	-	PBMCs	0.76	RAISING	0.14	-
384	HAM184	HAM	-	PBMCs	8.36	RAISING	0.25	-
385	HAM185	HAM	-	PBMCs	6.39	RAISING	0.32	-
386	HAM186	HAM	-	PBMCs	2.87	RAISING	0.08	-
387	HAM187	HAM	-	PBMCs	14.79	RAISING	0.13	-
388	HAM188	HAM	-	PBMCs	10.73	RAISING	0.10	-
389	HAM189	HAM	-	PBMCs	10.56	RAISING	0.11	-
390	HAM190	HAM	-	PBMCs	2.13	RAISING	0.20	-
391	HAM191	HAM	-	WBCs	1.39	RAISING	0.12	-
392	HAM192	HAM	-	PBMCs	1.92	RAISING	0.14	-
393	HAM193	HAM	-	WBCs	3.30	RAISING	0.13	-
394	HAM194	HAM	-	PBMCs	3.22	RAISING	0.24	-
395	HAM195	HAM	-	PBMCs	4.31	RAISING	0.24	-
396	HAM196	HAM	-	PBMCs	2.03	RAISING	0.07	-
397	HAM197	HAM	-	PBMCs	4.00	RAISING	0.09	-
398	HAM198	HAM	-	PBMCs	3.25	RAISING	0.13	-
399	HAM199	HAM	-	PBMCs	5.02	RAISING	0.09	-
400	HAM200	HAM	-	PBMCs	0.73	RAISING	0.09	-
401	HAM201	HAM	-	PBMCs	1.54	RAISING	0.12	-
402	HAM202	HAM	-	PBMCs	1.58	RAISING	0.11	-
403	HAM203	HAM	-	PBMCs	2.51	RAISING	0.32	-
404	HAM204	HAM	-	PBMCs	1.03	RAISING	0.22	-
405	HAM205	HAM	-	PBMCs	4.52	RAISING	0.10	-
406	HAM206	HAM	-	PBMCs	0.71	RAISING	0.37	-
407	HAM207	HAM	-	WBCs	1.10	RAISING	0.16	-
408	HAM208	HAM	-	PBMCs	5.17	RAISING	0.54	-
409	HAM209	HAM	-	PBMCs	8.32	RAISING	0.14	-
410	HAM210	HAM	-	PBMCs	0.17	RAISING	0.51	-
411	HAM211	HAM	-	PBMCs	4.52	RAISING	0.16	-
412	HAM212	HAM	-	PBMCs	6.28	RAISING	0.11	-
413	HAM213	HAM	-	PBMCs	1.82	RAISING	0.14	-
414	HAM214	HAM	-	PBMCs	3.57	RAISING	0.12	-
415	HAM215	HAM	-	PBMCs	3.32	RAISING	0.11	-
416	HAM216	HAM	-	PBMCs	12.23	RAISING	0.08	-
417	HAM217	HAM	-	WBCs	0.34	RAISING	0.32	-
418	HAM218	HAM	-	PBMCs	3.93	RAISING	0.13	-
419	HAM219	HAM	-	PBMCs	2.64	RAISING	0.05	-
420	HAM220	HAM	-	PBMCs	6.33	RAISING	0.22	-
421	HAM221	HAM	-	PBMCs	19.73	RAISING	0.14	-
422	HAM222	HAM	-	PBMCs	3.62	RAISING	0.14	-
423	HAM223	HAM	-	PBMCs	3.41	RAISING	0.17	-
424	HAM224	HAM	-	PBMCs	12.78	RAISING	0.19	-
425	ATL1	ATL	Acute	PBMCs	1.10	RAIS	1.00	-
426	ATL2	ATL	Acute	PBMCs	84.90	RAIS	1.00	-
427	ATL3	ATL	Acute	PBMCs	32.90	RAIS	1.00	-
428	ATL4	ATL	Acute	PBMCs	141.60	RAIS	0.75	-
429	ATL5	ATL	Chronic	PBMCs	83.90	RAIS	1.00	-
430	ATL6	ATL	Acute	PBMCs	60.80	RAIS	1.00	-
431	ATL7	ATL	Acute	PBMCs	38.90	RAIS	1.00	-
432	ATL8	ATL	Acute	PBMCs	31.40	RAIS	0.99	-
433	ATL9	ATL	Acute	PBMCs	72.10	RAIS	0.95	-
