ARCHITECT SYSTEM

en

*r*HTLV-I/II

REF 6L61

84-6470/R2

B6L610

*r*HTLV-I/II

Customer Service
For additional product information, please contact your local customer service organization.

This package insert must be read carefully before product use. Package insert instructions must be followed. Reliability of assay results cannot be guaranteed if there are any deviations from the instructions in this package insert.

Key to symbols used

REF	List Number	ASSAY CD-ROM	Assay CD-ROM
IVD	*In Vitro* Diagnostic Medical Device	SN	Serial Number
LOT	Lot Number	CONTROL NO.	Control Number
	Expiration Date	REAGENT LOT	Reagent Lot
2°C 8°C	Store at 2-8°C	REACTION VESSELS	Reaction Vessels
	Caution, consult accompanying documents	SAMPLE CUPS	Sample Cups
		SEPTUM	Septum
	Manufacturer	REPLACEMENT CAPS	Replacement Caps

See **REAGENTS** section for a full explanation of symbols used in reagent component naming.

ABBOTT
Diagnostics Division

NAME

ARCHITECT *r*HTLV-I/II

INTENDED USE

The ARCHITECT *r*HTLV-I/II assay is a chemiluminescent microparticle immunoassay (CMIA) for the qualitative detection of antibodies to HTLV-I and HTLV-II in human serum and plasma.

SUMMARY AND EXPLANATION OF THE TEST

HTLV-I and HTLV-II are closely related human type C retroviruses.[1,2] HTLV-I has been etiologically associated with neoplastic conditions and a variety of demyelinating neurologic disorders including: adult T-cell leukemia (ATL),[3] tropical spastic paraparesis (TSP),[4,5] and/or HTLV-I associated myelopathy (HAM)[6] and more recently HTLV-I associated polymyositis, arthritis, and infective dermatitis.[7-9] Association of HTLV-II with leukemia pathogenesis is not established; however, there is some evidence of an association with a neuro-degenerative disease similar to HAM/TSP[10] and occasionally also with lymphoproliferative disease.[11]

HTLV-I infection is endemic in south Japan[12], the Caribbean[13], in some regions of Africa[14], Central and South America[15] and also found in Melanesia[16] and central and northern Australia[17], while HTLV-II is endemic to a number of indigenous American Indian populations.[15] Both HTLV-I and HTLV-II are distributed worldwide among populations at high risk of infection, such as intravenous drug abusers, sex workers and patients attending sexually transmitted disease clinics.[18,19] Transmission of both HTLV-I and HTLV-II is by sexual contact, exposure to infected cellular blood components by transfusion or intravenous drug use or perinatally by breast feeding. Detection of antibodies against HTLV-I and HTLV-II serves to aid in the diagnosis of HTLV infection and to protect the safety of blood supply.

BIOLOGICAL PRINCIPLES OF THE PROCEDURE

The ARCHITECT *r*HTLV-I/II assay is a two-step immunoassay for the qualitative detection of antibodies to HTLV-I and HTLV-II in human serum and plasma using CMIA technology with flexible assay protocols, referred to as Chemiflex.

Sample and assay diluent are combined. An aliquot of the pretreated sample and HTLV-I/HTLV-II coated paramagnetic microparticles are combined in a new reaction vessel. Anti-HTLV-I/HTLV-II antibodies present in the sample bind to the HTLV-I/HTLV-II synthetic peptide and HTLV-II recombinant antigen coated microparticles.

After washing, the acridinium-labeled conjugates (HTLV-I/HTLV-II synthetic peptide and HTLV-I recombinant antigen) bind to the anti-HTLV-I/HTLV-II antibodies. Following another wash cycle, pre-trigger and trigger solutions are added to the reaction mixture.

The resulting chemiluminescent reaction is measured as relative light units (RLUs). A direct relationship exists between the amount of anti-HTLV-I/HTLV-II antibodies in the sample and the RLUs detected by the ARCHITECT *i* System optics.

The presence or absence of anti-HTLV-I/HTLV-II in the sample is determined by comparing the chemiluminescent signal in the reaction to the cutoff signal determined from an active calibration. If the chemiluminescent signal of the specimen is greater than or equal to the cutoff signal, then the sample is considered reactive for anti-HTLV-I and/or anti-HTLV-II.

