Subject: Re: ICD 10 search of Owen Clinic Patients
Date: Monday, July 22, 2019 at 2:15:06 PM Pacific Daylight Time
From: Maile Karris
To: Rawlings, Stephen
CC: Mathur, Kushagra, Gianella Weibel, Sara

Yup now you have to submit a request to cfar clinical core and attach the irb approval. It has to specifically say in the rp that allows investigators to generate a list of eligible participants and that this list will be given to providers

Sent from my iPhone

On Jul 22, 2019, at 2:05 PM, Rawlings, Stephen <strawlings@ucsd.edu> wrote:

> Dear Maile,
>
> Sara mentioned that you were willing to help us get a search done of the Owen patient database for patients with ICD10 codes that could suggest they are candidates for Last Gift.
>
> Kush, a medical student helping with the project, helped put together this list of ICD10 codes that we want to start with. Is it reasonable to run these against the clinic list? Is there anything else you need from us?

Condition	ICD-10 Code
Palliative Care	Z51.5
ALS	G12.21
Secondary Malignant Neoplasm of Brain	C79.31
Malignant neoplasm of brain, unspecified	C71.9
Hypertensive heart and chronic kidney disease with heart failure and with stage 5 chronic kidney disease, or end stage renal disease	I13.2
Neoplasm of unspecified behavior of digestive system	D49.0

Malignant neoplasm of bronchus and lung	C34

Thank you!

Cheers,
Stephen

UNIVERSITY OF CALIFORNIA, SAN DIEGO
HUMAN RESEARCH PROTECTIONS PROGRAM

Date: August 6, 2019

To: Dr. David Smith

Re: Project #160563
The Last Gift: Development of an End-of-life Translational Model to Characterize the HIV Reservoir

Dear Dr. Smith:

Your July 23, 2019 request to amend Project 160563 has been reviewed and approved using the expedited review process. This amendment included the request for waiver of consent and partial waiver of HIPAA for recruitment purposes. Your cover letter stated, "Due to the narrow and specific inclusion and exclusion criteria, per 46 CFR 46.116, for prescreening purposes only, we request a waiver of informed consent to interrogate the EPIC database and identify potential prospective participants who meet eligibility criteria. We also request a wavier of individual authorization for pre-screening recruitment purposes only of individual HIPAA/PHI. Justifications for this request are made on the research plan and in the body of this cover memo. We also made some personnel updates."

Your determination that this amendment will not require a change to the risk management procedures, informed consent document, or the risk/benefit ratio has been accepted.

The documents submitted for review included the following: cover letter, Amendment Request Form, revised Research Plan (clean and tracked changes), Biomedical Standard Facesheets

Please note that the amendment approval date does not alter the study expiration date. A modification is given approval only to the expiration date that was received at the most recent initial or continuing review. Also, please check your most recent initial or continuing review approval letter and ensure that continuing review materials are submitted approximately 45 days prior to that expiration.

In addition, IRB amendment approval does not constitute **other institutional required "approvals."** Should your study involve other review entities/committees such as Office of Clinical Trials Administration; Office of Coverage Analysis Administration; Independent Review Committee; Protocol Review Monitoring Committee; committees under Environmental Health & Safety such as Institutional Biosafety Committee and Human Exposure Review Committee; and/or Rady Children's Hospital – San Diego, Research Administration; it is the researchers responsibility to ensure that these entities/committees have been informed of the amendment request, as appropriate.

Thank you for keeping us informed.

On behalf of the UCSD Institutional Review Boards,

/nm

Kip Kantelo
Director
UCSD Human Research Protections Program
858-246-HRPP (858-246-4777); hrpp@ucsd.edu

UCSD Human Research Protections Program
New Biomedical Application
RESEARCH PLAN

1. PROJECT TITLE

The Last Gift: Development of an End-of-life Translational Model to Characterize the HIV Reservoir and the HIV RNA Rebound across Tissues

2. PRINCIPAL INVESTIGATOR

Davey Smith, MD
Professor of Medicine
Division of Infectious Diseases and Global Public Health
University of California San Diego

Other collaborators:
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University of California San Diego

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Karine Dube
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Chapel Hill, NC 27599

Jeff Taylor
AntiViral Research Center Community Advisory Board Co-Chair

University of California San Diego

Andy Kaytes
AntiViral Research Center Community Advisory Board Chair
University of California San Diego

3. FACILITIES

This study will be carried out primarily at the following sites:

a. UCSD Antiviral Research Center (AVRC)
220 Dickinson Street, Suite A
San Diego, CA 92103

b. UCSD Owen Clinic
UC San Diego Health – Hillcrest
Medical Offices South
4168 Front Street
San Diego, CA 92103

Prospective and longitudinal data collection and clinical evaluations will be carried out primarily at sites (a) and (b) at UCSD. Additional potential study sites include a total of more than 175 other facilities in San Diego County, including hospice facilities, hospitals, retirement communities, and private residences. Because the total number of participants enrolled to this protocol is vastly smaller than the number of potential end-of-life care facilities, we propose to obtain an appropriate and standardized hospice or care facility Memorandum of Understanding (MOU) from the medical director or signing official for each of these centers prior to enrolling (and consenting) the potential study participant (Appendix A: MOU).

Specimen Analysis
Stein Clinical Research Building
Center for AIDS Research (CFAR)
University of California San Diego
9500 Gilman Drive
La Jolla CA, 92093-0679

Data generation (only using de-identified tissue samples)
University Hospital Zurich (Günthard)
Rämistrasse 100
8091 Zurich, Switzerland

Data Analysis (only using de-identified data)
The Harvard T.H. Chan School of Public Health (DeGruttola)
677 Huntington Avenue
Boston, MA 02115

4. ESTIMATED DURATION OF THE STUDY

The study's duration is expected to be 5 years.

5. LAY LANGUAGE SUMMARY OR SYNOPSIS (no more than one paragraph)

This study is designed to evaluate what factors might influence the levels of HIV DNA in blood and across the body during antiretroviral therapy (ART) as well as HIV RNA rebound dynamics in various tissues after ART interruption. To do this, we will engage and enroll people living with HIV who are very sick and have less than six months to live. These participants will be very interested in helping HIV researchers understand more about

how HIV lives throughout the human body (for example in gut, lymph nodes, genital tract, brain and other sites). Therefore, as part of this study, we will enroll 30 motivated people living with HIV and we will follow and characterize them during the last few months of their life and then characterize the HIV that can be found throughout their body after they die.

6. SPECIFIC AIMS

Our objectives:

- To establish a cohort of people living with HIV (referred to as *"The Last Gift"*) who are terminally ill and motivated to participate in HIV cure research during the last few months of their life.
- Ante-mortem: To characterize the participants during their terminally-ill period including (1) use of medications and other substances (e.g. antiretroviral therapy [ART], pain medications, others), (2) thoughts and feelings about end-of-life research for HIV, (3) virologic and immunologic measures in the blood.
- Post-mortem: To characterize the virologic and immunologic milieu throughout the participants' body (at autopsy).

Rationale for involvement of terminally ill, HIV infected persons. The choice to involve a terminally ill population is motivated by: i) the absence of any reasonable expectation of clinical benefit by the volunteers, ii) the desire that many terminally-ill persons voice to "give back" and contribute in some way prior to their death. Local work in this area demonstrates that the concept of this research is widely accepted among local HIV communities (see summary of survey results described below). Finally, this study will allow us to characterize the full-body HIV reservoir in relation to ART use and use of other substances in these altruistic volunteers. Such information would be extremely important in future cure-related studies.

7. BACKGROUND AND SIGNIFICANCE

To cure HIV, we need a better understanding of the distribution of the HIV DNA reservoirs throughout the body and how these HIV reservoirs contribute to viral rebound after discontinuation of ART. Extensive investigations in humans have been unable to fully characterize the large and complex reservoirs that must be eradicated to achieve a cure, in part because most studies have necessarily been limited to sampling of blood, with limited cerebrospinal fluid (CSF), genital secretion or gut sampling.

As part of this study, we will methodically characterize the size, distribution, activity and mechanisms of persistence of the HIV reservoir throughout the body (blood, brain, genital tract, gut, etc.) and determine the associations between the characteristics of these HIV reservoirs and drug consumption. Specifically, we will leverage this innovative model to address the following important open questions:

Reservoir Sampling Problem. A critical barrier to eradicating HIV is our limited understanding of viral persistence in anatomic reservoirs and how external factors, like substances of potential abuse, can shape their composition. Because ART does not eradicate latently infected cells, viremia generally rebounds within 2-4 weeks after ART is interrupted. This replication competent virus that remains in cells during ART represents the major barrier to curing HIV. Further, even if strategies currently in development succeed in purging HIV from CD4+ T cells, residual virus will likely remain in the central nervous system (CNS), lymph nodes, adipose, and other tissues. Most human studies have characterized non-blood HIV reservoirs using limited biological samples from otherwise healthy individuals living with HIV (e.g. semen, CSF, small biopsies from gut or lymph nodes), or autopsy specimens with little pre-mortem characterization. The glaring differences between these cohorts have confounded our understanding of HIV reservoirs throughout the body. It is also unclear, to what extend these tissue reservoirs might contribute to HIV RNA rebound after ART interruption.

Last Gift solution. To overcome this limitation, we will develop a unique clinical resource, called the *'The Last*

Gift' cohort. This cohort will comprise altruistic individuals living with HIV on ART who have a terminal illness (e.g. solid organ cancer, cardiovascular disease) and who have less than six months to live (according to their primary care physician). In these volunteers, we will measure cellular and tissue reservoirs of HIV in blood (ante-mortem) and compare these reservoirs in blood and anatomic compartments (at autopsy) to best understand how HIV reservoirs persist during ART. If participants interrupt ART before death, we will also characterize rebounding HIV RNA populations across the body.

Replication Competence Problem. During ART, the HIV DNA population exists in multiple forms: (i) intact and replication competent, (ii) intact but replication incompetent, and (iii) not intact. Further, <1% of infected $CD4^+$ T cells carry replication-competent (intact) HIV DNA. While we have a reasonable idea about the composition of the HIV DNA reservoir in circulating blood cells and (to a lesser extent) lymphoid tissues, little is known about HIV reservoirs in other tissues. The current gold standard to measure replication competent provirus in blood is the Quantitative Viral Outgrowth Assay (QVOA). However, QVOA is limited by the cost, labor and time it takes to perform the assay, and because it cannot measure intact viral genomes that are not inducible by *in vitro* stimulation. The abundance of intact proviruses that are not inducible by currently available agents means that the *QVOA largely underestimates* the size of the replication competent reservoir. The variability in the frequency of inducible replication-competent proviruses across individuals and time-points, also suggests that QVOA is unreliable, even in blood. These issues are even more relevant in solid tissues, which are usually obtained from autopsies and are not amenable to in vitro stimulation.

Last Gift solution. Next generation sequencing (NGS) technology can overcome many of the described limitations of the QVOA for tissue specimens. Specifically, the single-molecule real-time sequencing platform can sequence the 9,749 base pairs (bp) needed to cover the full-length (FL) HIV DNA. We will use this technology to determine which proviruses contain fully intact genomes and to measure the relative viral diversity in blood and in tissues. Intact HIV sequences from blood and tissues will be cloned into pNL4-3 vectors to test their replication and fitness competence.

Reservoir Persistence Problem. Most HIV reservoirs reside outside of the bloodstream, and cellular mechanisms of HIV persistence in humans likely differs across anatomic compartments. Existing strategies to reactivate latent provirus have been largely tested using cells from peripheral blood, primarily because of the sampling and assay limitations associated with other tissues. Also, candidate interventions for eradication studies have been selected mainly on the basis of mechanisms of latency identified using primate models and cells from the peripheral blood of individuals living with HIV; however, epigenetic control of HIV transcription likely varies between: infected cells of different lineages (e.g. T cells vs. monocytes), various tissues, and T cells of various maturation stages. Other mechanisms that contribute to HIV persistence also likely differ throughout the body including: homeostatic proliferation of HIV-infected cells, residual HIV transcription, and proliferation of CD4 T cells with selective viral integrants. To evaluate which interventions can impact HIV reservoirs across the body, mechanisms of viral persistence need to be compared across relevant tissues.

Last Gift solution. The 'Last Gift' cohort will provide unparalleled opportunity to characterize the human mechanisms that regulate HIV latency and persistence throughout the body. We hypothesize that the maintenance of HIV latency in tissue CD4 T cells and macrophages is controlled, at least in part, through similar mechanisms as in peripheral blood cells, but this will need to be specifically evaluated. To this end, we will simultaneously characterize and compare putative mechanisms of HIV persistence in blood and selected anatomic compartments, including epigenetic profiles, measures of clonal expansion and residual HIV transcription.

Opioid Use and HIV Reservoirs. Substance abuse is a worldwide public health concern, and opiates are

widely abused addictive drugs. According to the CDC, heroin use has increased by 63% from 2002 to 2013 among the US population. The strongest risk factor for heroin abuse is prior abuse of prescription opiates, and prescription opiates are one of the most abused substances in the US with 3-8% of adults reporting use of these substances in 2013. Convergent evidence from multiple groups has shown that morphine and synthetic opioids potentiate HIV infection of human monocyte-derived macrophages, in part by inducing increased expression of galectin-1. Galectin-1 directly binds to HIV in a β-galactoside-dependent fashion through recognition of clusters of N-linked glycans on the viral envelope gp120, accelerating viral adhesion and entry into susceptible cells. Thus, exposure to opioid medications, particularly in the presence of active viral replication, might increase the HIV reservoir in myeloid cells. To date, however, this hypothesis has not been tested in humans, and the impact of opioids on HIV reservoirs in different tissues, particularly the brain, where endogenous opioid signaling occurs, has not been specifically examined.

Last Gift solution. Prescription opiates are used to relieve pain and suffering associated with terminal illness. These are the same prescription drugs that are commonly abused by individuals not needing them for pain relief. Investigating reservoirs among individuals living with HIV who use prescription opioids offer an opportunity to understand how such substances impact the HIV reservoir.

Preliminary Data:
In preparation to this application and to demonstrate feasibility, we have: (i) surveyed HIV-uninfected and (ii) HIV-infected individuals concerning hypothetical biomedical research in the last six months of life that has no benefit for them but may help others.