434	ATL10	ATL	Acute	PBMCs	45.60	RAIS	1.00	-
435	ATL11	ATL	Acute	PBMCs	28.80	RAIS	1.00	-
436	ATL12	ATL	Acute	PBMCs-derived CADM1+ T-cells	-	RAIS	0.97	-
437	ATL13	ATL	Acute	PBMCs-derived CADM1+ T-cells	-	RAIS	1.00	-
438	ATL14	ATL	Acute	PBMCs-derived CADM1+ T-cells	-	RAIS	1.00	-
439	ATL15	ATL	Acute	PBMCs-derived CADM1+ T-cells	-	RAIS	0.71	-
440	ATL16	ATL	Acute	PBMCs-derived CADM1+ T-cells	-	RAIS	1.00	-
441	ATL17	ATL	Acute	PBMCs-derived CADM1+ T-cells	-	RAIS	1.00	-
442	ATL18	ATL	Acute	PBMCs-derived CADM1+ T-cells	-	RAIS	0.72	-
443	ATL19	ATL	Acute	PBMCs-derived CADM1+ T-cells	-	RAIS	0.92	-
444	ATL20	ATL	Chronic	PBMCs-derived CADM1+ T-cells	-	RAIS	1.00	-
445	ATL21	ATL	Chronic	PBMCs-derived CADM1+ T-cells	-	RAIS	0.84	-
446	ATL22	ATL	Chronic	PBMCs-derived CADM1+ T-cells	-	RAIS	1.00	-
447	ATL23	ATL	Chronic	PBMCs-derived CADM1+ T-cells	-	RAIS	1.00	-
448	ATL24	ATL	Chronic	PBMCs-derived CADM1+ T-cells	-	RAIS	0.91	-
449	ATL25	ATL	Chronic	PBMCs-derived CADM1+ T-cells	-	RAIS	1.00	-
450	ATL26	ATL	Chronic	PBMCs-derived CADM1+ T-cells	-	RAIS	1.00	-
451	ATL27	ATL	Chronic	PBMCs-derived CADM1+ T-cells	-	RAIS	0.88	-
452	ATL28	ATL	Acute	PBMCs	61.06	RAIS	1.00	-
453	ATL29	ATL	Acute	PBMCs	65.00	RAIS	0.90	-
454	ATL30	ATL	Acute	PBMCs	100.51	RAIS	0.92	-
455	ATL31	ATL	Acute	PBMCs	88.04	RAIS	0.98	-
456	ATL32	ATL	Acute	PBMCs	56.81	RAIS	1.00	-
457	ATL33	ATL	Acute	PBMCs	69.07	RAIS	1.00	-
458	ATL34	ATL	Acute	PBMCs	55.51	RAIS	0.73	-
459	ATL35	ATL	Chronic	PBMCs	99.85	RAIS	1.00	-
460	ATL36	ATL	Chronic	PBMCs	72.91	RAIS	1.00	-
461	ATL37	ATL	Chronic	PBMCs	82.83	RAIS	1.00	-
462	ATL38	ATL	Chronic	PBMCs	87.54	RAIS	0.69	-
463	ATL39	ATL	Chronic	PBMCs	2.12	RAIS	1.00	-
464	ATL40	ATL	Chronic	PBMCs	242.77	RAIS	0.99	-
465	ATL41	ATL	Acute	PBMCs	87.10	RAIS	0.74	-
466	ATL42	ATL	Acute	PBMCs	39.70	RAIS	1.00	-
467	ATL43	ATL	Acute	PBMCs	2.70	RAIS	0.98	-
468	ATL44	ATL	Acute	PBMCs	69.50	RAIS	0.56	-
469	ATL45	ATL	Lymphoma	Lymph node	32.50	RAIS	1.00	-
470	ATL46	ATL	Acute	PBMCs	31.90	RAIS	0.90	-

471	ATL47	ATL	Acute	PBMCs	0.90	RAIS	1.00	-
472	ATL48	ATL	Acute	Bone marrow	11.70	RAIS	1.00	-
473	ATL49	ATL	Acute	PBMCs	20.60	RAIS	1.00	-
474	ATL50	ATL	Chronic	PBMCs	3.90	RAIS	0.70	-