The immunodominant region of gp21 is 100% identical between HTLV-I and HTLV-II viral genome, and the overall homology between the two gp21 proteins is 86%. Additionally the homology between the two gp46 peptides is 65%, therefore the selected rare reagents (synthetic peptides (gp46) and recombinant antigens (gp21)) in this assay are capable to detect antibodies for HTLV-I and HTLV-II simultaneously.

For additional information on system and assay technology refer to the ARCHITECT System Operations Manual, Section 3.

REAGENTS

Reagent Kit, 1 x 100 Tests, 1 x 500 Tests and 4 x 500 Tests

NOTE: Some kit sizes are not available in all countries or for use on all ARCHITECT *i* Systems. Please contact your local distributor.

ARCHITECT *r*HTLV-I/II Reagent Kit (6L61).

- **MICROPARTICLES** 1 or 4 Bottle(s) (6.6 mL per 100-test bottle/ 27.0 mL per 500-test bottle) HTLV-I/HTLV-II synthetic peptide and HTLV-II recombinant antigen coated microparticles in TRIS buffered saline. Preservatives: ProClin 950 and sodium azide.
- **CONJUGATE** 1 or 4 Bottle(s) (5.9 mL per 100-test bottle/26.3 mL per 500-test bottle) acridinium-labeled HTLV-I/HTLV-II synthetic peptide and acridinium-labeled HTLV-I recombinant antigen in HEPES buffer with protein stabilizers and detergent. Preservative: ProClin 950.
- **ASSAY DILUENT** 1 or 4 Bottle(s) (7.7 mL per 100-test bottle/39.2 mL per 500-test bottle) *r*HTLV-I/II assay diluent containing TRIS buffer and detergent. Preservatives: ProClin 950 and sodium azide.

Other Reagents

ARCHITECT *i* Pre-Trigger Solution

- **PRE-TRIGGER SOLUTION** Pre-Trigger Solution containing 1.32% (w/v) hydrogen peroxide.

ARCHITECT *i* Trigger Solution

- **TRIGGER SOLUTION** Trigger Solution containing 0.35N sodium hydroxide.

ARCHITECT *i* Wash Buffer

- **WASH BUFFER** Wash Buffer containing phosphate buffered saline solution. Preservative: antimicrobial agents.

WARNINGS AND PRECAUTIONS

- **IVD**

Safety Precautions

- **CAUTION:** This product requires the handling of human specimens. It is recommended that all human-sourced materials be considered potentially infectious and handled with appropriate biosafety practices.

All of the components of this kit contain methylisothiazolones, which are components of ProClin. These components are classified per applicable European Community (EC) Directives as: Irritant (Xi). The following are the appropriate Risk (R) and Safety (S) phrases.

R43 May cause sensitization by skin contact.
S24 Avoid contact with skin.
S35 This material and its container must be disposed of in a safe way.
S37 Wear suitable gloves.
S46 If swallowed, seek medical advice immediately and show this container or label.

- Some components of this product contain sodium azide. For a specific listing, refer to the **REAGENTS** section of this package insert. Contact with acids liberates very toxic gas. This material and its container must be disposed of in a safe way.
- For product not classified as dangerous per European Directive 1999/45/EC as amended - Safety data sheet available for professional user on request.
- For information on the safe disposal of sodium azide and a detailed discussion of safety precautions during system operation, refer to the ARCHITECT System Operations Manual, Section 8.

Handling Precautions

- Do not use reagent kits beyond the expiration date.
- **Do not pool reagents within a kit or between reagent kits.**
- Before loading the ARCHITECT *r*HTLV-I/II Reagent Kit on the system for the first time, the microparticle bottle requires mixing to resuspend microparticles that have settled during shipment. For microparticle mixing instructions, refer to the **PROCEDURE, Assay Procedure** section of this package insert.
- **Septums MUST be used to prevent reagent evaporation and contamination and to ensure reagent integrity. Reliability of assay results cannot be guaranteed if septums are not used according to the instructions in this package insert.**
- To avoid contamination, wear clean gloves when placing a septum on an uncapped reagent bottle.
  - Once a septum has been placed on the reagent bottle, **do not invert the bottle** as this will result in reagent leakage and may compromise assay results.
  - Over time, residual liquids may dry on the septum surface. These are typically dried salts, which have no effect on assay efficacy.
- For a detailed discussion of handling precautions during system operation, refer to the ARCHITECT System Operations Manual, Section 7.