- Uninfected survey data: Our IRB-approved survey (Protocol number: 150457) included 440 U.S. citizens between the ages of 25 and 44 years; 50% were women, mostly white (77%) and with 60% having a salary <$50,000/year. Over 90% reported that they "*would consider participating in a study that would potentially help others but not themselves*" if they had a terminal illness and only six months left to live; 88% reported that they "*would endure blood draws*" for research. Interestingly, 40% reported that they "*would be willing to reduce their lifespan by a week or more as a consequence of research*", and 90% "*would donate their body to science after death*".

- HIV-infected and healthy: Our IRB-approved survey (Protocol number: 150457) included a random sample of 97 adults living with HIV receiving care at the UCSD Owen Clinic, of whom 6.3% were women; 39% self-identified as white non-Hispanic, 30% as Hispanic, and 18.6% as African American. Most reported having a salary <$50,000/year and being diagnosed with HIV for over 10 years. Over 80% responded that they "*would consider participating in a study that would potentially help others but not themselves*" if they had a terminal illness and only six months left to live, and "*would endure blood draws*" for such research. Interestingly, 58% reported that they "*would be willing to reduce their lifespan by a week or more as a consequence of research*", and over 70% reported they "*would donate their body to science after death*"

8. PROGRESS REPORT

Not Applicable

9. RESEARCH DESIGN AND METHODS

Study population (peri-mortem cohort, *"The Last Gift"*): As part of this study, we will enroll 30 individuals living with HIV who are terminally-ill with six months or less to live, as determined by their primary care provider. Based on a survey of UCSD Owen patients entering hospice care over the past year, roughly half chose to interrupt ART before their death, while the other half continued their ART until death.

Participants in this study will be co-enrolled into the UCSD California NeuroAIDS Tissue Network (CNTN, PIs: David Moore, PhD and Cristian Achim, MD, PhD, CNTN IRB Project #171024). They will

undergo all the procedures specified in the CNTN protocol separately from the procedures that they complete as part of this study. Participants may withdraw from this study without jeopardizing participation in CNTN.

Study design: For each participant, we will obtain blood samples once every 1-4 weeks (20-60mL) (or twice weekly during viral rebound if ART is interrupted) during the last 6 months of life to evaluate **ante-mortem**: (1) blood plasma HIV RNA levels; (2) HIV DNA levels, viral genetics by next generation sequencing (NGS), and replication competence by QVOA and clonal expression. When it clinically appears death is imminent, blood draw may be taken up to daily with the option to refuse by the participants or NOK. A weight adjusted table of the maximum blood draw volume allowed (Clinical + Research) is provided in Appendix B. If participant agrees, we will also collect stool for microbiome analysis and genital secretion. Study visits and assessments are summarized in Appendix C: Schedule of Evaluations.

Ante-mortem Assessments (Appendix C: Table 1):

- Screening Evaluation: will include informed consent and verification of eligibility checklist. The screening evaluation must be completed within 30 days of the baseline (Day 0) visit.
- Baseline Visit (Day 0-30): Because study participants may fatigue during the collection of study data, baseline (Day 0) data may be collected between day 0 and day 30 and may occur during multiple visits.
    - Clinical data collection will include: demographics, HIV risk factors, estimated duration of HIV infection, smoking history, medical history, sexually transmitted infection and hepatitis history, substance use assessment (as indicated on PRISM/CIDI), current and past ART history, and concomitant medications.
    - Limited physical examination: a physical exam will be performed targeted to clinical signs and reported symptoms.
    - Blood collection will include: blood for CD4/CD8 count and HIV viral load (total 10 mL). Blood will also be collected for banking of plasma and peripheral blood mononuclear cells (target volume 30 mL).
    - Urine collection: a urine sample will be collected for toxicology if the subject is able to provide the sample.
    - Opioid CRFAn opiate case report form (CRF) will be completed to the best of the subject's ability .
    - A stool sample (or stool swab in those unable to provide a stool sample) and genital secretion sample will be collected at baseline in participants who agree to provide these samples (stool, genital secretion, vaginal specimen collection protocols, Appendix H-1, H-2, H-3 and H-4). Any time a stool/stool swab, semen and/or vaginal secretion sample is collected, we will ask the participant to complete a specialty questionnaire related to the specific sample being collected. This questionnaire will address issues that may influence the characteristics of the sample that was collected including the participant's diet, recent antibiotic use, and recent sexual history.
    - Questionnaires: an End-of-Life (EOL) questionnaire (Appendix D – modules 1, 2, 4, 5 – 45-60 min) will be administered over one or multiple visits depending on the participants' desire and compliance. Either the study staff or the study participant can complete the questionnaire (if s/he is able). The participant can decide to interrupt the questions anytime if s/he is tired or wishes to stop. The EOL questionnaire will include questions about demographic characteristics, reasons behind participation in the study, attitudes towards HIV cure research, understanding of the study, perceptions of risks and

benefits, facilitators and barriers, willingness to participate in research, quality of life and meaning of participation. This questionnaire will also ask questions about participants' attitudes about the death with dignity law in California (medical aid to end life). Interviewers are available to discuss any concerns or anxieties that this topic may raise for participants and to provide referrals to a clinician (psychologists, psychiatrists or masters-level clinician) at the HNRC should the participant become distressed during the course of the interviews or express suicidal ideation. This will be important for recruitment of future participants and to understand how participants perceive the study.

  - In consenting patients, the baseline questionnaire will be digitally recorded. The principal investigator, co-investigators, and research assistants will review transcripts and audiotapes will be destroyed upon completion of the study. Video recording will be offered as an alternative for remote interviews (if in person interview is not possible) using HIPAA compliant teleconferencing tool, specifically UC-wide approved Zoom (UCOP executed a BAA with Zoom on behalf of the entire UC system in 2016, see https://cio.ucop.edu/new-uc-zoom-agreement-for-video-web-and-audio-conferencing/, https://zoom.us/docs/doc/Zoom-hipaa.pdf). If the participant declines audio or video recording, the questionnaire will be completed by hand only. We will store all audio and video files in a password-protected folder and follow the utmost confidentiality procedures (see below). All audio and video files and tapes will be under lock and key. A professional transcriber will transcribe all interviews data verbatim. Once transcriptions are completed, we will verify all transcripts against the audio files and make corrections as necessary using the tracked changes function in Word. Once the verification of the transcripts is complete, we will conduct a content analysis aimed at identifying key themes and categories, prior to data coding. We will then proceed to coding and analyzing the data.

- Release of Information: written consent for sharing of all medical and HIV related data will be obtained in order to share (send and receive) relevant information between care providers and the study team.
- Depression survey: A Beck Depression Inventory (BDI) will be collected unless the data was collected during a CNTN visit within 3 months of the Last Gift baseline visit.
- Quality of Life assessment (Appendix E): A Quality of Life in Seriously Ill Patients questionnaire will be collected unless the data was collected during a CNTN visit within 3 months of the Last Gift baseline visit.
- Surrogate form (Appendix F): self-certification of surrogate decision makers will be recorded unless the data was collected during a CNTN visit within 3 months of the Last Gift baseline visit.
- Study design and purpose will be discussed with appropriate hospice staff and participants next of kin. An "In the Event of Death" form will be completed (Appendix G) and provided to the responsible party who will notify CNTN staff (who will notify LG staff) immediately upon being notified of participant's death.
- Study staff will discuss end of life issues including advanced health care directives, cremation/burial referrals, Physician's Orders for Life-Sustaining Treatment (POLST), and organ donation/autopsy consent with all participants.

- On Study:

- Study visits will occur every 1-4 weeks (less frequent visits will be performed in patients who are assessed to be clinically stable, while more frequent visits will be performed for patients who are thought to be closer to death). Study visits will include the following:
  - Substance use assessment, current ART use and adherence since last visit, concomitant medications, and adverse event monitoring.
  - Limited physical examination: a physical exam will be performed targeted to clinical signs and reported symptoms.
  - Blood collection will include: blood for HIV viral load (total 6 mL) and for banking of plasma and peripheral blood mononuclear cells (target volume 30 mL).
  - Urine collection: a urine sample will be collected for toxicology once a month during study if the patient is able to provide the sample.
  - Opioid CRF: An opiate CRF will be completed to the best of the patient's ability.
  - A stool sample (or stool swab in those unable to provide a stool sample) and genital secretion sample will be collected at every 4 weeks (+/- one week) in participants who agree to provide these samples (stool/stool swab, genital secretion, vaginal specimen collection protocols, Appendix H-1, H-2, H-3 and H-4). Any time a stool/stool swab, semen and/or vaginal secretion sample is collected, we will ask the participant to complete a specialty questionnaire related to the specific sample being collected. This questionnaire will address issues that may influence the characteristics of the sample that was collected including the participant's diet, recent antibiotic use, and recent sexual history.
  - Follow-up questionnaires: a follow-up End-of-Life questionnaire (30 min) will be administered once a month during study (Appendix D, Module 6). As above, a digital audio (and possibly video) recording will be performed in consenting patients, and a pen and paper questionnaire will be performed for patients that do not consent to audio recording.
  - Study design and purpose will be discussed with appropriate hospice staff and participants next of kin.

- ART Interruption (Appendix C, Table 2):
  - At any point during study that the participant makes the decision to interrupt ART, twice weekly study visits will occur until virologic relapse is demonstrated (VL>10,000 copies/mL). The first ART interruption visit will occur as soon as possible after ART is discontinued.
    - Blood collection will include: blood for HIV viral load (total 6 mL) and for banking of plasma and peripheral blood mononuclear cells (target volume 20 mL) twice per week. . The target draw of 20mL is twice a week, but it is a case-by-case decision by study staff. We will limit blood draws if subject has a very low Hb or if we are close to exceeding the maximum allowed blood in a 30-day period.
  - Once virologic relapse is demonstrated, the participant will resume the "parent" schedule of evaluations (as above, Appendix C, Table 1).

- End of Study (Appendix C, Table 3):
  - In patients who elect to discontinue study participation, an end-of-study visit will be performed

as indicated in Appendix C, Table 1). Study participants may withdraw from the study at any time. Specimens and data collected on study prior to withdrawal will be used unless the participant requests otherwise on the informed consent document. If a subject withdraws or is discontinued from the study, we will not support costs for cremation and provision of two death certificates.

- Post-mortem (Appendix C, Table 3):
  - Upon receiving notice of participant's death, the Last Gift Autopsy protocol (Appendix I) will be initiated and relevant study staff will be immediately notified (Appendix J).
  - Blood collection will include: blood for HIV viral load and for banking of plasma and peripheral blood mononuclear cells (target volume 30 mL).
  - Participants in this study will undergo autopsy via their participation in CNTN.
  - Last Gift autopsy tissue samples will be collected from a wide variety of anatomic sites for HIV DNA levels, viral genetics by NGS, and replication competence by clonal expression and QVOA.

Study Discontinuation:
Participants may be discontinued without their consent under the following circumstances:

1. If the participant moves out of region.

2. If the participant refuses an autopsy or withdraws consent for an autopsy.

3. If the participant's next of kin refuses autopsy of participant.

4. If the participant dies under circumstances such that Last Gift investigators believe that rapid autopsy would no longer result in meaningful/useful data.

5. If the participant does not comply with study visits.

Post-mortem histological data: Similar to published CNTN procedures (https://www.nntc.org/), the pathology protocol was developed with a focus on nervous system evaluation and expanded to also explore other specimen resources that can be obtained from the autopsy. The protocol was designed to: 1) comprehensively sample tissues that are susceptible to injury from HIV and represent an important HIV DNA reservoir; 2) preserve tissues for a wide range of research methodologies; and 3) whenever possible collect tissue within 6-8 hours of death to maximize probability to maintain cells alive for induction and outgrow assays. Briefly, the protocol will harvest tissue samples from different brain regions, spinal cord, muscle, peripheral nerves, GALT, lymph nodes, spleen, liver, bone marrow, heart, kidney, lungs, adipose tissue and genital tract for snap freezing and routine formalin fixation. Fixed tissues are examined by a board-certified pathologist (Dr. Hansel) who renders appropriate neuropathologic and systemic diagnoses that are tabulated into the study database. The neuropathologic examination includes specific categorization of key diagnoses such as HIV encephalitis (HIVE), microglial nodule encephalitis, opportunistic infections, neoplasms and vascular disease [60, 61]. Appendix K provides a summary of the planned data generation.

Data Generation and Analysis
The size and distribution of the HIV reservoir during suppressive ART will be determined by measuring and comparing levels of: (i) total HIV DNA, (ii) intact and not intact HIV DNA sequences, (iii) proviral genetics, and (iv) replication competent proviruses in blood (before and after death) and in anatomic compartments (after death), and (v) proviral epigenetic marks in blood (before and after death) and in anatomic compartments (after

death)

i. *Cellular HIV DNA and RNA transcripts* in PBMC and other tissues will be quantified by ddPCR. Since each participant will be on ART for different periods of time, which can influence HIV DNA levels, we will compute HIV DNA levels in each anatomic tissue *relative to* HIV DNA levels in paired PBMC. While not perfect (different infected cell types in each tissue, which likely have different levels of integrated provirus and different turnover), this normalization will assist intra- and inter- host comparisons.

ii. *Intact and not intact HIV DNA sequences* will be characterized and quantified by FL HIV DNA NGS procedures. In brief, we will use our innovative assay to deeply sequence provirus in blood and solid tissues and determine if sampled HIV DNA variants are intact or not intact and the genetics of these variants.

iii. *Proviral genetics* will be characterized using the same sequences as above (iii) to determine molecular diversity, cellular tropism, presence of DRM….

iv. *Replication competent proviruses* will be measured in resting CD4 T cells collected before and after death using QVOA. This assay is the current 'gold standard' to measure the frequency of CD4 T cells that can be induced to produce infectious virus after a single round of *in vitro* stimulation. *Since the QVOA procedures might not work in solid tissues*, we will also use our sequence-based assay to measure and to genetically characterize replication competent provirus.

v. *Proviral epigenetic marks* in PBMC and other tissues will be measured using three different assays: bisulfite capture and sequencing of the HIV provirus to measure DNA methylation, ChIP-seq followed by HIV probe-based capture to measure histone modifications, and ATAC-seq followed by probe-based capture to measure open chromatin in the HIV provirus. These measures will be normalized to proviral load and correlated with intact proviral DNA both on and off ART to evaluate epigenetic control of the HIV provirus.