475	ATL51	ATL	Acute	PBMCs	6.90	RAIS	0.75	-
476	ATL52	ATL	Acute	PBMCs	41.20	RAIS	0.69	-
477	ATL53	ATL	Smoldering	PBMCs	15.50	RAIS	0.75	-
478	ATL54	ATL	Chronic	PBMCs	9.75	RAIS	0.99	-
479	ATL55	ATL	Lymphoma	PBMCs	8.75	RAIS	1.00	-
480	ATL56	ATL	Acute	PBMCs	20.60	RAIS	0.66	-
481	ATL57	ATL	Chronic	PBMCs	22.90	RAIS	1.00	-
482	ATL58	ATL	Chronic	PBMCs	23.30	RAIS	1.00	-
483	ATL59	ATL	Acute	PBMCs	6.00	RAIS	0.82	-
484	ATL60	ATL	Acute	PBMCs	42.95	RAIS	0.83	-
485	ATL61	ATL	Smoldering	PBMCs	18.65	RAIS	0.78	-
486	ATL62	ATL	Smoldering	PBMCs	45.85	RAIS	0.83	-
487	ATL63	ATL	Smoldering	PBMCs	7.00	RAIS	0.62	-
488	ATL64	ATL	Acute	PBMCs	38.90	RAIS	1.00	-
489	ATL65	ATL	Acute	PBMCs	99.70	RAIS	1.00	-
490	ATL66	ATL	Lymphoma	Lymph node	40.70	RAIS	0.96	-
491	ATL67	ATL	Lymphoma	Lymph node	53.25	RAIS	0.90	-
492	ATL68	ATL	Lymphoma	PBMCs	5.00	RAIS	0.99	-
493	ATL69	ATL	Acute	PBMCs	9.90	RAIS	0.74	-
494	ATL70	ATL	Acute	PBMCs	26.05	RAIS	1.00	-
495	ATL71	ATL	Acute	PBMCs	31.85	RAIS	1.00	-
496	ATL72	ATL	Smoldering	PBMCs	7.57	RAIS	0.92	-
497	ATL73	ATL	Lymphoma	PBMCs	1.20	RAIS	1.00	-
498	ATL74	ATL	Smoldering	PBMCs	3.70	RAIS	0.93	-
499	ATL75	ATL	Smoldering	PBMCs	7.90	RAIS	1.00	-
500	ATL76	ATL	Chronic	Bone marrow	26.10	RAIS	0.98	-
501	ATL77	ATL	Chronic	PBMCs	14.65	RAIS	1.00	-
502	ATL78	ATL	Acute	PBMCs	77.55	RAIS	0.93	-
503	ATL79	ATL	Chronic	PBMCs	29.20	RAIS	0.66	-
504	ATL80	ATL	Smoldering	PBMCs	13.50	RAIS	1.00	-
505	ATL81	ATL	Smoldering	PBMCs	15.70	RAIS	1.00	-
506	ATL82	ATL	Lymphoma	PBMCs	20.85	RAIS	1.00	-
507	ATL83	ATL	Acute	PBMCs	75.60	RAIS	0.70	-
508	ATL84	ATL	Acute	Lymph node	68.15	RAIS	0.99	-
509	ATL85	ATL	Acute	PBMCs	23.55	RAIS	0.90	-
510	ATL86	ATL	Lymphoma	PBMCs	19.80	RAIS	0.72	-
511	ATL87	ATL	Acute	PBMCs	14.95	RAIS	0.56	-
512	ATL88	ATL	Smoldering	PBMCs	33.45	RAIS	0.97	-
513	ATL89	ATL	Chronic	PBMCs	78.85	RAIS	0.94	-
514	ATL90	ATL	Smoldering	PBMCs	23.45	RAIS	0.97	-
515	ATL91	ATL	Smoldering	PBMCs	15.15	RAIS	0.95	-
516	ATL92	ATL	Lymphoma	PBMCs	13.45	RAIS	0.86	-
517	ATL93	ATL	Smoldering	PBMCs	4.25	RAIS	0.61	-
518	ATL94	ATL	Chronic	PBMCs	38.95	RAIS	0.87	-
519	ATL95	ATL	Chronic	PBMCs	124.75	RAIS	1.00	-
520	ATL96	ATL	Acute	PBMCs	7.15	RAIS	1.00	-
521	ATL97	ATL	Smoldering	PBMCs	9.15	RAIS	0.66	-