Storage Instructions

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The ARCHITECT *r*HTLV-I/II Reagent Kit must be stored at 2-8°C in an upright position and may be used immediately after removal from 2-8°C storage.
- When stored and handled as directed, reagents are stable until the expiration date.
- The ARCHITECT *r*HTLV-I/II Reagent Kit may be stored on board the ARCHITECT *i* System for a maximum of 30 days. After 30 days, the reagent kit must be discarded. For information on tracking onboard time, refer to the ARCHITECT System Operations Manual, Section 5.
- Reagents may be stored on or off the ARCHITECT *i* System. If reagents are removed from the system, store them at 2-8°C (with septums and replacement caps) in an upright position. For reagents stored off the system, it is recommended that they be stored in their original trays and boxes to ensure they remain upright. **If the microparticle bottle does not remain upright (with a septum installed) while in refrigerated storage off the system, the reagent kit must be discarded.** After reagents are removed from the system, initiate a reagent scan to update the onboard stability timer.

Indications of Reagent Deterioration

When a control value is out of the specified range, it may indicate deterioration of the reagents or errors in technique. Associated test results are invalid and samples must be retested. Assay recalibration may be necessary. For troubleshooting information, refer to the ARCHITECT System Operations Manual, Section 10.

INSTRUMENT PROCEDURE

- The ARCHITECT *r*HTLV-I/II assay file must be installed on the ARCHITECT *i* System from the ARCHITECT *i* Assay CD-ROM before performing the assay. For detailed information on assay file installation and on viewing and editing assay parameters, refer to the ARCHITECT System Operations Manual, Section 2.
- For information on printing assay parameters, refer to the ARCHITECT System Operations Manual, Section 5.
- For a detailed description of system procedures, refer to the ARCHITECT System Operations Manual.

SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

Specimen Types

The specimen collection tubes listed below were verified to be used with the ARCHITECT *r*HTLV-I/II assay. Other specimen collection tubes have not been tested with this assay.

- Human serum (including serum collected in serum separator tubes and tubes containing Kaolin)
- Human plasma collected in:
  - plasma separator tubes (lithium heparin)
  - potassium EDTA
  - sodium citrate
  - sodium heparin
  - lithium heparin
  - potassium oxalate
  - CPDA-1
  - ACD
  - CPD
- Liquid anticoagulants may have a dilution effect resulting in lower concentrations for individual patient specimens.
- The ARCHITECT *i* System does not provide the capability to verify specimen type. It is the responsibility of the operator to verify that the correct specimen types are used in the ARCHITECT *r*HTLV-I/II assay.

Specimen Conditions

- Do not use specimens with the following conditions:
  - heat-inactivated
  - pooled
  - grossly hemolyzed (> 500 mg/dL)
  - obvious microbial contamination
  - cadaver specimens or any other body fluids
- For accurate results, serum and plasma specimens should be free of fibrin, red blood cells, and other particulate matter. Serum specimens from patients receiving anticoagulant or thrombolytic therapy may contain fibrin due to incomplete clot formation.
- Use caution when handling patient specimens to prevent cross contamination. Use of disposable pipettes or pipette tips is recommended.
- For optimal results, inspect all specimens for bubbles. Remove bubbles with an applicator stick before analysis. Use a new applicator stick for each specimen to prevent cross contamination.
- No qualitative performance differences were observed between experimental controls and a minimum of 10 nonreactive and 10 spiked reactive specimens tested with elevated levels of bilirubin (20 mg/dL), triglycerides (3000 mg/dL), protein (12 g/dL), red blood cells (0.4% v/v), or hemoglobin (500 mg/dL).

Preparation for Analysis

- Follow the tube manufacturer's processing instructions for serum and plasma collection tubes. Gravity separation is not sufficient for specimen preparation.
- Mix thawed specimens thoroughly by low speed vortexing or by inverting 10 times. Visually inspect the specimens. If layering or stratification is observed, continue mixing until specimens are visibly homogeneous.
- To ensure consistency in results, specimens must be transferred to a centrifuge tube and centrifuged at ≥ 10000 RCF (Relative Centrifugal Force) for 10 minutes before testing if
  - they contain fibrin, red blood cells, or other particulate matter
  - they require repeat testing, or
  - they were frozen and thawed.