The activity of the HIV reservoir during ART will be determined by measuring cell-free HIV RNA levels in blood plasma, CSF supernatant and genital secretion using a single copy assay, and cellular HIV RNA transcription in isolated CD4 T cells and appropriately stored anatomic tissues using ddPCR. Similar to above, these measures will be compared between blood samples (collected before and after death) and across various tissues from anatomic compartments (after death).

Epigenetic mechanisms of HIV persistence during ART in CD4 T cells and monocytes from blood, and various tissue compartments will be identified using targeted ChIP experiments to measure HIV LTR occupancy by specific transcriptional repressors and nucleosome modifications at the LTR. Bisulfite sequencing will be performed to determine contribution of CpG dinucleotide methylation in the HIV LTR to the persistence of HIV during ART. Clonal expansion mechanisms of HIV persistence during ART will be assessed by using sequencing technologies to measure frequency of unique integration sites of HIV within the human genome in blood and various tissues.

We will devote considerable resources to determine the size of replication competent HIV DNA in the brain tissue and to investigate unique mechanisms of HIV persistence in the brain. We will use highly sensitive in situ hybridization (ISH) techniques, and laser-capture micro-dissection (LCM) to target coding and noncoding RNA in brain tissue and study their cellular distribution and association with viral protein products and markers of neuroinflammation. We will assess levels of glial activation (GFAP, Iba1, HLA-DR), oxidative stress (sestrin 2) and blood-brain barrier integrity (occludin and Z01). We will perform ISH experiments on formalin-

fixed paraffin-embedded brain tissue. To isolate single cells (e.g. astrocytes vs. microglial cells) or focal regions of interest (e.g. microglial nodules or perivascular inflammatory infiltrates) for in depth molecular pathology and sequencing analysis we will use LCM followed by DNA PCR, mRNA arrays and sequencing procedures.

Prescription histories and calculate an index of cumulative drug exposure, e.g. morphine milligram equivalents (MME) (100). (ii) Collect detailed reports of current and past use of substances including opiates (prescribed or not), marijuana, stimulants, and alcohol (as indicated by M.I.N.I. (101) and urine toxicology during our regular ante-mortem visits. (iii) In post-mortem samples, we will quantify opiates, marijuana, methamphetamine, and cocaine in brain, gut, genital tract and lymph node samples, by organic extraction of 100 mg frozen tissue in 1 M NaOH and cyclohexane followed by gas chromatography/mass spectrometry or other appropriate validated assays.

How opiate use affects the size, distribution and activity of the HIV reservoirs within the body will be determined by comparing levels of: (i) total HIV DNA, (ii) intact and not intact HIV DNA sequences, (iii) proviral sequences, (iv) replication competent proviruses in CD4+ T cells, (v) levels of HIV RNA transcription in blood samples collected before and after death and in anatomic compartments after death in relation to the measures of substance use, in particular opiates. Simple associations between levels of drug and HIV reservoir size (HIV DNA levels) and activity (HIV RNA levels) will be assessed using Pearson correlation, separately for each sampled tissue. The strength of associations between each drug and HIV reservoir size and activity will be also compared between tissues using a generalized estimating approach (GEE), which permits correlated outcomes, to regress reservoir measures on drug levels across tissue compartments.

Fluid Banking, Autopsies, and Organ Tissue Collection and Banking

For participants enrolled in-life, data and blood collected during ante-mortem evaluation and data resulting from laboratory analysis of fluids will be banked. Autopsy data, additional data abstracted during post-mortem medical charts review, tissue, fluids and data resulting from laboratory analysis of tissues and fluids will also be banked. For individuals with documented autopsy consent and HIPAA authorization obtained through hospital services or other end-of-life planning, autopsy, tissue and fluid collection, and data resulting from laboratory analysis of tissues and fluids will also be banked. Post mortem neuroradiological procedures may be performed on some tissues. These procedures include postmortem imaging and 3D histological analysis. Data from these analyses will be banked. We will only perform autopsy and tissue acquisition for 'The Last Gift' study if pre-consent has been obtained and documented. Likewise, we will only access health records for autopsy and organ donors when authorization has been obtained and documented.

The Principal Investigator may authorize the release of anonymous data, fluids, and/or tissues stored in the bank to investigators conducting IRB approved research.

10. HUMAN SUBJECTS

We will enroll 30 appropriate individuals living with HIV in the 'Last Gift' cohort.

Inclusion criteria

- Age≥18, HIV infected
- Estimated survival of less than six months according to their primary care physician (i.e., hospice eligible).
- Capacity to provide informed consent in English (or if lacking capacity, has next of kin with capacity to provide informed consent in English)

- Co-enrolled in CNTN and agree to an autopsy and organ donation upon death via CNTN. Participant Informed Consent for autopsy will be reviewed and discussed with next of kin in order to minimize concerns or conflicts at the time of death.

Exclusion Criteria

- Unwilling or unable to comply with study-related procedures
- Any factor or factors that in the opinion of the local investigator that could prevent compliance with study requirements.

NOTE: Persons who are eligible but decline enrollment will be asked to complete a brief social-behavioral questionnaire (15 min, Appendix D, Module 3) in order to collect information about their reasons for declining study participation. The goal of this questionnaire is to better understand the rationale of persons who do and do not agree to participate in end-of-life research.

This study will not include recruitment of the following vulnerable populations: pregnant women, fetuses, neonates, prisoners, children, groups with known cognitive impairment, or institutionalized individuals.

11. RECRUITMENT AND PROCEDURES PREPARATORY TO RESEARCH

The Last Gift study will enroll 30 HIV-positive, hospice eligible (i.e., terminally ill) patients who are also enrolled in CNTN. Patients will also be recruited directly from local clinic and care providers (Appendix L: outreach flyer to be posted in clinics), though simultaneous or prior enrollment to CNTN is an eligibility requirement for the Last Gift Study. Drs. Smith, Little and Gianella will provide outreach educational seminars and recruitment flyers to San Diego County care providers and case managers that may care for terminally ill patients who may be appropriate candidates for enrollment*. We will also post recruitment flyers at local hospice facilities, clinics, and retirement communities and post online educational materials to study volunteers. We will work closely with Drs. Moore and Achim and their CNTN recruitment team to engage these participants to co-enroll them in the Last Gift study. Potentially eligible participants will be provided a description of the study by Dr. Smith (PI of this study) or another qualified study team member, who will address study specific questions.

In addition, due to the narrow and specific inclusion and exclusion criteria, for pre-screening recruitment purposes ONLY, we are also requesting a waiver of informed consent to interrogate the EPIC database and identify potential prospective research participants who meet the eligibility criteria for enrollment as listed in Item 10 Human Subjects.

The investigator believes the pre-screening to be used for recruitment meets the following requirements for this request per 46 CFR 46.116:

1. The (pre-screening) procedure is considered no more than minimal risk to the potential subjects, since we will not perform any procedure and the probability and magnitude of harm or discomfort anticipated in the research are not greater than those ordinarily encountered in daily life.
2. The waiver or alternation will not adversely affect the rights and welfare of the subjects.
3. The (pre-screening) research could not practicably be carried out without the waiver or alternation; and.
4. Once the potential participants are identified, we will contact their PCP and ask them to distribute one of our IRB-approved flyers. If interested, study participants will contact the study team and schedule a screening visit (per IRB-approved study protocol). Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

Recruitment procedures will also involve the review of subject records by designated study personnel (e.g., investigators and/or study coordinators) in order to identify potentially eligible subjects. Since Protected Health Information (PHI) will be accessed via the hospital's medical record database prior to contacting the potential subject about the research study, we are requesting a waiver of HIPAA authorization for access to PHI for purposes of prescreening only.

Standard HIPAA authorization to collect research data from the subject's medical record will be obtained at the time of informed consent.

A brief subset of preliminary eligibility criteria such as age, gender, and sexually transmitted disease diagnosis in the past 12 months, will be reviewed by study personnel to determine subjects' preliminary eligibility for the research study. No written record of this information will be created. There will be no direct contact of the potential research subject by the pre-screener (i.e., study staff). The pre-screener will ask the subject's treating physician to approach the subject. The treating physician will further discuss the research study with the potential subject and ask whether they would like to be contacted by study staff to discuss the trial (i.e., counseling) and/or provide the potential subject with the study staff's contact information. Eligibility may be formally determined at the time of counseling, but any research-specific screening procedures will only be performed after informed consent is obtained and a standard, stand-alone HIPAA authorization form is signed.

Due to the narrow and specific inclusion and exclusion criteria , we also request a waiver of individual authorization for pre-screening recruitment purposes ONLY of individual HIPPA/Protected Health Information. The following conditions apply:

1. The (pre-screening) research involves no more than minimal risk, since we will not perform any procedure and the probability and magnitude of harm or discomfort anticipated in the research are not greater than those ordinarily encountered in daily life.
2. Granting of waiver for recruitment purposes only will not adversely affect privacy rights and welfare of the individuals whose records will be used.
3. The pre-screening could not practicably be conducted without a waiver.
4. The pre-screening could not practicably be conducted without use of PHI.
5. The privacy risks are reasonable relative to the anticipated benefits of research.
6. An adequate plan to protect identifiers from improper use and disclosure is included in Item 16.
7. Participant identifiers/sensitive information shall be removed/destroyed as soon as they are no longer needed and in accordance with AVRC policy. The investigators have procedures in place to periodically review collected participant identifiers/sensitive information to ensure it is still required to satisfy a particular purpose or carry out a function.
8. The participants' PHI will not be re-used or disclosed for other purposes.
9. Once the potential participants are identified, we will contact their PCP and ask them to distribute one of our IRB-approved flyers. If interested, study participants will contact the study team and schedule a screening visit (per IRB-approved study protocol). Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

To ensure that recruitment methods to "The Last Gift" cohort are sensitive to the feelings of the Last Gift eligible individuals and are not considered coercive, Susanna Concha-Garcia (or other qualified study staff) will perform an in-depth qualitative interview with each consenting participant to examine their opinions and

perceptions regarding the relative risks and benefits of the proposed clinical study (Appendix D: End of Life Qualitative Interview Guide). Interviews will be performed at study entry to the Last Gift study, after obtaining informed consent. Results from this interview will inform our outreach strategies, content, and management of Last Gift cohort participants who are enrolled to studies. *NOTE: Recruitment and enrollment of study participants within a specific institute will only happen after we receive written approval from the medical directors or administrators at each community. Specific letters of cooperation will be solicited from these institutions, and copies of these letters will be submitted to the IRB for record-keeping purposes. When working at a facility that is covered by the Privacy Rule, we will request for partial waiver of HIPPA to allow pre-screening of candidates. Pre-screening criteria will be compliant with HIPPA regulations. During the course of the project we expect to iteratively involve new centers and communities and recruit participants accordingly. We will keep the IRB informed of additional centers and field sites for research, including written approval from each new facility provider or administrator.

12. INFORMED CONSENT

This protocol and the informed consent document and any subsequent modifications will be reviewed and approved by the UCSD Institutional Review Board responsible for oversight of the study. Written informed consent will be obtained from the subject from Dr. Smith or another member of the study staff. At the time potential participants contact us regarding the study, any questions they may have will be answered by a member of the study staff. If the potential subject is still interested in participating, a clinic visit will be scheduled. The participant will be informed of the time that needs to be allotted for their first visit in which the informed consent will be administered.

The informed consent will describe the purpose of the study, the procedures to be followed, and the risks and benefits of participation. This information will be explained to the study participant in a face-to-face setting by the individual consenting the participant. Participants will be encouraged to ask questions throughout the consent process and encouraged to discuss their participation with trusted advisors, such as family members, close friends, etc. Participants will be allotted sufficient time to consider whether or not to participate in the research study. After allowing the potential participant time to read the informed consent the study staff and/or investigator will answer and address any questions or concerns the participant may have. Once all questions and concerns have been addressed and the participant wishes to participate, they will be asked to sign the informed consent.

Individuals unable to speak English will be excluded from participating in a study. The decision to limit enrollment to English speaking persons is related to: 1) difficulty ensuring proper translation of the risks and benefits involved in study participation, and 3) lack of a transcription service that will provide transcription of foreign language interviews described above. If this research model turns out to be successful and accepted within the community, we will consider opening the enrollment to non-English speaking participants.

Also, during the consent process, the Health Insurance Portability and Accountability Act (HIPAA) Authorization will be addressed. A copy of the consent and HIPAA Authorization form as well as the Notice of Privacy Practices booklet will be given to the participant.

13. ALTERNATIVES TO STUDY PARTICIPATION

Participants may choose not to join this study.

14. POTENTIAL RISKS

Risks of Participating in This Study: Although we will make every effort to protect the participant's privacy and confidentiality it is possible that the participant's status could become known to others. This could cause problems between the participant and the participant's family and/or community and could cause the participant

to be discriminated against.

Breach of Confidentiality. Information that a participant is HIV-infected could, if disclosed, be economically or socially damaging, physically or psychologically harmful, or embarrassing to the participant. Additionally, certain information solicited in interviews and/or questionnaires related to risk behaviors could have similar adverse effects if disclosed. We believe it is important to minimize these risks in every way possible. The Last Gift research staff will adhere to their ethical obligation to protect both the patient participants and the general community from harm as it relates to ongoing high-risk behaviors of participants.

Risks of Blood Draws: The participant may experience temporary discomfort from the blood draws. The needle sticks may cause local pain, bleeding, bruising and swelling, as well as lightheadedness, dizziness and rarely, blockage of the vein, fainting and/or a local infection.

Vaginal Secretions Collection Risks: Women may have some discomfort or feel embarrassed when they give vaginal fluid sample.

Semen Collection Risks: Men may have some discomfort or feel embarrassed when they give semen sample.

Stool Collection Risks: Subjects may have some discomfort or feel embarrassed when they give stool samples.

Risk of Questionnaire/Interview: Participants will be asked questions that might seem sensitive or personal during this study. They can skip or stop answering questions that make them feel tired or uncomfortable. The participants might experience anxiety or frustration during the planed interviews. To minimize potential sadness or other emotional discomfort, participants will be informed that the interview can be terminated at any time if they desire. If at any time during the interview the participant expresses undue feelings of discomfort or pressure, his/her interview will be terminated. Staff personnel are trained to recognize the symptoms of anxiety and frustration and not to press participants to answer questions that seem unduly distressing. Interviews, exams and assessments are rescheduled or omitted if a participant reports symptoms of becoming overly distressed, fatigued, or frustrated by his/her efforts. Participants will be advised that none of the information obtained from their visit will be shared except in the form of generalized examples of particular themes or aggregate statistics with any personal identifiers. The only exception would be in the unlikely event of a clinical emergency in which case the research team would be required to take necessary action to prevent harm.