522	ATL98	ATL	Smoldering	PBMCs	66.50	RAIS	0.78	-
523	ATL99	ATL	Chronic	PBMCs	57.65	RAIS	1.00	-
524	ATL100	ATL	Lymphoma	PBMCs	21.00	RAIS	1.00	-
525	ATL101	ATL	Acute	PBMCs	7.05	RAIS	0.73	-
526	ATL102	ATL	Acute	PBMCs	55.30	RAIS	0.72	-
527	ATL103	ATL	Chronic	PBMCs	53.15	RAIS	0.99	-
528	ATL104	ATL	Smoldering	PBMCs	13.65	RAIS	0.82	-
529	ATL105	ATL	Acute	PBMCs	8.60	RAIS	0.82	-
530	ATL106	ATL	Acute	PBMCs	12.25	RAIS	0.68	-
531	ATL107	ATL	Chronic	PBMCs	68.15	RAIS	1.00	-
532	ATL108	ATL	Smoldering	Skin	25.40	RAIS	0.93	-
533	ATL109	ATL	Lymphoma	PBMCs	4.75	RAIS	0.84	-
534	ATL110	ATL	Smoldering	PBMCs	36.40	RAIS	0.54	-
535	ATL111	ATL	Chronic	PBMCs	46.95	RAIS	0.78	-
536	ATL112	ATL	Smoldering	PBMCs	28.05	RAIS	0.53	-
537	ATL113	ATL	Acute	PBMCs	36.30	RAIS	1.00	-
538	ATL114	ATL	Acute	PBMCs	8.65	RAIS	0.75	-
539	ATL115	ATL	Acute	PBMCs	25.40	RAIS	0.94	-
540	ATL116	ATL	Acute	PBMCs	18.45	RAIS	0.74	-
541	ATL117	ATL	Smoldering	PBMCs	6.95	RAIS	0.94	-
542	ATL118	ATL	Smoldering	PBMCs	7.10	RAIS	0.96	-
543	ATL119	ATL	Acute	PBMCs	14.60	RAIS	0.81	-
544	ATL120	ATL	Chronic	PBMCs	17.70	RAIS	1.00	-
545	ATL121	ATL	Smoldering	PBMCs	11.65	RAIS	0.75	-
546	ATL122	ATL	Acute	PBMCs	44.45	RAIS	0.66	-
547	ATL123	ATL	Chronic	PBMCs	4.25	RAIS	0.75	-
548	ATL124	ATL	Acute	PBMCs	21.90	RAIS	1.00	-
549	ATL125	ATL	Lymphoma	Lymph node	15.95	RAIS	0.97	-
550	ATL126	ATL	Acute	PBMCs	40.65	RAIS	1.00	-
551	ATL127	ATL	Acute	PBMCs	15.45	RAIS	1.00	-
552	ATL128	ATL	Acute	PBMCs	6.50	RAIS	0.59	-
553	ATL129	ATL	Acute	PBMCs	13.75	RAIS	1.00	-
554	ATL130	ATL	Chronic	PBMCs	51.65	RAIS	0.88	-
555	ATL131	ATL	Acute	PBMCs	10.40	RAIS	0.64	-
556	ATL132	ATL	Acute	PBMCs	15.10	RAIS	1.00	-
557	ATL133	ATL	Chronic	PBMCs	6.75	RAIS	0.87	-
558	ATL134	ATL	Chronic	PBMCs	77.50	RAIS	0.66	-
559	ATL135	ATL	Lymphoma	Lymph node	44.25	RAIS	1.00	-
560	ATL136	ATL	Lymphoma	PBMCs	30.15	RAIS	0.99	-
561	ATL137	ATL	Smoldering	PBMCs	26.25	RAIS	0.49	-
562	ATL138	ATL	Chronic	PBMCs	44.35	RAIS	0.78	-
563	ATL139	ATL	Acute	PBMCs	6.95	RAIS	0.84	-
564	ATL140	ATL	Acute	PBMCs	7.65	RAIS	0.94	-
565	ATL141	ATL	Smoldering	PBMCs	7.40	RAIS	0.78	-
566	ATL142	ATL	Acute	PBMCs	33.00	RAIS	1.00	-
567	ATL143	ATL	Smoldering	PBMCs	4.05	RAIS	0.63	-
568	ATL144	ATL	Chronic	PBMCs	17.80	RAIS	1.00	-