  Transfer clarified specimen to a sample cup or secondary tube for testing.
- Centrifuged specimens with a lipid layer on the top must be transferred to a sample cup or secondary tube. Care must be taken to transfer only the clarified specimen without the lipemic material.

Storage

- Specimens may be stored on or off the clot, red blood cells, or separator gel for up to 14 days refrigerated at 2-8°C or for up to 3 days at 15-30°C.
- If testing will be delayed more than the recommended storage time, remove serum or plasma from the clot or red blood cells, and store frozen (-20°C or colder).
- No qualitative performance differences were observed between experimental controls and a minimum of 10 nonreactive or spiked reactive specimens subjected to 6 freeze/thaw cycles; however, multiple freeze/thaw cycles should be avoided.

Shipping

- Before shipping specimens, it is recommended that specimens be removed from the clot, red blood cells, or separator gel.
- When shipping specimens, package and label specimens in compliance with applicable state, federal, and international regulations covering the transport of clinical specimens and infectious substances.
- Specimens may be shipped ambient. Do not exceed the storage time limitations listed above.

PROCEDURE

Materials Provided

- 6L61 ARCHITECT *r*HTLV-I/II Reagent Kit

Materials Required but not Provided

- ARCHITECT *i* System
- ARCHITECT *i* System **ASSAY CD-ROM**
- 6L61-01 ARCHITECT *r*HTLV-I/II Calibrator
- 6L61-10 ARCHITECT *r*HTLV-I/II Controls
- ARCHITECT *i* **PRE-TRIGGER SOLUTION**
- ARCHITECT *i* **TRIGGER SOLUTION**
- ARCHITECT *i* **WASH BUFFER**
- ARCHITECT *i* **REACTION VESSELS**
- ARCHITECT *i* **SAMPLE CUPS**
- ARCHITECT *i* **SEPTUM**
- ARCHITECT *i* **REPLACEMENT CAPS**
- Pipettes or pipette tips (optional)

For information on materials required for maintenance procedures, refer to the ARCHITECT System Operations Manual, Section 9.

Assay Procedure

- Before loading the ARCHITECT *r*HTLV-I/II Reagent Kit on the system for the first time, the microparticle bottle requires mixing to resuspend microparticles that have settled during shipment. After the first time the microparticles have been loaded, no further mixing is required.
  - **Invert the microparticle bottle 30 times.**
- Visually inspect the bottle to ensure microparticles are resuspended. If microparticles remain adhered to the bottle, continue inverting the bottle until the microparticles have been completely resuspended.
  - **If the microparticles do not resuspend, DO NOT USE. Contact your local Abbott representative.**
- Once the microparticles have been resuspended, place a septum on the bottle. For instructions on placing septums on bottles refer to the **Handling Precautions** section of this package insert.
- Load the ARCHITECT *r*HTLV-I/II Reagent Kit on the ARCHITECT *i* System.
  - Verify that all necessary assay reagents are present.
  - Ensure that septums are present on all reagent bottles.
- Order calibration, if necessary.
  - For information on ordering calibrations, refer to the ARCHITECT System Operations Manual, Section 6.
- Order tests.
  - For information on ordering patient specimens and controls and for general operating procedures, refer to the ARCHITECT System Operations Manual, Section 5.
- The minimum sample cup volume is calculated by the system and is printed on the Orderlist report. No more than 10 replicates may be sampled from the same sample cup. To minimize the effects of evaporation, verify adequate sample cup volume is present before running the test.
  - Priority: 183 µL for the first ARCHITECT *r*HTLV-I/II test plus 133 µL for each additional ARCHITECT *r*HTLV-I/II test from the same sample cup.
  - ≤ 3 hours on board: 183 µL for the first ARCHITECT *r*HTLV-I/II test plus 133 µL for each additional ARCHITECT *r*HTLV-I/II test from the same sample cup.
  - > 3 hours on board: additional sample volume is required. For information on sample evaporation and volumes, refer to the ARCHITECT System Operations Manual, Section 5.
  - If using primary or aliquot tubes, use the sample gauge to ensure sufficient patient specimen is present.
- Prepare calibrator and controls.
  - Mix ARCHITECT *r*HTLV-I/II Calibrator and Controls by gentle inversion before use.
  - To obtain the recommended volume requirements for the ARCHITECT *r*HTLV-I/II Calibrator and Controls, hold the bottles **vertically** and dispense 20 drops of calibrator or 10 drops of each control into each respective sample cup.
- Load samples.
  - For information on loading samples, refer to the ARCHITECT System Operations Manual, Section 5.
- Press RUN.
- For additional information on principles of operation, refer to the ARCHITECT Operations Manual, Section 3.
- For optimal performance, it is important to perform routine maintenance as described in the ARCHITECT System Operations Manual, Section 9. When a laboratory requires more frequent maintenance, follow those procedures.