Data collection forms carry only study identification numbers. All records are stored securely in locked rooms and/or locking file cabinets. Standard measures exist for all computerized records that limit data access to selected research project personnel. The electronic data are protected by four separate levels of password access, specifically: 1) to an individual machine, 2) to the server machine, 3) to the central database, and 4) within the database to each data table assigned by the database administrator to an individual user.

Participants will be clearly informed that the interviews will be audio (and possibly video) recorded and that digital audio recording is only used for the purpose of transcribing their interview. Participants will also be informed that the audio and video recording can be stopped at any time, and that any/all portions of the audio recording can be erased at the patient's request. The audio files created during the qualitative interview will be uploaded electronically using participant study numbers only. The audio interviews will be transcribed and archived via a professional transcription service called M*Modal, a vendor currently approved and in use by UCSD. The use of M*Modal applications requires password-protected authentication prior to any transmission of files and applies 128-bit encryption and SSL-secured web applications. All M*Modal databases are located on a secured internal network that is protected by Cisco Secure PIX Hardware Firewalls with utilization of the SQL Server Security Model. The M*Modal physical data centers are housed in tier one data centers with geographic redundancy (SAS 70 approved). Once the audio recording has been transcribed, the audio and video

recorded is deleted.

Unknown Risks: Participants might have side effects or discomforts that are not listed in this form. Some side effects may not be known yet. New ones could happen. Participants are to tell the study doctor or staff right away when they have any problems.

15. RISK MANAGEMENT PROCEDURES AND ADEQUACY OF RESOURCES

All laboratory specimens, evaluation forms, reports and other records will be identified by a coded number only to maintain participant confidentiality. All records will be kept in a locked file cabinet. All computer entry and networking programs will be done with coded numbers only. Clinical information will not be released without written permission of the participant, the sponsor, or the UCSD IRB.

In the event of reported or suspected abuse or neglect, research staff will report such information to the appropriate authorities. Research staff training includes procedures for reporting.

Phlebotomy will be performed by experienced phlebotomists.

16. PRIVACY AND CONFIDENTIALITY CONSIDERATIONS INCLUDING DATA ACCESS AND MANAGEMENT

The AVRC research staff has undergone the CITI Biomedical Human Research, and Good Clinical Practice (GCP) training along with the HIPAA training.

The research staff will protect Patient Protected Health Information (PHI) or other Personal Identification Information (PII) of any individual in general, obtained from as part of the University or Healthcare or other work-related records, for whatever purpose, as private and confidential, and will make every effort to safeguard such information from unauthorized access or dissemination. Steps in place to protect this information are outlined below (Data Security).

Certificate of Confidentiality: A Certificate of Confidentiality from The U.S. Department of Health and Human Services (DHHS) has been issued.

Consent Process/Study Visits
For confidentiality purposes the consent process and exams will be conducted in an exam room by one of the study staff members. The laboratory procedures will be done in the blood draw room or an exam room by an experienced phlebotomist. Genital sample and stool collection will be performed at home, or in the privacy of our clinic.

Data Security
Any data collected as part of this study that is stored at the AVRC and/or is transferred via the internet will follow our data security process as outlined below.

With the fast-developing technology, dependable and comprehensive data security measures are key components to defy the perceived threats of Internet hackers and accidental disclosure of confidential information. In the following we provide a summary of the key features pertinent to this project.

- An anonymous participant identification number is used for all data collection, recording, and submission to the project database.
- Data that contain any participant identifiers (e.g., name or contact information) other than the unique identifier are password protected and accessible only to staff members whose job requires knowledge of such data.
- Laboratories are instructed not to disseminate any participant identifiers in any communications with, or

data submissions to, any other AVRC collaborators. Any data transfer over the Internet uses encryption.

- Data transfer and all Web-based utilities use secure access (user and server authentication, 128-bit SSL encryption). This type of encryption is the same as is used for Web-based transactions that involve credit cards or Web banking.

Research Laboratory Specimen Identification Policy
All research laboratory specimens leaving the AVRC to an outside laboratory will be de-identified.

Procedures
1. The Lab Manager will create a study specific AVRC internal lab requisition. The requisition will be saved and accessible via the AVRC internal computer system's shared drive.
2. Each research nurse will access and print the study specific requisition(s) via the shared drive.
3. Each research nurse will then complete the study specific requisition with the participant's name, DOB, medical record number (MR#), PID, AVRC number and study week.
4. The requisition will then be delivered by the research nurse to the AVRC lab.
5. The AVRC laboratory staff will then complete the appropriate form for the corresponding laboratory to which the specimen will be sent, using two coded identifiers, the participant's ID number (in the name field) and AVRC number (in the medical record number 's field).
6. The AVRC laboratory staff will prepare and label specimen tubes using the same two coded identifiers, the participant's ID number (in the name field) and AVRC number (in the medical record number's field). No personal health identifiers will be included on the specimen label (i.e., no name, initials, DOB, MR#, etc.).
7. Prior to the blood draw, the phlebotomist will verbally verify the participant's name and DOB. The phlebotomist will confirm the coded specimen tube(s) identifiers with the coded form identifiers.
8. Coded specimens are transported to the appropriate lab either by AVRC staff or shipped via FedEx, under IATA regulations.
9. All study specific completed AVRC internal lab requisitions will be retained in a locked and secured area for a period of six months and thereafter shredded.

All stored samples are accessible only to the AVRC laboratory personnel and the appropriate study members. Samples are stored under the coded identifiers as detailed above frozen and in freezers equipped with locks until they are shipped to the central laboratory under contract with the sponsor. The freezers are located in the AVRC and CTF building behind locked doors with cypher or key pad entry.

The stored samples are shipped as outlined above and are then secured under the sponsor's SOPs for storage of human biological samples.

Qualitative Interviews/Questionnaires
Participants will not be identified in any way, as we will use study identification number in all field notes and transcription services, while pseudonyms will be used in all reports of study results. Audio and video recordings will be kept in a secure database until they are transcribed. Only the principal investigator, co-investigators, and the research assistants will be the authorized people who will have access to the digital recordings prior to transcription. After transcription is completed, all recordings will be erased.

Data Sharing with CNTN
Data collected in this study will be shared with the CNTN and vice versa.

Health Information Exchange: A risk of loss of confidentiality does exist. However, study staff will do everything in their power to protect participants' privacy. Participants will further be notified that UCSD participates in a health information exchange (HIE) and that the HIE shares medical records with other doctors outside UCSD to help improve overall medical care. Research tests that are performed at UCSD, including records from this research study, may be shared on the HIE.

17. POTENTIAL BENEFITS

There is no guarantee that the participant will directly benefit from being in this study or upon completion of the study. However, what is learned from this study may help other people living with HIV by improving our knowledge about HIV persistence.

18. RISK/BENEFIT RATIO

It is the opinion of the investigators that the b benefits to society outweigh the risks to the individual study participants.

19. EXPENSE TO PARTICIPANT

There is no cost to participants for clinic visits, examinations, or laboratory tests, which are part of this study and beyond standard care. All medical costs for participant's treatment outside this study will be charged to the participant, or their insurance company.

20. COMPENSATION FOR PARTICIPATION

Participant reimbursement: Participants will be compensated $25 for the enrollment study visit with collection of data regarding drug use and ART adherence. Additional compensation will include:

- $10 for each study visit that includes a blood draw
- $30 for completion of baseline questionnaire (one time) and $10 for each follow up questionnaire (monthly)
- $10 for completion of the decliner questionnaire (one time)
- $10 for each genital secretion collection procedure performed
- $10 for each stool sample collection procedure performed
- $20 for each next of kin questionnaire (up to two questionnaires)

Additionally, we will support costs for cremation (if desired by the participant) up to $1,000, and provision of two death certificates to next of kin for participants who undergo study autopsy. Family will be able to choose among a list of 2-3 cremation facilities (pre-selected by the study team). Family will be responsible to pick up the ashes (in a basic cardboard box). Costs for an urn will not be covered as part of the study and will be responsibility of the family.

There is no expense to the participant, or their family or relatives for any study procedures, including autopsy. Autopsy costs and costs for transportation of the body to and from the autopsy site are covered as part of this study.

If a subject withdraws or is discontinued from the study, we will not support costs for cremation and provision of two death certificates. Subjects will receive compensation for all procedures they complete prior to ending the study.

21. PRIVILEGES/CERTIFICATIONS/LICENSES AND RESEARCH TEAM RESPONSIBILITIES

Drs. Davey Smith and Susan Little currently have privileges at UCSD Medical Center in the Department of

Medicine; Division of Infectious Disease and are licensed and certified by the State of California to perform all the medical procedures discussed in the protocol at UCSD. In addition to having privileges with UCSD Medical Center, Drs. Susan Little, and Davey Smith have privileges at the VA Medical Center.

Sara Gianella Weibel is a Swiss federally approved and board certificated physician and will be responsible for overseeing the success of the project from identifying participants through post mortem analysis.

David J. Moore, Ph.D. – Dr. Moore, a neuropsychologist, serves as the Principal Investigator for CNTN and is responsible for overseeing all aspects of the ante-mortem CNTN protocol, including tracking participant accrual and retention. He will also be in charge of managing the tissue request procedures, as well as overseeing quality assurance for neuropsychological data.

Cristian Achim, M.D., Ph.D. – Dr. Achim, a neuropathologist, serves as Co-PI of CNTN and oversee all aspects of the post-mortem CNTN protocol. In addition, Dr. Achim will provide scientific expertise in the neuropathological markers of aging and inflammation.

Nadir Weibel PhD – Dr. Weibel is a Research Assistant Professor of Computer Science. Dr. Weibel will direct the Data Management Core and with his team will ensure that all data generated as part of this study will be served by an appropriate interface to enable easy data storage, data retrieval, analysis and visualization, as well as, when appropriate, data sharing with the research community through an open data framework.

Celsa Spina PhD - Dr. Spina is a UCSD researcher who has served over the past 21 years as the Director of the combined CFAR and VASDHS Flow Cytometry Research Core facility to coordinate UCSD, VA, and VMRF flow cytometry resources. She will help with the immunological part of this study.

Antoine Chaillon MD, PhD - Dr. Chaillon is currently an Assistant Project Scientist at the University of California, San Diego (UCSD). Dr. Chaillon has extensive experience in sequence analysis, phylogeny and viral evolution, and he was uniquely successful in applying these techniques to characterize HIV evolution and the viral dynamics between anatomic compartments and blood plasma.

Sarah LaMere, DVM, Ph.D. – Dr. LaMere is a Postdoctoral Fellow at the University of California, San Diego (UCSD). Dr. LaMere is a veterinarian and an epigeneticist who focuses on epigenetic mechanisms of HIV latency. Dr. LaMere will be examining tissue and peripheral blood samples for epigenetic marks specific to the integrated provirus. Additionally, she will correlate her findings to viral load and rebound following treatment interruption.

Benjamin S. Murrell, Ph.D. Dr. Murrell is an Assistant Adjunct Professor with extensive expertise in computational biology and, more generally, the quantitative analysis of complex biological data. Dr. Murrell will be integral in the analysis of all generated full-length env sequencing data. He has developed a computational platform for pre-processing long-read HIV sequence data which will form the foundation of the analyses in this proposal. He will ensure the analytical and statistical rigor of this proposal. He will work with Dr. Chaillon on the bioinformatics part of this project.

Karin Metzner MD - Dr. Metzner is a Professor of Medicine in Department of Infectious Diseases and Hospital Epidemiology at the University Hospital of Zurich. Dr. Metzner will be responsible for virologic evaluations of samples collected in the Last Gift Cohort.

Dr. Jesus Rivera-Nieves, MD, is a professor of medicine at UCSD in the division of Gastroenterology. Dr. Rivera-Nieves will serve as a sub-investigator and assist with processing gut samples and generating data.

Huldrych Günthard, MD – Dr. Günthard is a professor of Medicine, the President of the Swiss HIV Cohort Study and a senior staff physician within the Division of Infectious Diseases and Hospital Epidemiology at the

University Hospital Zurich. Dr. Günthard will also be responsible for virologic evaluations of samples collected in the Last Gift Cohort.

Victor DeGruttola SM, ScD - Dr. DeGruttola. is a Professor of Biostatistics at Harvard School of Public Health and will lead the team of seasoned investigators with a range of expertise including: characterizing and modeling rebound dynamics, quantifying and modeling reservoirs, sequence analysis, and analyzing immunology and virology data.

Jukka-Pekka Onnela - Dr. Onnela will work closely with Dr. DeGruttola on the development of a global host model (based on a network model) that describes the migration of cells and dissemination of HIV using data from studies of clonal expansion and of viral phylogeny.

Alison Hill, PhD - Dr. Hill will provide guidance regarding mechanistic and the development of efficient statistical methods for identifying biomarkers that predict rebound dynamics.

Rui Wang, PhD - Dr. Wang will be working closely with Dr. De Gruttola and the quantitative methods research project team to develop, validate and apply new analytic methods for discovering biomarkers that can guide curative process, determining of HIV reservoir size and the impact of treatment interruption and re-initiation on these reservoirs, delineating immunological mechanisms of HIV reservoir resistance, and creating a global host model that incorporates all relevant information to guide study designs aimed at eradicating or controlling HIV reservoirs.

Stephen Rawlings, MD, PhD Rawlings has a PhD in HIV-1 latency and techniques for studying and eradicating HIV-1 reservoirs as well as an MD. Dr. Rawlings will assist in the virologic evaluations of samples collected in the Last Gift Cohort.

John Zaia, MD is the director for Gene Therapy at the City of Hope, a comprehensive treatment center and research facility in Duarte CA. Dr. Zaia will perform immunological experiments using blood and tissues from study participants.

Ben Gouaux, B.A. – Mr. Gouaux is the study coordinator for the project and will assist Dr. Moore in fulfilling tissue requests and coordinating activity of the various cores. Mr. Gouaux will also act as liaison with staff at the subcontract sites to ensure successful collaboration.