569	ATL145	ATL	Acute	PBMCs	61.10	RAIS	0.85	-
570	ATL146	ATL	Acute	PBMCs	10.10	RAIS	0.75	-
571	ATL147	ATL	Acute	PBMCs	21.55	RAIS	0.70	-
572	ATL148	ATL	Chronic	PBMCs	26.06	RAIS	0.91	-
573	ATL149	ATL	Smoldering	PBMCs	24.78	RAIS	0.59	-
574	ATL150	ATL	Acute	PBMCs	37.14	RAIS	0.97	-
575	ATL151	ATL	Acute	PBMCs	39.52	RAIS	0.65	-
576	ATL152	ATL	Lymphoma	Lymph node	26.43	RAIS	1.00	-
577	ATL153	ATL	Acute	PBMCs	39.92	RAIS	1.00	-
578	ATL154	ATL	Acute	PBMCs	28.71	RAIS	0.52	-
579	ATL155	ATL	Acute	PBMCs	46.37	RAIS	0.98	-
580	ATL156	ATL	Acute	PBMCs	15.95	RAIS	0.91	-
581	ATL157	ATL	Acute	PBMCs	46.15	RAIS	0.94	-
582	ATL158	ATL	Acute	PBMCs	23.33	RAIS	0.93	-
583	ATL159	ATL	Acute	PBMCs	2.88	RAIS	0.67	-
584	ATL160	ATL	Smoldering	PBMCs	14.83	RAIS	0.68	-
585	ATL162	ATL	Smoldering	PBMCs	23.18	RAIS	0.74	-
586	ATL163	ATL	Smoldering	PBMCs	4.59	RAIS	0.48	-
587	ATL164	ATL	Acute	PBMCs	25.71	RAIS	0.86	-
588	ATL165	ATL	Chronic	PBMCs	46.53	RAIS	0.89	-

589	ATL166	ATL	Acute	PBMCs	5.46	RAIS	0.66	-
590	ATL167	ATL	Chronic	PBMCs	31.02	RAIS	0.71	-
591	ATL168	ATL	Smoldering	PBMCs	17.09	RAIS	0.99	-
592	ATL169	ATL	Chronic	PBMCs	41.03	RAIS	1.00	-
593	ATL170	ATL	Acute	PBMCs	12.12	RAIS	0.64	-
594	ATL171	ATL	Acute	PBMCs	31.68	RAIS	1.00	-
595	ATL172	ATL	Chronic	PBMCs	31.42	RAIS	0.73	-
596	ATL173	ATL	Chronic	PBMCs	114.75	RAIS	0.98	-
597	ATL174	ATL	Acute	PBMCs	19.48	RAIS	1.00	-
598	ATL175	ATL	Acute	PBMCs	25.57	RAIS	0.90	-
599	ATL176	ATL	Chronic	PBMCs	12.28	RAIS	1.00	-
600	ATL177	ATL	Chronic	PBMCs	36.17	RAIS	0.88	-
601	ATL178	ATL	Acute	PBMCs	50.10	RAIS	0.99	-
602	ATL179	ATL	Lymphoma	Lymph node	4.47	RAIS	0.58	-
603	ATL180	ATL	Acute	PBMCs	68.58	RAIS	0.89	-
604	ATL181	ATL	Smoldering	PBMCs	28.33	RAIS	0.89	-
605	ATL182	ATL	Acute	PBMCs	24.24	RAIS	0.55	-
606	ATL183	ATL	Smoldering	PBMCs	48.89	RAIS	1.00	-
607	ATL184	ATL	Acute	PBMCs	14.91	RAIS	0.95	-
608	ATL185	ATL	Acute	PBMCs	9.28	RAIS	0.58	-
609	ATL186	ATL	Acute	PBMCs	17.99	RAIS	0.66	-
610	ATL187	ATL	Smoldering	PBMCs	19.11	RAIS	0.82	-
611	ATL188	ATL	Chronic	PBMCs	34.66	RAIS	1.00	-
612	ATL189	ATL	Chronic	PBMCs	3.90	RAIS	0.97	-
613	ATL190	ATL	Lymphoma	Lymph node	88.03	RAIS	0.97	-
614	ATL191	ATL	Chronic	PBMCs	28.47	RAIS	0.95	-