Specimen Dilution Procedures

Specimens cannot be diluted for the ARCHITECT *r*HTLV-I/II assay.

Calibration

- To perform an ARCHITECT *r*HTLV-I/II calibration, test the calibrator in replicates of three. A single sample of each *r*HTLV-I/II control level must be tested to evaluate the assay calibration. Ensure that assay control values are within the concentration ranges specified in the control package insert. The calibrator should be priority loaded.
- Once an ARCHITECT *r*HTLV-I/II calibration is accepted and stored, all subsequent samples may be tested without further calibration unless:
  - A reagent kit with a new lot number is used.
  - Controls are out of range.
- For detailed information on how to perform an assay calibration, refer to the ARCHITECT System Operations Manual, Section 6.

QUALITY CONTROL PROCEDURES

The recommended control requirement for the ARCHITECT *r*HTLV-I/II assay is that a single sample of each control be tested once every 24 hours each day of use. If laboratory quality control procedures require more frequent use of controls to verify test results, follow those procedures.

Each laboratory should establish control ranges to monitor the acceptable performance of the assay. The ARCHITECT *r*HTLV-I/II Control values must be within the acceptable ranges specified in the control package insert. If a control is out of its specified range, the associated test results are invalid and must be retested. Recalibration may be indicated.

Verification of Assay Claims

For protocols to verify package insert claims refer to the ARCHITECT System Operations Manual, Appendix B. The ARCHITECT *r*HTLV-I/II assay belongs to method group 5, except functional sensitivity.

RESULTS

The ARCHITECT *i* System calculates the cutoff (CO) using the mean chemiluminescent signal (RLU) from three replicates of the Calibrator 1 multiplied by 0.25 and stores the result.

Calculation

The ARCHITECT *r*HTLV-I/II assay calculates results based on a cutoff determined by the following calculation.

- Cutoff RLU = Calibrator 1 mean RLU value x 0.25
- S/CO = Sample RLU/Cutoff RLU
- The cutoff RLU is stored for each reagent lot calibration.
- The ARCHITECT *i* System calculates a result based on the ratio of the sample RLU(s) to the cutoff RLU for each specimen and control.

Interpretation of Results

- Specimens with S/CO values < 1.00 are considered nonreactive (NR).
- Specimens with S/CO values ≥ 1.00 are considered reactive (R).

NOTE: All specimens that are initially reactive must be centrifuged and retested in duplicate. Refer to the **SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS** section in this package insert.

For details on configuring the ARCHITECT *i* System to use grayzone interpretations, refer to the ARCHITECT System Operations Manual, Section 2. The grayzone interpretation from the ARCHITECT interpretations screen is not used by the ARCHITECT System unless a grayzone is configured.

Flags

Some results may contain information in the Flags field. For a description of the flags that may appear in this field, refer to the ARCHITECT System Operations Manual, Section 5.

LIMITATIONS OF THE PROCEDURE

- If the assay results are inconsistent with clinical evidence, additional testing is suggested to confirm the result.
- Heterophilic antibodies in human serum can react with reagent immunoglobulins, interfering with *in vitro* immunoassays.[20] Patients routinely exposed to animals or to animal serum products can be prone to this interference and anomalous values may be observed. Additional information may be required for diagnosis.