Susanna Concha-Garcia, B.A., is a Senior Community Health Program Representative Supervisor who has completed certification in the Protection of Human Research Subjects, CITI Biomedical Human Research, UCSD HIPAA training and has received specialized training to conduct and document the informed consent process for this study; she has been authorized by the Principal Investigator to serve in this role.

Karine Dube, DrPH, Mphil – is a social scientist with expertise in global health ethics. She will be involved in development and analysis of the End of Life questionnaire.

Melanie Harris will serve as the overall project coordinator and she will oversee day-to-day operation, organization, communication, and coordination of collaborative activities.

Demetrius DelaCruz will be responsible for communication among the investigators and for outreach to outside researchers, community members, and industry partners, including the establishment and maintenance of a Collaboratory website.

Helene Le, CPhT will serve as the primary IRB and Regulatory Affairs Coordinator for the project and will be responsible for all regulatory documents.

Joseph Lencioni, MABMH will serve as the back-up IRB and Regulatory Affairs Coordinator for the project

and will be responsible for regulatory documents.

The nurses at the AVRC will be involved with the consent process and study visits. The study nurses are all licensed by the State of California. Prior to the study opening at the AVRC, one of the study nurses will be assigned to the study and provide any in-service necessary to the other AVRC nurses who will be here back-up when the main study nurse is absent due to illness or vacations. The nursing staff for this study includes; Alina Burgi, RN and Steven Hendrickx, RN.

Kushagra Mathur and Bryan Le are medical students who will be helping out with recruitment, consenting, and providing questionnaires under direct supervision of Drs. Smith and Gianella.

Deedee Pacheco is the site Lab Manager and will be responsible for processing all samples.

All site phlebotomists are certified to perform phlebotomy in the State of California. The site phlebotomists are DeLys Brooks, Rebecca Gonzalez, Christopher Houston and Ernesto De Leon Marquez.

Michelle Troung and Fakhira Anwar will serve as data managers for this study. Both Michelle and Fakhira will have access to identifiable data as part of their study duties.

The PI, co-PIs, and nurses at the AVRC have completed the required UCSD research training to include CITI Human Subjects and GCP training along with the UCSD IRB HIPAA tutorial.

22. BIBLIOGRAPHY

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23. FUNDING SUPPORT FOR THIS STUDY

This trial is supported by the grants P01 AI131385, 1 R24 AI106039, P30 AI036214, DP1 DA034978, R01 MH097520. The financial contact for this study is Melanie Harris. She can be reached at 619-300-7104

24. BIOLOGICAL MATERIALS TRANSFER AGREEMENT

There will be an MTA for the transfer of specimens from UCSD to the University Hospital Zurich (Günthard) and another set up for the transfer of data from UCSD to Harvard University (DeGruttola). Angela Kozakowski is the contact for this study. She can be reached at (619) 543-5019.

25. INVESTIGATIONAL DRUG FACT SHEET AND IND/IDE HOLDER

Not Applicable

26. IMPACT ON STAFF

The Antiviral Research Center (AVRC) is an HIV/AIDS research facility. The nurses and other study personnel assigned to this study are funded by the abovementioned grants.

27. CONFLICT OF INTEREST

Not Applicable

28. SUPPLEMENTAL INSTRUCTIONS FOR CANCER-RELATED STUDIES

Not Applicable

29. OTHER APPROVALS/REGULATED MATERIALS

Copy of ZPHI Ethics Committee approval provided from Zurich.

30. PROCEDURES FOR SURROGATE CONSENT AND/OR DECISIONAL CAPACITY ASSESSMENT

Procedures to assess decisional capacity will be the same as CNTN (assessment of informed consent) since all Last Gift study participants will be also enrolled in CNTN. Similar to CNTN, if the participant cannot pass this assessment, then it triggers an alternate person listed in the surrogacy form.

APPENDIX A
HOSPICE MEMORANDUM OF UNDERSTANDING (MOU)

Includes MOU and an extensive list of healthcare and hospice programs in San Diego County from which participants may be enrolled.

UNIVERSITY OF CALIFORNIA - SAN DIEGO (UCSD)
Hospice Memorandum of Understanding (MOU)

TITLE: "The Last Gift": Development of an End-of-life Translational Model to Characterize the HIV Reservoir

About the Last Gift Study

In our efforts to better understand HIV and work towards a cure, the Last Gift project focuses on studying where the virus hides in the human body when dormant (i.e. when patients are on antiretroviral treatment). This study is an NIH-funded and Institutional Review Board approved study from now until 2022. The Last Gift project is enrolling altruistic HIV-infected people who are receiving hospice care for a terminal illness and who are interested in participating in HIV research that will not benefit themselves but potentially benefit others.

Participants agree to a full body donation for research purposes and their consent may be withdrawn at any time. Given that our study relies on examining the human body, **we request permission from the hospice care facility to perform routine blood draws on participants. These blood draws will be performed by our experienced phlebotomists.** The Last Gift staff will also meet with the participant at least once a week to gather information on the participant's social and clinical factors. The blood samples drawn will be used by our study staff to gain insight as to how HIV behaves in blood and compare it to the virus in tissues after death. Both those taking antiretroviral therapy and those that are not will be included in the study. A copy of the informed consent form from the participant will be provided, as well as the Last Gift study protocol.

Therefore, this document serves as a request from the hospice facility or provider to:

- Grant the UCSD Last Gift team permission to visit UCSD Last Gift patients in the facility.
- Allow the UCSD Last Gift team to collect detailed reports on social and clinical factors until the time of patient death through regular visits.
- Allow trained UCSD Last Gift personnel to draw blood on participant according to our schedule of evaluation.
- Allow the UCSD Last Gift team access twenty-four hours a day and seven days a week.
- Allow the UCSD Last Gift team to transport the body at the time of the participant's death to an authorized location in order to perform a rapid autopsy.

We will provide a medical release form signed by the participant or legally designated agent to the facility or hospice provider.

By having an authorized medical professional sign below, the director and the facility they represent are agreeing to the requests listed above.

APPENDIX A
Last Gift Hospice List
LAST GIFT HOSPICE OUTREACH

LAST GIFT HOSPICE OUTREACH							
COMPANY	Administrator	DIRECTOR OF NURSING (DON)	MEDICAL DIRECTOR	ADDRESS/LOCATIONS	PHONE	FAX	COMMENTS
ELIZABETH HOSPICE https://elizabethhospice.org/		Liz Sumner RN, BSN, MA ORGL Director, Clinical Services	George Delgado, MD, FAAFP, HMDC Chief Medical Officer	1) 2820 Roosevelt Rd, San Diego, CA 92106	1) (800) 797-2050		Identifies HIV/AIDS care. Provides info & supports End of Life Option Act, Many facilities throughout San Diego County
				2) 500 LA TERRAZA BLVD ESCONDIDO, CA 92025	(800) 797-2050		
Fraternity House & Nchaelle House www.fraternityhouse-inc.org	Larry Graff , Executive Director	Cristal Kacirek, Intake Coordinator & Program Manager		20702 Elfin Forest Rd, Escondido CA 92029	1) (760) 736-0292 2) Cristal 760-736-0292		Exclusively HIV & AIDS, chronically ill, hospice care. Susanna's contact: Cristal Kacirek @ Faternity House
				687 Riviera Ct, Vista, CA 92084	(760) 758-9165		
Sharp.com/hospice				1) Parkview Home 5788 Lyden Way	1) 619-667-1900 2) 1-800-681-9188		Susanna's contact: Veva Arroyo, Business Development Specialist Sharp HospiceCare, Transitions & Advance Care Planning T. (619)667-1969 F. (619)667-1981
				2) Lakeview			
				3) Bonita View	(619) 434-6816		
	Pablo Velez, RN, PhD, CEO & Sr VP			Sharp Chula Vista Medical Center	(619) 502-5800		
	Susan Stone, Sr VP & CEO			Sharp Coronado Hospital	619) 522-3600		
	Tim Smith, Senior VP & CEO			Sharp Memorial Hospital			
	Scott Evans, PharmD, MHA, CEO & Sr VP			Sharp Grossmont Hospital 5555 Grossmont Center Drive La Mesa, CA 91942	1) Sharp Grossmont Hospital Palliative Care 619-740-4154		

					2) Sharp Hospice 8881 Fletcher Pkwy #336, La Mesa, CA 91942		Coordination
www.silverado.com		Loren S. Novak, DO, Medical Director of Silverado Hospice San Diego,		1) 3750 Convoy St #200a, San Diego, CA 92111	1) 888-328-4558 2) 858-565-1005		
				2) Corporate Office 6400 Oak Canyon, Suite 200, Irvine, CA 92618	(888) 328-5400		
Silverado Encinitas Memory Care Community				2) 335 Saxony Rd, Encinitas, CA 92024	2) 760-270-9917		Dementia & hospice care
Silverado Escondido Memory Care Community				3) 1500 Borden Rd., Escondido, CA 92026	3) (760) 456-5137		Dementia & hospice care
Kaiser Permanente Hospice Care				San Diego Mission Road Kaiser 10990 San Diego Mission Road San Diego, CA 92108	1) 619-528-5000 Home health 2) 619-641-4100 hospice		Coordinated through Primary Care Doctor. Coordination for home health care, hospice home care. Susanna's contact: Melanie A Ross LCSW Kaiser Permanente Department of Internal Medicine/ID 3250 Fordham St San Diego CA 92110 619-221-6046
VITAS HEALTHCARE				9655 Granite Ridge Dr #300, San Diego, CA 92123	(858) 499-8901		Susanna's contact: Ben Janzen, Dr. Theol., PhD Bereavement Services Manager Program 95 Chaplain, APC, SCA 9655 Granite Ridge Dr, Ste 300, San Diego, CA 92123 858-499-8901
SCRIPPS HOSPICE				4311 Third Ave San Diego, CA 92103	(800) 304-4430		
SONATA HOSPICE www.sonatahospice.com/				1) Serra Mesa 8825 Aero Dr San Diego, CA 92123	(858) 277-2161		
				2) 5333 Mission Center Road, Suite 210 San Diego, CA 92108	858-277-2161	Fax: (858)275-5928	
LifeHOUSE San Diego Healthcare Center http://www.lifehousehs.com				2828 Meadow Lark Dr., San Diego, CA 92123	858.277.6460		
Hospice of North Coast www.hospicenorthcoast.org				2525 PIO PICO DR CARLSBAD, CA 92008	(760) 431-4100		Hospice care & HIV care
				2) Pacifica House			

VA Health Systems							Susanna's contact: 1) Keirre da Luz, MSW is case manager keirre.daluz@va.gov 2) Kimberley Woodworth (new) kimberley.woodworth@va.gov

LAST GIFT DOCTORS

DOCTORS				
DOCTOR & WEBSITE	ADDRESS/LOCATIONS	PHONE	FAX	COMMENTS
1. Dr. Jeannette Aldous	King Chavez Health Center, San Ysidro Health Center, Scripps Memorial Encinitas	(760)230-2251 and (619)428-4463		
2. Dr. Joel Trambley	Hillcrest Family Health Center, 4090 4th Ave., San Diego (Hillcrest), CA 92103, 619.515.2545	1). (619)515-2300 2)619.515.2545		
3. Dr. Chris Holt	AIDS Healthcare Foundation	(619)245-2350		
4. Dr. Adam Zweig	AIDS Healthcare Foundation	(619)245-2350		
5. Dr. Samuel Poniachik, Dr. Denise Gomez, and Dr. Laure Jefferis	5. North County Health Services	(760)736-6767		
6. Dr. Loretta Stenzel	Vista Community Clinic	(760) 631-5220		
7. Dr. Victor Souza	• Vista Community Clinic, Scripps Carlsbad Office	760-966-2499		
8. Dr. Frank Gilman	• Sharp Rees-Stealy Point Loma	(858) 499-2712		
9. San Diego HIV/STD/Hepatitis Branch		619-293-4700		
	San Ysidro Health Services/Casa South Bay, 4004 Beyer Blvd, San Ysidro, CA 92173	619-662-4161		
	UCSD Owen Clinic, 4168 Front St. San Diego, CA 92103	619.543.3995		

Appendix B
Maximum Blood Draw Collection Allowed

CMRC IRB MAXIMUM ALLOWABLE TOTAL BLOOD DRAW VOLUMES (CLINICAL + RESEARCH)						
Body Wt (Kg)	**Body Wt (lbs)**	**Total blood volume (mL)**	**Maximum allowable volume (mL) in one blood draw (= 3.0% of total blood volume)**	**Total volume (clinical + research) maximum volume (mL) drawn in a 30-day period**	**Minimum Hgb required at time of blood draw**	**Minimum Hgb required at time of blood draw if subject has respiratory/CV compromise**
31-35	68-77	2480-2800	74-84	248-280	7.0	9.0-10.0
36-40	79-88	2880-3200	86-96	288-320	7.0	9.0-10.0
41-45	90-99	3280-3600	98-108	328-360	7.0	9.0-10.0
46-50	101-110	3680-4000	110-120	368-400	7.0	9.0-10.0
51-55	112-121	4080-4400	122-132	408-440	7.0	9.0-10.0
56-60	123-132	4480-4800	134-144	448-480	7.0	9.0-10.0
61-65	134-143	4880-5200	146-156	488-520	7.0	9.0-10.0
68-70	145-154	5280-5600	158-168	528-560	7.0	9.0-10.0
71-75	156-185	5680-6000	170-180	568-600	7.0	9.0-10.0
76-80	167-176	6080-6400	182-192	608-640	7.0	9.0-10.0
81-85	178-187	6480-6800	194-204	648-680	7.0	9.0-10.0
86-90	189-198	6880-7200	206-216	688-720	7.0	9.0-10.0
91-95	200-209	7280-7600	218-228	728-760	7.0	9.0-10.0
96-100	211-220	7680-8000	230-240	768-800	7.0	9.0-10.0

Adapted from: http://www.feinsteininstitute.org/wp-content/uploads/2013/02/Maximum-Blood-Draw-Limits.pdf