615	ATL192	ATL	Acute	PBMCs	21.91	RAIS	1.00	-
616	ATL193	ATL	Acute	PBMCs	30.83	RAIS	0.77	-
617	ATL194	ATL	Smoldering	PBMCs	9.95	RAIS	0.73	-
618	ATL195	ATL	Chronic	PBMCs	13.27	RAIS	0.76	-
619	ATL196	ATL	Acute	PBMCs	17.67	RAIS	1.00	-
620	ATL197	ATL	Smoldering	PBMCs	20.37	RAIS	0.59	-
621	ATL198	ATL	Smoldering	PBMCs	48.30	RAIS	0.71	-
622	ATL199	ATL	Lymphoma	Lymph node	30.87	RAIS	0.87	-
623	ATL200	ATL	Acute	PBMCs	4.21	RAIS	1.00	-
624	ATL201	ATL	Smoldering	PBMCs	5.20	RAIS	0.76	-
625	ATL202	ATL	Acute	PBMCs	29.56	RAIS	1.00	-
626	ATL203	ATL	Acute	Lymph node	16.70	RAIS	1.00	-
627	ATL204	ATL	Acute	PBMCs	28.70	RAIS	0.78	-
628	ATL205	ATL	Acute	PBMCs	29.80	RAIS	1.00	-
629	ATL206	ATL	Chronic	PBMCs	2.93	RAIS	1.00	-
630	ATL207	ATL	Acute	PBMCs	87.75	RAIS	1.00	-
631	ATL208	ATL	Acute	PBMCs	14.36	RAIS	0.97	-
632	ATL209	ATL	Acute	PBMCs	24.84	RAIS	1.00	-
633	ATL210	ATL	Smoldering	PBMCs	4.84	RAIS	0.93	-
634	ATL211	ATL	Smoldering	PBMCs	4.77	RAIS	0.67	-
635	ATL212	ATL	Chronic	PBMCs	90.58	RAIS	0.60	-
636	ATL213	ATL	Chronic	PBMCs	24.35	RAIS	0.59	-
637	ATL214	ATL	Smoldering	PBMCs	5.68	RAIS	0.68	-
638	ATL215	ATL	Smoldering	PBMCs	23.77	RAIS	0.71	-
639	ATL216	ATL	Smoldering	PBMCs	6.24	RAIS	0.67	-
640	ATL217	ATL	Acute	PBMCs	12.60	RAIS	1.00	-
641	ATL218	ATL	Smoldering	PBMCs	25.63	RAIS	0.50	-
642	ATL219	ATL	Chronic	PBMCs	4.25	RAIS	0.80	-
643	ATL220	ATL	Smoldering	PBMCs	9.50	RAIS	0.67	-
644	ATL221	ATL	Chronic	PBMCs	70.84	RAIS	0.72	-
645	ATL222	ATL	Acute	PBMCs	34.25	RAIS	0.65	-
646	ATL223	ATL	Acute	PBMCs	58.91	RAIS	1.00	-
647	ATL224	ATL	Acute	PBMCs	22.85	RAIS	1.00	-
648	ATL225	ATL	Chronic	PBMCs	24.46	RAIS	1.00	-
649	ATL226	ATL	Acute	PBMCs	19.61	RAIS	1.00	-
650	ATL227	ATL	Acute	PBMCs	41.12	RAIS	1.00	-
651	ATL228	ATL	Acute	PBMCs	45.59	RAIS	0.82	-
652	ATL229	ATL	Acute	PBMCs	93.89	RAIS	0.92	-
653	ATL230	ATL	Acute	PBMCs	16.24	RAIS	1.00	-
654	ATL231	ATL	Acute	PBMCs	55.13	RAIS	1.00	-
655	ATL232	ATL	Acute	PBMCs	76.00	RAIS	1.00	-
656	ATL233	ATL	Acute	PBMCs	117.83	RAIS	1.00	-
657	ATL234	ATL	Acute	PBMCs	45.70	RAIS	0.96	-
658	ATL235	ATL	Acute	PBMCs	48.91	RAIS	1.00	-
659	ATL236	ATL	Acute	PBMCs	81.40	RAIS	1.00	-
660	ATL237	ATL	Acute	PBMCs	14.37	RAIS	0.77	-
661	ATL238	ATL	Acute	PBMCs	51.97	RAIS	1.00	-
