LIZ SPEECH

DEVELOPMENT OF HUMAN RETROVIROLOGY

HUMAN T LEUKEMIA VIRUS STRAIN I	(1980)
HUMAN T LEUKEMIA VIRUS STRAIN II	(1981)
LYMPHADENOPATHY ASSOCIATED VIRUS (LAV)	(1983)
HUMAN T LYMPHOTROPIC VIRUS STRAIN III	(1984)
AIDS RELATED RETROVIRUS (ARV)	(1984)
SIMIAN T LYMPHOTROPIC VIRUS STRAIN III	(1985)

FURTHER STUDIES

ELECTRON MICROSCOPY

CHARACTERIZATION BY IMMUNOFLUORESCENCE

LONG TERM PROPAGATION IN CELL LINES

PURIFICATION BY SUCROSE GRADIENT CENTRIFUGATION

ELISA

CHARACTERIZATION AND COMPARISON OF MAJOR PROTEINS

CLONING AND COMPARISON OF ISOLATES

RT ASSAY - HTLV-3 CELL LINE (H9)

	CPM (mean)
8/9/85	187,963
8/13/85	194,436
9/5/85	663,801
9/12/85	225,839

* mean of blanks (RPMI) less than 5,000 cpm

RT ASSAY - REPRESENTATIVE EXPERIMENT 10/11/85

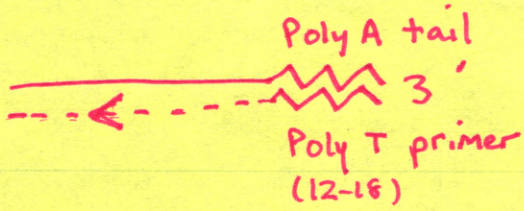
Tube #	Content	CPM
1	med	278
2	med	520
3	H9 sup	207,420
4	H9 sup	168,514
5	ARC day 6	3,530
6	ARC day 6	3,697
7	ARC day 24	38,681
8	ARC day 24	36,628
9	Normal day 6	1,521
10	Normal day 6	1,988
11	Normal day 24	2,673
12	Normal day 24	2,906

SPECIFIC AIMS

(1) TO ISOLATE AND PROPAGATE RETROVIRUSES FROM NEW ONSET SLE

(2) TO CHARACTERIZE ISOLATES AND ASSESS ANY ETIOLOGIC RELATIONSHIP

CLINICAL	LABORATORY
GLOMERULOPATHY	HYPERGAMMAGLOBULINEMIA
ITP	POLYCLONAL ACTIVATION
SICCA SYNDROME	TUBULO-RETICULAR STRUCTURES
CEREBRITIS	ELEVATED IMMUNE COMPLEXES
LYMPHADENOPATHY	ACID LABILE INTERFERON
	T CELL IMBALANCE



template primer

poly-~~A~~ (adenosine) -oligo-dT 12-18 and poly-C-oligo-dG 12-18

over

poly dA - oligo - dT 12-18

FEATURE USUALLY DISTINGUISHES RETROVIRAL ENZYMES FROM cellular DNA polymerases & E coli polymerases (bacterial)

^{3}H TTP ~~-~~ (correct: deoxy adenosine) tritiated thymidine 5' triphosphate INCORPORATION into DNA

COUNTS x 10^3 makes a complementary STRAND OF C DNA FROM

tRNA transfer RNA

MgCl

dATP 2' deoxyadenosine triphosphate

deoxy ATP

DIRECTORY OF RESEARCH GRANTS (DRG)

ORYX PRESS

2214 North Central at Encanto

Phoenix $85004 - 1483

I/M ME, PI of ATEU at UCLA, ~~NOW LONGER ACTING~~ CHIEF OF DIV. Funded by NIH.
JOINING ME FOR THIS PANEL ON Research: Problems & Pr
to my immed right Dr. Harold GINZBURG, CHIEF OF Epi BRANCH OF AIDS Program
Dr. Lawrence MICKEY, OFFICE OF TECHNOLOGY ASSESSMENT
~~AIDS has changed from~~
Each OF US will ~~take 7 minutes FOR opening~~
introduce ~~slightly different but related research~~
our topics and IF time allows we'll follow wi
discussion amongst the panelists.
Dr. GINZBURG will begin with an intro to drug testi
~~ON the~~ treatment IND FOR ~~the~~ new drug azidoth
~~NIH~~ promising
~~I will then describe the task of the NIAID ATE~~ talk about
~~of the anticipated problems.~~
~~Dr. Mickey will present the research agenda as pa~~ ss.
I'll NOW turn the floor over to ~~call~~ ON Dr. G.