Appendix C
LAST GIFT SCHEDULES OF EVALUATION

Assessments & Laboratory	Screening (n-30)	Baseline (Day 0-30)	Every 1-4 Wks [3,5]	End of Study[4]
LG Assessments				
Informed Consent/HIPAA	X			
Eligibility Checklist	X			
Demographics[1]		X		
Smoking History[1]		X		
Medical History[1]		X		
STI & Hepatitis History[1]		X		
Substance Use Assessment		X	X	X
Sexual Behavior Assessment[1]		X		
ART History[1]		X		
ART Adherence Monitoring		X	X	X
Change in ART Form[2]		X	X	X
Concomitant Medications		X	X	X
Adverse Event Monitoring		X	X	X
Limited Physical Exam		X	X	X
Additional Actions				
Review study with next of kin		X	X	
Discuss all legal and regulatory affairs		X	X	
Discuss with Hospice personnel (if appropriate		X	X	
Laboratories				
CD4/CD8 Subset Panel		X		X
HIV RNA PCR (Viral Load)		X	X	X
Specimen Collection				
Plasma/PBMC Bank		X	X	X
Urine Collection		X	X	X
Stool collection		X	X[6]	X
Genital secretion collection		X	X[6]	X
Vaginal swab collection		X	X[6]	X
LG Surveys & Forms				
Release of Information (to send & receive)	X			
LG Screening Questionnaire		X		
Beck Depression Survey		X	X	X
QOL Assessment		X	X	
Opioid CRF		X	X	
Surrogate Form		X		
Study Termination Form				X
Stipends				
Stipend for Study Visit with blood draw[3]		X	X	
Stipend for EOL Questionnaires		X	X	
Stipend for stool/genital secretions		X	X	X

Assessments & Laboratory	Screening (n-30)	Baseline (Day 0-30)	Every 1-4 Wks [3,5]	End of Study[4]

1 Take over from CNTN and update if more than 6 months old
2 A separate schedule of evaluations required at any time ART is interrupted
3 Compensation rates: S25, the basline and blood draw, $10 for follow up visits with blood draw, $10 for genital secretion samples, and $10 for each stool sample collected. $30 for an in-depth interview (stipend remains the same even if interview is split across multiple days) and $10 for follow-up questionnaire.
4 Repeated every 1-4 weeks until death, 4 If Death occurs on study, initiate the Autopsy Schedule of Evaluations (Table 3)
5 Regular study visits may be paused at the discretion of the investigator if the participant's medical condition stabilizes or deteriorates.
6. Stool, GS, and Vaginal Swabs will be collected once every 4 weeks (+/- 1 one week)

Table 2. Interruption of ART Schedule

ART Interruption Schedule	Day of ART Interruption	Wk 1	Wk 2[1]	Resume Main LG SOE
Laboratories				
HIV RNA PCR (Viral Load)	X	XX	XX	X
Specimen Collection				
Plasma/PBMC Bank	X	XX	XX	X
Stipends				
Stipend for PBMC/Plasma Bank[2]	X	X	X	

1 Twice weekly, if possible, sampling repeated weekly until virologic rebound is documented. The draw is a case-by-case decision by study staff. We will limit blood draws if subject has a very low Hb or if we are close to exceeding the maximum allowed blood in a 30-day period.
2 SOE = Schedule of Evaluations

Table 2. Close to death schedule

Close to death schedule	Up to daily
Laboratories	
HIV RNA PCR (Viral Load)	X
Specimen Collection	
Plasma/PBMC Bank	X
Stipends	
Stipend for PBMC/Plasma Bank[2]	X

Table 4. Last Gift Autopsy Schedule of Evaluations

Autopsy Assessments & Samples	Within 6 hrs of death	Post Autopsy Events
Sample collections		
Intra-cardiac serum	X	
CSF (Intraventricular)	X	

Table 4. Last Gift Autopsy Schedule of Evaluations

Autopsy Assessments & Samples	Within 6 hrs of death	Post Autopsy Events
Brain (various regions) *	X	
Skeletal muscle*	X	
Spleen*	X	
Lymph nodes (various regions) *	X	
Liver*	X	
Bone marrow*	X	
Adipose tissue (subcutan and pericardial) *	X	
Heart*	X	
Lung*	X	
Kidney*	X	
Prostate/Testes or Cervix*	X	
Body Processing		
Cremation		X
Stipends		
**Cremation and 2 death certificates (up to 1,000)		X

*All samples will be frozen immediately in liquid nitrogen with and without OTC compound (embedding media for frozen tissue specimens to ensure optimal cutting temperature.

**Participant or their family may opt out of cremation if they have pre-existing burial plans that do not conflict with the participants wishes.

Appendix D
END OF LIFE SOCIAL SCIENCES QUESTIONNAIRE

1) Baseline Questionnaire (for enrolled participants)
2) Decliners' Survey (for those who decline enrollment)
3) ART Interruption Questionnaire
4) Follow-up Questionnaire (for enrolled participants)
5) Beck Depression Inventory Questionnaire

Appendix E

Quality of Life of Seriously Ill Patients

QUAL-E 2005 (Steinhauser et al.)

Measuring the Quality of Life of Seriously Ill Patients

I'd like you to think back over the last month. Please tell me the three physical symptoms or problems that have bothered you the most during that time. Some examples are pain, nausea, lack of energy, confusion, depression, anxiety, and shortness of breath.

Symptom #1_____ **Symptom #3**_____

Symptom #2_____

- If no symptoms were elicited, then state the following:
  So, just to be sure, over the last month, you have had no physical or emotional symptoms that bothered you.

If correct, skip to question #5.

Which of these symptoms or problems has bothered you the most this past week?

1. During the last week, how often have you experienced _____?

Rarely	*A few times*	*Fairly often*	*Very often*	*Most of the time*
1	*2*	*3*	*4*	*5*

2. During the last week, on average, how severe has _____ been?

Very mild	*Mild*	*Moderate*	*Severe*	*Very severe*
1	*2*	*3*	*4*	*5*

3. During the last week, how much has _____ interfered with your ability to enjoy your life?

Not at all	*A little bit*	*A moderate amount*	*Quite a bit*	*Completely*
1	*2*	*3*	*4*	*5*

4. How worried are you about _____ occurring in the future?

Not at all	*A little bit*	*A moderate amount*	*Quite a bit*	*Completely*
1	*2*	*3*	*4*	*5*

5. In general, how important are your PHYSICAL SYMPTOMS OR PROBLEMS to your overall quality of life?

Not at all	*A little bit*	*A moderate amount*	*Quite a bit*	*Completely*
1	*2*	*3*	*4*	*5*

Below is a list of statements that other people with a serious illness have said may be important. Please tell me how true each statement is for you.

6. Although I cannot control certain aspects of my illness, I have a sense of control about my treatment decisions.

Not at all	*A little bit*	*A moderate amount*	*Quite a bit*	*Completely*
1	*2*	*3*	*4*	*5*

7. I participate as much as I want in the decisions about my care.

Not at all	*A little bit*	*A moderate amount*	*Quite a bit*	*Completely*
1	*2*	*3*	*4*	*5*

8. Beyond my illness, my doctor has a sense of who I am as a person.

Not at all	*A little bit*	*A moderate amount*	*Quite a bit*	*Completely*
1	*2*	*3*	*4*	*5*

9. In general, I know what to expect about the course of my illness.

Not at all	*A little bit*	*A moderate amount*	*Quite a bit*	*Completely*
1	*2*	*3*	*4*	*5*

10. As my illness progresses, I know where to go to get answers to my questions.

Not at all	*A little bit*	*A moderate amount*	*Quite a bit*	*Completely*
1	*2*	*3*	*4*	*5*

11. In general, how important is feeling like an ACTIVE PARTICIPANT in your HEALTH CARE to your overall quality of life?

Not at all	*A little bit*	*A moderate amount*	*Quite a bit*	*Completely*
1	*2*	*3*	*4*	*5*

12. I worry that my family is not prepared to cope with the future.

Not at all	*A little bit*	*A moderate amount*	*Quite a bit*	*Completely*
1	*2*	*3*	*4*	*5*

13. I have regrets about the way I have lived my life.

Not at all	*A little bit*	*A moderate amount*	*Quite a bit*	*Completely*
1	*2*	*3*	*4*	*5*

14. At times, I worry that I will be a burden to my family.

Not at all	*A little bit*	*A moderate amount*	*Quite a bit*	*Completely*
1	*2*	*3*	*4*	*5*

15. Thoughts of dying frighten me.

Not at all	*A little bit*	*A moderate amount*	*Quite a bit*	*Completely*
1	*2*	*3*	*4*	*5*

16. I worry about the financial strain caused by my illness.

Not at all	*A little bit*	*A moderate amount*	*Quite a bit*	*Completely*
1	*2*	*3*	*4*	*5*

17. In general, how important are CONCERNS ABOUT THE FUTURE to your overall quality of life?

Not at all	*A little bit*	*A moderate amount*	*Quite a bit*	*Completely*
1	*2*	*3*	*4*	*5*

18. I have been able to say important things to those close to me.

Not at all	*A little bit*	*A moderate amount*	*Quite a bit*	*Completely*
1	*2*	*3*	*4*	*5*

19. I make a positive difference in the lives of others.

Not at all	*A little bit*	*A moderate amount*	*Quite a bit*	*Completely*
1	*2*	*3*	*4*	*5*

20. I have been able to help others through time together, gifts, or wisdom.

Not at all	*A little bit*	*A moderate amount*	*Quite a bit*	*Completely*
1	*2*	*3*	*4*	*5*

21. I have been able to share important things with my family.

Not at all	*A little bit*	*A moderate amount*	*Quite a bit*	*Completely*
1	*2*	*3*	*4*	*5*

22. Despite my illness, I have a sense of meaning in my life.

Not at all	*A little bit*	*A moderate amount*	*Quite a bit*	*Completely*
1	*2*	*3*	*4*	*5*

23. I feel at peace.

Not at all	*A little bit*	*A moderate amount*	*Quite a bit*	*Completely*
1	*2*	*3*	*4*	*5*

24. There is someone in my life with whom I can share my deepest thoughts.

Not at all	*A little bit*	*A moderate amount*	*Quite a bit*	*Completely*
1	*2*	*3*	*4*	*5*

25. In general, how important is the feeling that your LIFE IS COMPLETE to your overall quality of life?

Not at all	*A little bit*	*A moderate amount*	*Quite a bit*	*Completely*
1	*2*	*3*	*4*	*5*

Now, I have one last question.

26. How would you rate your OVERALL QUALITY OF LIFE?

Very Poor	*Poor*	*Fair*	*Good*	*Excellent*
1	*2*	*3*	*4*	*5*

References

Two phases of validation:

1. Factor structure
Steinhauser KE, Bosworth HB, Clipp EC, McNeilly M, Christakis NA, Tulsky JA. Initial assessment of a new measure of quality of life at the end of life (QUAL-E). Journal of Palliative Medicine. 2002, 5(6):829-42.

2. Construct divergent and convergent validatity
Steinhauser KE, Clipp EC, Bosworth HB, McNeilly M, Christakis NA, Voils CI, Tulsky JA. Measuring quality of life at the end of life: Validation of the QUAL-E. Palliative and Supportive Care, 2004, Vol .2 (2):3-14.

APPENDIX F
Surrogate Certification

Self-Certification of Surrogate Decision Makers for Potential Subject's Participation in University of California Research

Section 1:
I am willing to serve as a surrogate decision maker for _____
(Potential Subject)
to participate in _____
(Title of research project and IRB #)
research conducted by _____
(Principal Investigator)

Section 2:

Category of Potential Surrogate

Check ( ) the category that best describes your relationship to the potential subject:

For the categories listed above yours, provide the name(s) of other relatives. *(For example, if you are the adult son or daughter of the potential subject, provide the names of adults, if any, who are best described by categories 1-4 only)*

1. Agent named in the potential subject's advanced health care directive. 1. _____
2. Conservator or guardian of the potential subject, with authority to make health care decisions for the potential subject 2. _____
3. Spouse of the potential subject. 3. _____
4. Domestic partner of the potential subject 4. _____
5. Adult son or daughter of the potential subject 5. _____
6. Custodial parent of the potential subject 6. _____
7. Adult brother or sister of the potential subject 7. _____
8. Adult grandchild of the potential subject 8. _____
9. Adult whose relationship to the potential subject does not fall within one of the above listed categories and is best described as: _____ (Example: cousin, aunt, etc.) 9. _____

Section 3:
The following section information must be completed only for surrogate consent to participate in research in non-emergency settings:
(Check the statement which best describes the basis of your knowledge of the potential subject)

_____ I live with the potential subject and have done so for _____ years.

_____ I have discussed participation in research with the potential subject and believe that I can carry out his/her preferences.

_____ Other (please describe): _____
_____

Section 4:
Potential Surrogate's Contact Information:

Name: _____
Address: _____
_____

Home Phone: ( ) _____
Work Phone: ( ) _____
Cell Phone: ( ) _____
E-mail: _____

_____ ___/___/___ _____ ___/___/___
Signature of Potential Surrogate Date Signature of Witness Date

APPENDIX G
In Event of Death

UNIVERSITY OF CALIFORNIA, SAN DIEGO UCSD

BERKELEY • DAVIS • IRVINE • LOS ANGELES • MERCED • RIVERSIDE • SAN DIEGO • SAN FRANCISCO SANTA BARBARA • SANTA CRUZ

HIV Neurobehavioral Research Program
Office (619) 543-5000
Fax: (619) 543-8099

220 Dickinson Street, Suite B
San Diego CA 92103-8231

IN THE EVENT OF DEATH

As an important component of a research project on the neurobehavioral effects of Human Immunodeficiency Virus (HIV) infection,

_____

has consented to an autopsy at UCSD Medical Center. We would appreciate your assistance with the following procedure. As soon as possible after death (***regardless of day, date or time of day***), please page:

The On-Call Representative at 858-616-1214 24hr pager or 619-438-4996 24hr cell

Pager instructions: After the tone, dial in the number from which you are calling including the area code, hit the # key and hang up. Please make no other calls until you are called back. If someone does not call you back within fifteen minutes, try this step one more time.

If you have tried twice and received no answer to your pages, please call the Message Center at UCSD Medical Center at 619-543-6737, and ask to page:

Ronald Ellis, M.D. on beeper #5769
or
Scott Letendre, M.D. on beeper #5796

When your call is returned, the person answering will need the following information:

- The UCSD Medical Record Number, if known. (If unknown, date of birth)
- The name and telephone number of the mortuary if one has been chosen.