662	ATL239	ATL	Acute	PBMCs	89.12	RAIS	1.00	-
663	ATL241	ATL	Acute	PBMCs	66.80	RAIS	1.00	-
664	ATL242	ATL	Acute	PBMCs	35.86	RAIS	0.82	-
665	ATL243	ATL	Acute	PBMCs	32.15	RAIS	1.00	-
666	ATL244	ATL	Acute	PBMCs	79.02	RAIS	1.00	-
667	ATL245	ATL	Acute	PBMCs	17.34	RAIS	0.75	-
668	ATL246	ATL	Acute	PBMCs	19.92	RAIS	0.51	-
669	ATL247	ATL	Acute	PBMCs	92.66	RAIS	1.00	-
670	ATL248	ATL	Acute	PBMCs	67.96	RAIS	1.00	-
671	ATL249	ATL	Acute	PBMCs	107.07	RAIS	0.94	-
672	ATL250	ATL	Chronic	PBMCs	82.34	RAIS	1.00	-
673	ATL251	ATL	Chronic	PBMCs	80.63	RAIS	1.00	-
674	ATL252	ATL	Chronic	PBMCs	57.30	RAIS	1.00	-
675	ATL253	ATL	Chronic	PBMCs	75.79	RAIS	0.91	-
676	ATL255	ATL	Chronic	PBMCs	64.30	RAIS	1.00	-
677	ATL256	ATL	Chronic	PBMCs	81.29	RAIS	1.00	-
678	ATL257	ATL	Chronic	PBMCs	58.20	RAIS	0.83	-
679	ATL258	ATL	Chronic	PBMCs	55.75	RAIS	0.75	-
680	ATL259	ATL	Chronic	PBMCs	121.62	RAIS	1.00	-
681	ATL260	ATL	Chronic	PBMCs	81.90	RAIS	0.98	-
682	ATL261	ATL	Chronic	PBMCs	85.04	RAIS	0.62	-
683	ATL262	ATL	Chronic	PBMCs	42.70	RAIS	0.89	-
684	ATL263	ATL	Chronic	PBMCs	65.45	RAIS	1.00	-
685	ATL264	ATL	Chronic	PBMCs	57.44	RAIS	1.00	-
686	ATL265	ATL	Chronic	PBMCs	73.60	RAIS	0.99	-
687	ATL266	ATL	Chronic	PBMCs	13.37	RAIS	1.00	-
688	ATL267	ATL	Chronic	PBMCs	72.31	RAIS	1.00	-
689	ATL268	ATL	Chronic	PBMCs	71.26	RAIS	1.00	-
690	ATL269	ATL	Smoldering	PBMCs	9.40	RAIS	1.00	-
691	ATL270	ATL	Smoldering	PBMCs	19.09	RAIS	0.81	-
692	ATL271	ATL	Smoldering	PBMCs	9.65	RAIS	0.96	-
693	ATL272	ATL	Smoldering	PBMCs	17.98	RAIS	0.78	-
694	ATL273	ATL	Smoldering	PBMCs	30.77	RAIS	0.79	-
695	ATL275	ATL	Smoldering	PBMCs	6.69	RAIS	1.00	-
696	ATL276	ATL	Smoldering	PBMCs	111.53	RAIS	1.00	-
697	ATL277	ATL	Smoldering	PBMCs	35.67	RAIS	0.82	-
698	ATL278	ATL	Smoldering	PBMCs	30.99	RAIS	0.69	-
699	ATL279	ATL	Smoldering	PBMCs	29.43	RAIS	1.00	-
700	ATL280	ATL	Smoldering	PBMCs	8.39	RAIS	0.71	-
701	ATL282	ATL	Smoldering	PBMCs	26.24	RAIS	0.87	-
702	ATL283	ATL	Smoldering	PBMCs	24.73	RAIS	1.00	-
703	ATL284	ATL	Smoldering	PBMCs	16.02	RAIS	0.75	-
704	ATL285	ATL	Smoldering	PBMCs	10.21	RAIS	0.72	-
705	ATL286	ATL	Smoldering	PBMCs	11.20	RAIS	0.95	-
706	ATL287	ATL	Smoldering	PBMCs	11.10	RAIS	0.69	-

707	ATL288	ATL	Smoldering	PBMCs	3.27	RAIS	1.00	-