SPECIFIC PERFORMANCE CHARACTERISTICS

Precision

The ARCHITECT *r*HTLV-I/II assay is designed to have an imprecision of ≤ 10% total** CV for specimens within the range of 1.00 to 6.00 S/CO. The study was performed at one internal and two external evaluation sites each using one instrument. A panel consisting of three different control lots and two human plasma specimens was tested in replicates of four across three reagent lots and one calibrator lot per site. A total of three different calibrator lots were used. Each combination of instruments, panel members, and reagent lots was tested in four runs. Data from this study are summarized in Table 1*.

Table 1

ARCHITECT *r*HTLV-I/II Precision

Panel Member	n	Mean S/CO	Within Run SD	Within Run %CV	Total** SD	Total** %CV
Negative Control	432	0.10	0.02	23.61	0.03	25.44
Positive Control	432	4.05	0.15	3.80	0.17	4.31
Human Plasma HTLV I	144	1.77	0.06	3.31	0.07	3.72
Human Plasma HTLV II	144	1.82	0.07	3.66	0.07	3.98

* Representative data; results in individual laboratories may vary from these data. Higher imprecision may be observed in high reactive samples without changes in qualitative results.

** Total is an accumulation of within run, between run and between day.

Specificity

The ARCHITECT *r*HTLV-I/II assay is designed to have a specificity of ≥ 99.5% on a blood donor population and ≥ 99.0% on a hospitalized/diagnostic population. A study was performed at two external sites and one internal site on a total of 5646 serum and plasma specimens collected from six blood-donation centers and 692 hospitalized/diagnostic specimens. Data from this study are summarized in Table 2*.

Table 2

ARCHITECT *r*HTLV-I/II Specificity

Category	n	IR [%]	RR [%]	Resolved Specificity	95% Confidence Interval
Plasma	3583	2 [0.06]	2 [0.06]	99.94% (3581/3583)	99.80% - 99.99%
Serum	2063	2 [0.10]	1 [0.05]	99.95% (2062/2063)	99.73% - 100%
Overall Blood Donors	5646	4 [0.07]	3 [0.05]	99.95% (5643/5646)	99.84% - 99.99%
HP/Diagnostics	692	1 [0.14]	1 [0.14]	99.86% (691/692)	99.20% - 100%

* Representative data; results in individual laboratories may vary from these data.

Sensitivity

The ARCHITECT *r*HTLV-I/II assay is designed to have a sensitivity equivalent or greater than a commercially available diagnostic kit.

A total of 301 anti-HTLV-I and 105 anti-HTLV-II reactive specimens were tested, resulting in a sensitivity of 100% (406/406), 95% confidence interval: 99.10% - 100%. (Representative data; results in individual laboratories may vary from these data). These values were determined in a study where pedigreed specimens from individuals with HTLV infection were tested.

Interference

Additional studies were performed to evaluate other potential interfering disease states on the Architect *r*HTLV-I/II assay. A total of 260 specimens were tested from following categories: Viral infection (HBV, HSV, CMV, HCV, EBV, HIV-1, HIV-2); fungal/yeast/protozoal/bacterial infection *(T. pallidum, T. gondii, E. coli, C. trachomatis, N. gonorrhea);* autoimmune (rheumatoid factor [RF], antinuclear antibodies [ANA]), other conditions (pregnant females all trimesters, multiparous females, elevated IgG, elevated IgM, monoclonal and polyclonal gammopathy, influenza vaccine recipients, hemodialysis patients, hemophiliacs, multiple transfusion recipients). Data from this study are summarized in Table 3*.

Table 3

ARCHITECT *r*HTLV-I/II Potential Interfering Substances

Interfering Substances	n	IR n	RR n	Apparent Specificity	95% Confidence Interval
Total	260	1[a]	1[a]	100% (259/259)	98.59% - 100%

[a] One multiple transfusion sample initially and repeatedly reactive on Architect *r*HTLV-I/II was confirmed positive with an alternative enzyme immunoassay and a Western Blot.

* Representative data; results in individual laboratories may vary from these data.