Costs associated with the autopsy, including transportation to the hospital and to the mortuary will be the responsibility of the HIV Neurobehavioral Research Program. All funeral costs are the responsibility of the participant or his/her family.

Should you have any questions regarding this document or the above named individual's desire for autopsy, please feel free to call the study representative at 877-543-8090, during business hours.

Ronald Ellis, M.D.
Principal Investigator, Neuromedical Core
HIV Neurobehavioral Research Program

FILE THIS LETTER WITH IMPORTANT LEGAL DOCUMENTS

VERSION: 02/2014

APPENDIX H-1
Collection of Semen Specimens
Last Gift Participant Instructions

Instruction for Collection of Semen

You have been asked to provide a semen sample using a semen collection kit. You will be required to return your specimen **within 2 hours of collection.** It is also important to remember to **store the pink "transport" fluid in the test tube in the refrigerator.** Below are instructions on how to collect and submit a semen specimen for testing. It is important to follow these instructions. Changing this protocol may cause issues with sample processing and inaccurate test results. The Last Gift team will be happy to answer any questions you may have.

NOTE: Read all instructions before beginning. Semen can be collected at home or in a dedicated private room at the AVRC.

Things to remember before semen collection

- **You must abstain from any form of ejaculation (intercourse or masturbation) for two days prior to specimen collection.**
- **Store the pink "transport" fluid in the test tube in the refrigerator.**
- **Collection of specimens must be done exclusively by masturbation.**
  - Condoms or lubricants (including saliva) should not be used, as they could contaminate or kill the sperm cells.
  - Withdrawal or interrupted intercourse is also detrimental, because a portion of the specimen may be contaminated with debris or cells from your partner. The entire ejaculate should be collected.

Semen Collection Procedure

1. Remove the test tube from the refrigerator 5-10 minutes before use and allow it to come to room temperature. Locate the specimen container within the plastic Ziploc bag.
2. Wash and dry your hands thoroughly, taking care to use soap and scrub under fingernails before producing specimen.
3. Remove the specimen container from the plastic Ziploc bag. Take the lid off the specimen container and carefully place the lid with the inside facing up.
4. Use the provided wipes to cleanse the penis prior to specimen collection.
5. After collecting the specimen, add the room temperature pink "transport" fluid from the test tube to the specimen container and then return the lid to the specimen container, taking care not to touch the inside of the lid.
6. Return the specimen container to the plastic Ziploc bag.

7. Place the plastic Ziploc bag containing the specimen container in the brown paper bag provided. Write your name on the outside of the paper bag.

Specimen Delivery Instructions

- **The fresh specimen should be delivered to the AVRC no later than two hours after collection.**
- **The specimen should be kept warm (body temperature) during transport to the office–do not refrigerate.**

If there are questions or concerns, please feel free to contact the AVRC lab staff during normal business hours at (619) 543-8080 or call Susanna Concha Garcia at (619) 543-5000.

APPENDIX H-2
Collection of Stool Specimens
Last Gift Participant Instructions

Instruction for Collection of Stool

You have been asked to provide a stool specimen using a stool collection kit. If you are unable to provide a specimen during your visit, you will be given a collection kit to take home. You will be required to return your specimen **within 2 hours of collection**. Below are instructions on how to collect and submit a stool specimen for testing. It is important that you follow these instructions. Changing this protocol may cause issues with sample processing and inaccurate test results. If you have any questions, the Last Gift team will be happy to explain how to properly collect a specimen.

NOTE: Read all instructions before beginning.

This kit contains one screw-capped tube. This tube will be used to transport your specimen to the testing site. Do not open the tube until you are ready to provide a specimen.

Your home collection kit contains the following:

- 1 Sterile stool collection container and frame (toilet commode)
- Latex gloves
- 1 labeled, sterile green screw-capped tube (with spoon)
- 1 Ziploc bag
- 1 brown paper bag
- 1 Transport pouch
- 1 date and time label
- 1 Ice pack

Preparation and Collection

1. Place ice pack in freezer at least 12 hours before use.
2. Urinate (into toilet) prior to collecting your specimen.
3. Raise toilet lid and seat.
4. Place commode frame on toilet rim ensuring that all four corners are supported by the toilet bowl (see Figure 1).
5. Place toilet seat down (see Figure 2).
6. When ready, remove lid from collection bowl.
7. Deposit your stool directly into the dry collection container. Do not urinate into the collection container. Do not collect specimen that has fallen into the toilet.

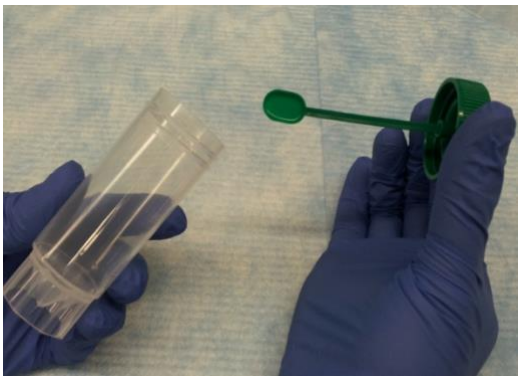
Figure 1

Figure 2

Transferring your specimen to lab tube

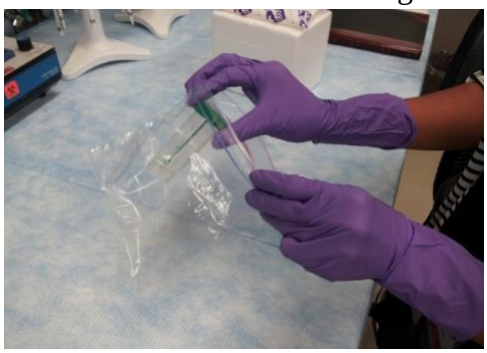
1. Using the spoon attached to the collection tube cap, scrape a dime-sized amount from the inside of your collected stool. Place into the collection tube (see Figure 3) and secure cap.

Figure 3



2. Wipe off any excess stool from the outside of container with paper towel or toilet paper. Discard towel or toilet paper.
3. Place collection tube with stool into the provided Ziploc bag (see Figure 4).

Figure 4



4. Record **Date & Time** of collection on the label located on the outside of the Ziploc.
5. Place tube in insulated transport pouch with frozen ice pack (see Figures 5 & 6).

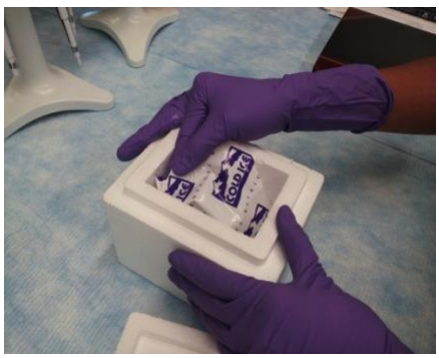


Figure 5

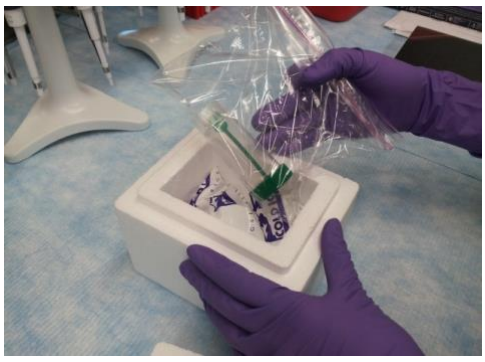


Figure 6

Disposal of remains

1. Flush leftover stool in toilet.
2. Dispose of the stool collection frame and gloves in trash.
3. Remember to wash your hands

Deliver specimen to AVRC for processing within 2 hours of collection.

If there are questions or concerns, please feel free to contact the AVRC lab staff during normal business hours at (619) 543-8080 or call Susanna Concha Garcia at (619) 543-5000.

APPENDIX H-3
Collection of Perirectal Swabs for Stool

Perirectal swab – Perirectal swab specimens will be collected by study staff for evaluation of stool microbiome (See Figure 1 for collection instructions).

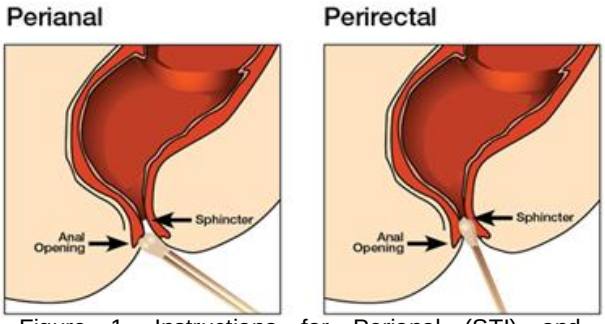


Figure 1. Instructions for Perianal (STI) and Perirectal (microbiome) sample collection

APPENDIX H-4
Collection of Vaginal Secretions
Last Gift Participant Instructions

Collection Materials

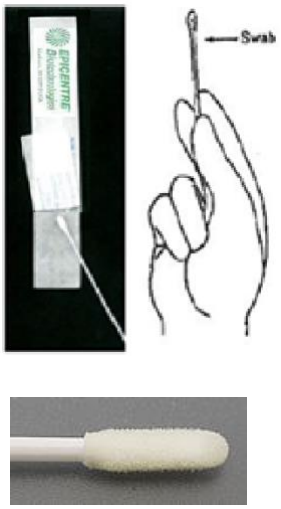
- Catch-All Sample Collection Swabs (Soft Pack) by Epicentre (www.epibio.com, Product ID QEC89100)
- 24 sterile 2 mL Cryovials by Sarsdedt (Cat #72.694.006) or similar

Vaginal Secretion Collection Instructions

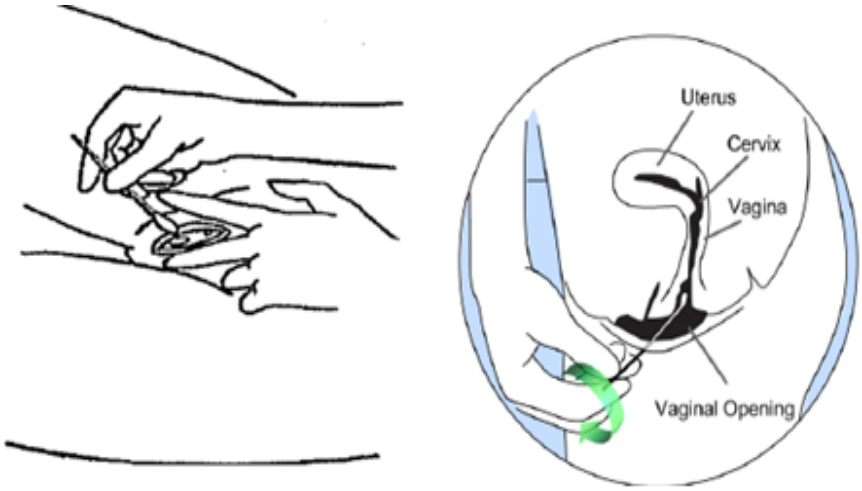
1. Remove the caps of the cryovial and set the cap aside on a clean surface with the screw top side facing up and flat side on surface. Do not throw the cap away. Keep the cryovial in a secured and upright position.

2. Partially peel open the Catch-All swab envelope, exposing the stick end of the swab.

3. Being careful not to lay the Catch-All swab down on any surface, remove the swab from the package once you are ready to collect the specimen.



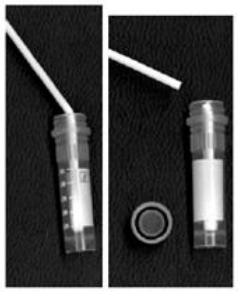
4. While separating the labia with one hand, use the other hand to hold the Catch-All swab shaft between the thumb and forefinger and insert the soft tip of the Catch-All swab into the vagina approximately 4-5 cm. Move the swab around the vagina for 10-20 seconds, attempting to touch all walls of the vagina.



5. Carefully withdraw the swab(s) from the vagina.

6. Insert each Catch-All swab into its own cryovial.

7. Break off the shaft of the Catch-All swab, leaving the soft end of the swab in the cryovial and throw the top stick portion away.



8. Put the cap back on the vial, and bring the vial to the laboratory for storage.

NOTE: If a swab or tube is dropped in this process, please replace the swab or tube and repeat the entire process above.

If there are questions or concerns, please feel free to contact the AVRC lab staff during normal business hours at (619) 543-8080 or call Susanna Concha Garcia at (619) 543-5000.

APPENDIX I
Last Gift Autopsy Protocol

(adapted by Sara Gianella and Donna Hansel)

Equipment

Safety.
Protective face masks or shield
Safety glasses
Protective footwear (booties)
Blue Gowns
Nitrile gloves
Hairnets
Cry gloves

Miscellaneous.
Metal bucket for flash freezing
Funnel
Extra Falcon Tubes (50 ml)
Liquid-nitrogen resistant tubes (2ml) (pink)
Disposable retractable scalpels
Freezer boxes
Extra labels
Aluminum foil
OCT (optimum cutting temperature)
Tweezers
Ethanol resistant marker

In Lab.
10L Liquid Nitrogen Dewar filled w/ LN2
2-methyl butane
Large Styrofoam box (for LN2)
2ml Tubes Labeled (pink top)
Ethanol resistant markers
70% Ethanol Bottle
Paraformaldehyde
Sucrose in 0.1M sodium cacodylate trihydrate
Glutaraldehyde
RNAlater
Tryzol

Procedures.

Before Autopsy.

- Using an ethanol-resistant marker or labels, pre-label falcon tubes, liquid-nitrogen-resistant tubes, and label tubes with patient number and tissue type (see list of abbreviations at the end of this document). Put them in freezer boxes (as many tubes fit per boxes - organ/region)
- Make sure LN2 dewar is filled and all equipment is fully stocked

Day of Autopsy.

- Organize transportation of all equipment and supplies to Hillcrest Hospital Morgue.
- Contact (as soon as possible) Sara Gianella, Susan Little, Donna Hansel, Virawudh (Soon) Soontornniyomkij and Michelli Oliveira (see Autopsy Notification Flow Sheet).

At the Morgue.

- Drop off equipment at loading dock outside the morgue
- Get dressed up, - Blue Gown, booties, hair covering, face shield/mask, double gloves.
- Pour LN2 into Styrofoam box
- Pour 2-methyl butane into large metal container

Amount of Tissues to be removed for Last Gift.

All fluids (CSF and intra-cardiac serum) will be collected and processed as part of CNTN and shared with Last Gift later.