708	ATL289	ATL	Acute	PBMCs	24.30	RAIS	0.98	-
709	ATL291	ATL	Chronic	PBMCs	45.15	RAIS	1.00	-
710	ATL292	ATL	Acute	Lymph node	22.50	RAIS	0.99	-
711	ATL293	ATL	Lymphoma	PBMCs	0.80	RAIS	0.51	-
712	ATL294	ATL	Acute	PBMCs, PBMCs-derived CADM1+ T-cells	213.26	RAISING	0.91	PVL in PBMCs, Cv in PBMCs-derived CADM1+ T-cells
713	ATL295	ATL	Acute	PBMCs, PBMCs-derived CADM1+ T-cells	109.70	RAISING	0.73	PVL in PBMCs, Cv in PBMCs-derived CADM1+ T-cells
714	ATL296	ATL	Acute	PBMCs, PBMCs-derived CADM1+ T-cells	340.26	RAISING	0.54	PVL in PBMCs, Cv in PBMCs-derived CADM1+ T-cells
715	ATL297	ATL	Chronic	PBMCs, PBMCs-derived CADM1+ T-cells	43.01	RAISING	1.00	PVL in PBMCs, Cv in PBMCs-derived CADM1+ T-cells
716	ATL298	ATL	Chronic	PBMCs, PBMCs-derived CADM1+ T-cells	99.27	RAISING	1.00	PVL in PBMCs, Cv in PBMCs-derived CADM1+ T-cells
717	ATL299	ATL	Chronic	PBMCs, PBMCs-derived CADM1+ T-cells	99.98	RAISING	1.00	PVL in PBMCs, Cv in PBMCs-derived CADM1+ T-cells
718	ATL300	ATL	Chronic	PBMCs, PBMCs-derived CADM1+ T-cells	96.53	RAISING	1.00	PVL in PBMCs, Cv in PBMCs-derived CADM1+ T-cells
719	ATL301	ATL	Smoldering	PBMCs, PBMCs-derived CADM1+ T-cells	65.76	RAISING	0.62	PVL in PBMCs, Cv in PBMCs-derived CADM1+ T-cells
720	ATL302	ATL	Smoldering	PBMCs, PBMCs-derived CADM1+ T-cells	21.72	RAISING	0.70	PVL in PBMCs, Cv in PBMCs-derived CADM1+ T-cells
721	ATL303	ATL	Smoldering	PBMCs, PBMCs-derived CADM1+ T-cells	12.87	RAISING	0.49	PVL in PBMCs, Cv in PBMCs-derived CADM1+ T-cells
722	ATL304	ATL	Smoldering	PBMCs	15.38	RAISING	0.60	-
723	ATL305	ATL	Smoldering	PBMCs	12.91	RAISING	0.59	-
724	ATL306	ATL	Chronic	PBMCs	22.87	RAISING	0.49	-
725	ATL307	ATL	Chronic	PBMCs	58.89	RAISING	0.59	-
726	ATL308	ATL	Smoldering	PBMCs	25.06	RAISING	0.70	Same subject as AC14
727	ATL309	ATL	Acute	PBMCs	20.12	RAISING	0.62	Same subject as HAM33
728	ATL310	ATL	Acute	PBMCs	18.06	RAISING	0.81	Same subject as HAM1
729	ATL311	ATL	Acute	PBMCs	106.24	RAISING	0.77	Same subject as HAM32
730	ATL312	ATL	Lymphoma	PBMCs, Lymph node	0.17	RAISING	0.94	PVL in PBMCs, Cv in Lymph node

PVL, proviral load; Cv, clonality value; ND, no data; PBMCs, peripheral blood mononuclear cells; WBCs, whole blood cells.