BIBLIOGRAPHY

1. Poiesz BJ, Ruscetti FW, Gazdar AF, et al. Detection and Isolation of Type C Retrovirus Particles from Fresh and Cultured Lymphocytes of a Patient with Cutaneous T-cell Lymphoma. *Proc Natl Aca Sci USA* 1980; 77:7415.
2. Poiesz BJ, Ruscetti FW, Reitz MS, et al. Isolation of a New Type C Retrovirus (HTLV) in Primary Uncultured Cells of a Patient with Sezarry T-cell Leukemia. *Nature (London)* 1981; 294:268.
3. Blattner WA, Takatsuki K, Gallo RC. Human T-Cell Leukemia-Lymphoma Virus and Adult T-Cell Leukemia. *JAMA* 1983; 250:1074.
4. Gessain A, Barin F, Vermant JC, et al. Antibodies to Human T-Lymphotropic Virus Type-I in Patients with Tropical Spastic Paraparesis. *Lancet* 1985; ii:407.
5. Rodgers-Johnson P, Gajdusek DC, Morgan OSC, et al. HTLV-I and HTLV-II Antibodies and Tropical Spastic Paraparesis. *Lancet* 1985; ii:1247.
6. Osame M, Usuku K, Izumo S, et al. HTLV-I Associated Myelopathy, A New Clinical Entity. *Lancet* 1986; I:1031.
7. Gessain A, Gout O. Chronic Myelopathy Associated with Human T-Lymphotropic Virus Type-I (HTLV-I). *Ann Intern Med* 1992; 117(11):933.
8. Wiley CA, Nerenberg M, Cros D, et al. HTLV-I Polymyositis in a Patient also Infected with the Human Immunodeficiency Virus. *N Engl J Med* 1989; 320 (15): 992.
9. Blattner WA. Epidemiology of HTLV-I and Associated Diseases. In: *Blattner WA, ed. Human Retrovirology: HTLV. New York:* Raven Press, 1990; 251.
10. Rosenblatt JD, Golde DW, et al. A Second Isolate of HTLV-II Associated with Atypical Hairy-cell Leukemia. *N Engl J Med* 1986, 315:372.
11. Jacobson S, Lehky T, et al. Isolation of HTLV-II from a Patient with Chronic, Progressive Neurological Disease Clinically Indistinguishable from HTLV-I Associated Myelopathy/tropical Spastic Paraparesis. *Ann Neurol.* 1993; 33:392.
12. The T- and B-Cell Malignancy Study Group. Statistical Analysis of Clinico-pathological, Virological and Epidemiological Data on Lymphoid Malignancies with Special Reference to Adult T-Cell Leukemia/ Lymphoma: A report of the Second Nationwide Study of Japan. *Jap. J Clin Oncol* 1985; 1593:517.
13. Newton M, Cruickshank K, Miller D. et al. Antibody to Human T Lymphotropic Virus Type I in West-Indian Born UK Residents with Spastic Paraparesis. *Lancet* 1987; I: 415.
14. Saxinger W, Blattner WA, Levine PH, et al. Human T-Cell Leukemia Virus (HTLV-I) Antibodies in Africa. *Science* 1984; 225:1473.
15. Maloney EM, Biggar RJ, Neel JV, et al. Endemic Human T-cell Lymphotropic Virus Type II Infection Among Isolated Brazilian Amerindians. *J Infect Dis* 1992; 166:100.
16. Yanagihara R, Jenkins CL, Alexander SS, More CA, et al. Human T-lymphotropic Virus Type I Infection in Papua New Guinea: High Prevalence Among the Hagahai Confirmed by Western Blot Analysis. *J. Infect. Dis* 1990; 162:649.
17. Bastian I, Gardner J, Webb D, Gardner I. Isolation of Human T-Lymphotropic Virus Type-I Strain from Australian Aboriginals. *J. Virol.* 1993; 67(2):843.
18. Wiktor SZ, Cannon RO, et al. Infection with Human T-Lymphotropic Virus Type I and II in Sexually Transmitted Disease Clinics in Baltimore and New Orleans. *J Infect Dis* 1992; 165:920.
19. Zella D, Mori L et al. HTLV-II Infection in Italian Drug Abusers. *Lancet* 1990, 336: 575.
20. Boscato LM, Stuart MC. Heterophilic Antibodies; A Problem for all Immunonoassays. *Clin Chem* 1988; 34(1):27.

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