Craig Gibson or designated alternative diener will extract the tissues listed below and hand them over to the Last Gift team in pre-labeled Falcon Tubes on Ice:

- Brain (right hemisphere): Frontal Cortex (motor and pre-motor), Parietal Cortex, Basal Ganglia, Occipital cortex, Hippocampus, approximatively 1x0.5x0.5 cm3 (1g) from each region will be devoted for Last Gift.
- Spinal Cord: Small sections from lumbosacral, thoracic, and if possible, cervical levels.
- Skeletal muscle: Two 2x2x2 cm3 sections are obtained from each site (proximal: vastus lateralis, and distal: gastrocnemius).
- Spleen: Two 2x2x2 cm3 sections are obtained.
- Lymph nodes: A minimum of 10 lymph nodes are obtained, with their sites of origin noted. If possible collect cervical, mediastinal, aortic (thoracic and abdominal), axillary, lung peri-hilar lymph nodes (and other lymph nodes if visible).
- Liver: Two 2x2x2 cm3 sections are obtained.
- Vertebral bone marrow: One 2x2x2 cm3 section is obtained from one mid-thoracic vertebral body.
- Adipose tissue from abdominal incision: Two 2x2x2 cm3 sections are obtained. Additionally, collect two 2x2x2 cm3 section of peri-cardial fat tissue.
- Heart: Two 2x2x2 cm3 sections are obtained from the myocardium of the left ventricle and from the right ventricle.
- Aorta: 4cm segment of the thoracic aorta.
- Gut: 4 cm segment from each section (esophagus, stomach, duodenum, terminal ileum, jejunum, left and right colon, rectum).
- Pancreas: Two 2x2x2 cm3 sections
- Lung: Two 2x2x2 cm3 sections are obtained from the lungs (each side).
- Kidney: Two 2x2x2 cm3 sections are obtained from the kidneys (each side) including cortex and medulla.
- Bladder: Two 2x2 cm2 sections
- Testes: One 2x2x2 cm3 section is obtained from each testis (for men)
- Prostate: One 2x2x2 cm3 section is obtained (for men)
- Seminal vesicle: One 2x2x2 cm3 section from each site.
- Cervix: One 2x2x2 cm3 section is obtained (for women)
- Uterus: Two 2x2 cm2 sections (for women)
- Ovaries: One 2x2x2 cm3 section from each site.

- Fallopian Tubes: Small sections from each site.
- Vagina: Two 2x2 cm^2 sections
- Thymus: One 2x2x2 cm^3 section (if visible)
- Blood or Blood Clots: Intra-cardiac blood/clot - as much as can be recovered from the heart
- Thyroid: One 2x2x2 cm^3 section
- Adrenal Glands: One 2x2x2 cm^3 section (one site)
- Additional samples: Two 2x2x2 cm^3 sections will be recovered from each body organ included in performance of a routine whole body (unrestricted) autopsy.

Freezing Procedures.
Tubes – flash frozen (OCT) and ~ 10 single tubes per organ/region (less for small organs or regions shared with CNTN).

Use caution when using the liquid nitrogen and 2-methyl butane, they are very cold and can cause cryogenic burns!!! Mark time of snap freezing for each organ!

- **For OCT sections**, add a few drops of OCT to the cryomold, place section in the mold in the desired orientation, and cover the section with OCT. Wrap TIGHTLY with aluminum foil.
- Place in the metal bucket attachment and submerge into the 2-methyl butane for approximately 60 seconds. Remove with long forceps and place in the appropriate Box.
- Transfer samples temporarily to a -80°C freezer
- **For non-OCT section**, transfer to cryomold, wrap TIGHTLY with aluminum foil, put in appropriate labelled bag, and store in the -80°C freezer. Put some of the tissue in buffers (Trizol, RNA later as appropriate).

3D immunofluorescence:
- **For our LM studies**, the tissue segments need to be removed and immediately placed into an ice-cold solution, for these samples we use **8% paraformaldehyde, 5% sucrose in 0.1M sodium cacodylate trihydrate.**
- **For EM studies**, the tissue segments need to be removed and immediately placed into an ice-cold solution of **3% glutaraldehyde, 1% paraformaldehyde, 5% sucrose in 0.1M sodium cacodylate trihydrate.** The samples can then be sealed in screw cap tubes completed filled with the same fixative and shipped to us as soon as possible on ice-packs (4°C) by overnight FedEx.
- Clean up dissection table and put instruments in sink.
- Use a funnel to transfer the 2-methyl butane back into its container. It is VERY IMPORTANT to warm the 2-methyl butane back to room temperature BEFORE putting the lid on. Put the container in the sink WITH THE LID OFF and run warm water over it until it warms up. Once it's warm, put the lid on.
- Dispose of the LN2 by dumping it slowly on the floor in a corner of the room that is out of the way.

Post-Autopsy Transportation.
- Frozen samples should be transported on dry ice
- Container should have dry ice and biological materials hazard stickers (category A)

Storage.
- Frozen samples should be stored at -150°C
- 2-methyl butane should return to fire safety cabinet

Database.

- Update patient info and tissue inventory in database

Call list.

Sara Gianella 858-784-15-76

Donna Hansel 858-242-00-94

Michelli Oliveira 619-730 5853

Susan Little 619-417-9206

Technicians

Description	Abbreviation
Adipose	ADP
Basal Ganglia	BSP
Blood Clots	BLC
Bone	BNE
Bone Marrow	BNM
Cervix	CER
Dorsal Root Ganglia	DRG
Frontal Cortex (motor)	FCM
Frontal Cortex (pre-motor)	FCP
Heart	HRT
Hippocampus	HPC
Ileum	ILM
Kidney	KDY
Large Bowel	LBL
Liver	LIV
Lung	LNG
Lymph Node (aortic)	LNA
Lymph Node (axillary)	LNX
Lymph Node (cervical)	LNC
Lymph Node (mediastinal)	LNM
Lymph Node (other)	LNO
Lymph Node (per-hilar)	LNP
Mesentery	MES
Motor Cortex	MTC
Occip Cortex	OCC
Pancreas	PNC
Parietal Cortex	PCT
Peritrach Lymph Nodes	PLN
Premotor Cortex	PRC
Prostate	PRO

Skeletal Muscle (distal)	SMD
Skeletal Muscle (proximal)	SMP
Spinal Cord Cervical	SCC
Spinal Cord Lumbosacral	SCL
Spinal Cord Thoracic	SCT
Spinal Cord Thoracic	SCT
Spleen	SPL
Testes	TST

APPENDIX J
Autopsy Notification Flow Sheet

Autopsy Flow Sheet Collect as much information at first contact as possible	HNRP Study ID CNTN ID (if different): LINK#
Date and Time of Call: / / AM/PM	Date and Time of Death: : AM/PM / / Probable Cause of Death:
Participant's name:	Contacted by Name & Ph# of Caller:
Facility (address) for DECEDENT Pick-Up (home, facility, morgue, medical examiner): Name/Contact Person (security, nurse, admissions) & Phone#:	Address/Location at TIME of DEATH (home, hospice, hospital, SNF): What is the name of the physician signing the death certificate?
UCSD MR #: (Patient Services 619-543-6570 to create # 24hrs)	Ask facility if this is a Medical Examiner (ME) Case? ☐No ☐Yes What is ME case #?
DOB: dd/mm/yyyy	When not an ME case ask facility for Medical Examiner Waiver#
Ask Caller for Next of Kin/POA/Partner's name & contact ph#: Ask facility if family is aware of Pt's death? Have they seen the body? If family wants to view body before transport, get estimated time of families arrival. Report to transport service and Craig Gibson & Ben Gouaux if delay.	Ask facility if mortuary/funeral home service has been arranged? ☐No ☐Yes Does family know about death? ☐No ☐Yes Get names & ph#s of next of kin and advanced healthcare directive agent

Consents:

	check/date		check/date
Fax Autopsy Consent (as needed) to facility if we pick up body		Obtain Surrogacy Consent Relative or Legal Document (Yes / No)	
Create UCSD Medical Record (888-309-8273) Research MR#		Release of body to Mortuary?	
Order Medical Records from facility		Need San Diego County Public Administrator? File online or with Decedent Affairs at UCSD?	

Mortuary/Crematorium Services:

Mortuary Address:	Contact Name:	Phone Number:

Information for HNRP Representative carrying CNTN Autopsy cell/pager: Before Transporting Decedent & Selection for Autopsy Send Email to CNTN Group:

		check/dates
CALL/TEXT Craig Gibson first, notify of potential autopsy to be scheduled and email Craig Gibson at apathservices@cox.net . Email Dr. Soontornniuomkil, MD, at vsoontor@ucsd.edu. USE the CNTN Autopsy cell phone only 619-438-4996. Drs. Bharti and Ellis use their own cell. CNTN Autopsy pager is 858-616-1214 (leave 10 digit number, hit # key, disconnect). EMAIL CNTN group CAchim, VSoon, CGibson, RElis, ABharti, BGouaux, DJMoore, SConchagarcia, JMarquieBeck, JMetcalf with brief details on time of death, date and cause of death.	619-708-2557 CG cell 619-334-8671 CG office fax 858-736-4291 Soon cell 858-822-4546 Soon office 619-543-2617 UCSD morgue	
For Last Gift Co-enrolled participants: Text the Last Gift autopsy team: Sara Gianella, Susan Little, Michelli Faria de Oliveira, Donna Hansel (text in order listed until response obtained)	858-784-1576 Sara Cell 619-417-9206 Susan Cell 619-730 5853 Michelli Cell 858-242-0094 Donna Cell	
After Consult with both Dr Soontornniuomkil & Craig Gibson about potential autopsy: ☐Yes approved for Autopsy ☐Not Approved for Autopsy		
If YES for autopsy – What is location of autopsy? ☐UCSD HILLCREST Morgue ☐Medical Examiner ☐OTHER _____ If decedent is not having an autopsy - Notify NOK & facility, we are not picking up decedent for autopsy	Estimated date & time of autopsy:	
Call Mike Looney for transportation of decedent, 92Mike Transport LLC OR Call Other Transport:	804-930-4277 MLooney cell	
FOR AUTOPSY AT UCSD (optional): Email ptregistration@ucsd.edu with decedent's Full Name, DOB, CC: Shelly Ebbert at sebbert@ucsd.edu of Decedent Affairs, with "RESEARCH AUTOPSY" date/time of arrival of decedent, with the UCSD Medical Record #, include mortuary plans if known. Call Security at 619-543-3762 to expect arrival of "Name of Decedent & Medical Record #" if known and Name of Transport Company making delivery.		

APPENDIX K
SUMMARY OF PLANNED DATA GENERATION

Table 1: Summary of laboratory data generated for 'Last Gift' participants who do and do not interrupt ART before death.

	ASSAYS	OUTCOME	SPECIMENS
Ante-mortem	**Mass Spec**	Levels of ART and other drugs	Blood plasma, urine
	Abbott m2000/ Aptima	Quantify cell-free HIV RNA	Blood plasma
	ddPCR	Quantify HIV DNA and cellular RNA	Isolated CD4 T cells
	FL HIV DNA NGS	Proviral genetics	Isolated CD4 T cells
	Targeted ChIP-Seq	Epigenetic profiling	PBMC
	Targeted ATAC-Seq	Epigenetic profiling	PBMC
	Bisulfite sequencing	DNA methylation patterns	PBMC
	Clonal Expression	Replication competence of FL HIV DNA	Isolated CD4 T cells
	Modified QVOA	Replication competence	Isolated CD4 T cells
	Env HIV RNA NGS	Migration dynamics	Blood plasma (Rebound)
	Env HIV DNA NGS	Origin of rebounding virus	Isolated CD4 T cells
	UIS Sequencing	Clonal expansion	Isolated CD4 T cells
	RNASeq, ddPCR	Gene expression	Isolated CD4 T cells
	Flow cytometry	Immunophenotyping	PBMC
	Meso Scale, ELISA	Soluble biomarkers	Blood plasma
Post-mortem	**Aptima assay**	Single copy cell-free HIV RNA	Blood plasma, CSF, genital secretion
	ddPCR	Quantify HIV DNA and cellular RNA	PBMC, Anatomic compartments*
	FL HIV DNA NGS	Proviral genetics	PBMC, Anatomic compartments*
	Clonal expression	Replication competence of FL HIV DNA	PBMC, Anatomic compartments*
	Modified QVOA	Replication competence	PBMC and tissue from 4 participants
	Env HIV RNA NGS	Migration dynamics	Blood plasma, CSF, genital secretion
	Env HIV DNA NGS	Origin of rebounding virus	PBMC, Anatomic compartments*
	UIS Sequencing	Clonal expansion	PBMC, Anatomic compartments*
	IHC/ISH, LCM	Cell type infected with HIV, activation	Brain tissue
	Mass spec	Levels of ART and other drugs	PBMC, Anatomic compartments*
	Transcriptomic, ddPCR	Global and targeted gene expression	PBMC, Anatomic compartments*
	Targeted ChIP-Seq	Epigenetic profiling	PBMC, Anatomic compartments*
	Targeted ATAC-Seq	Epigenetic profiling	PBMC, Anatomic compartments*
	Bisulfite sequencing	DNA methylation patterns	PBMC, Anatomic compartments*

Legend. ddPCR: droplet digital PCR, PBMC: peripheral mononuclear cells, GS: genital secretion, QVOA: quantitative viral outgrowth assay, NGS: next generation sequencing, FL: full-length, UIS: unique integration sites, ISH: in situ hybridization, LCM: laser capture microscopy, WB: Western Blot, CSF: cerebrospinal fluid, Mass spec: Mass spectrometry. *Compartments: post mortem PBMC will be sorted in T cells subsets (naïve, translational, memory and effector) and monocytes, gut associated lymphoid tissue (GALT) (i.e. duodenum, terminal ileum, right colon, rectum), Brain (multiple brain regions, white and gray matter), Lymph Nodes (inguinal, cervical, mediastinal and abdominal), Genital Tract (cervix, vagina, ovaries, uterus for women and prostate, testis, epididymis for men), Liver, Spleen, Fat, Lungs and CD34+ stem cells.

APPENDIX L
Advertising Modalities Planned

Includes:

1) Flyers to be circulated within the community
2) Last Gift business cards
3) Link to Last Gift Website with outreach video (http://lastgift.ucsd.edu/)