Bill
ATEU's

MY TALK

I ~~would first like to indicate that I am not~~ SPEAKING OFFICIALLY FOR the ATEU PROGRAM.
IN the last 2 yrs a high priority has been placed ON the I.D.
OF medically sound effective treatments FOR AIDS VIRUS INFECTIONS
as well as the complicating OI's and cancers. Mortality high.
Progress has been steady associated with improved understanding OF
the biology OF HIV.
IN 1985 NIAID ISSUED a call FOR proposals FOR ATEU CONTRACTS.
IN 7/86 14 were awarded FOR 5 yr. periods including 3 at UC Medical
Campuses.

What are these ATEU's?
~~The~~ ATEU's are CONTRACTS FOR the conduct OF specific clinical trials.
The UNIV personnel associated with these UNITS will test DRUGS FOR (A) HTLV-3 itself - a viral disease OF the immune system
(B) OI's & CANCERS

How do they work?
~~1st~~ AGENTS to be tested are chosen by a drug selection committee at NIH.
NEXT - INVESTIGATORS assoc with the ATEU's meet to originate and
draft protocols as a group.
NOT every CENTER will CONDUCT every protocol.

Where do we stand?
Effective 7/86.
Recruiting staff - NURSES, data, gearing up to do virologic & drug level testing
We have crafted 2 protocols FOR further testing OF AZT
to start early IN 1987. Likely other studies will explore anticipated
toxic interactions OF AZT with other commonly used drugs.

What are the problems?
1st draw distinction between tx eval UNITS which these are
and tx UNITS.
Their 1° charge is to test drugs, NOT to provide 1°, 2° or 3° care to all
pts IN their region. Widespread perception that these are treatment
UNITS. Hospitals could establish tx UNITS such as SF Gen.

I'M ME, PI of ATEU at UCLA, ~~NOW LONGER ACTING CHIEF OF DIV.~~ Funded by NIH.
JOINING ME FOR THIS PANEL ON Research: Problems & Prospects, are
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Dr. Lawrance MICKEY, OFFICE OF Technology Assessment Health Program
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~~ON the~~ treatment IND FOR ~~the~~ new drug azidothymidine (AZT).
~~NIH~~ ~~promising~~
~~I will then describe the task of the NIAID ATEU's and some~~
~~of the anticipated problems.~~ talk about
~~Dr. Mickey will present the research agenda as perceived from the Congress.~~
I'll NOW turn the floor over to ~~call~~ ON Dr. G.

Pathogenesis
treatment
Vaccine
Accelerated

MY TALK

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SAMPLE BIBLIOGRAPHY
AIDS: Workers' Compensation and Hospital Liability Issues

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Department of Medicine, University of California, San Francisco.
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(2) While ~~most~~ the ATEU's are NOT rx UNITS
~~Nevertheless~~ it is likely that their presence at our medical centers will increase the inpat and outpt load of HIV infected patients as we are increasingly identified as sites of leading edge technology

- Placebo controls have been a controversial issue in full blown AIDS a usually fatal disease. This was more of an issue before AZT was shown effective in one category.
~~This can be expected to increase~~
+ Thus issues for Medical staff of AIDS in the workplace will continue
- the ATEU's ~~will~~ should serve as further enhance oppty's for our ~~teaching~~ hospitals ~~represent an important oppty~~ to test COST-CONTAINMENT STRATEGIES: ~~and establishing standards for ICU utilization, length of stay, and identifying drugs which one will become~~ reimbursible - IN other words
There are ~~Another~~ problems associated with these clinical trials: ~~"ongoing care protocols"~~

(1) CONFIDENTIALY SAFEGUARDS FOR RESEARCH SUBJECTS
people who volunteer for research should not be at risk for disclosure. RISK of people who seek rx losing insurance. Especially for asympt. Ab⊕ who may enroll.

(2) because of the ~~urgent need~~ severity of disease for AIDS pressure to develop drugs for AIDS the database on some of the agents to be tested in tox/tol trials may be less extensive than usual. This could result in increased tox.

(3) INFORMED CONSENTS must take this into account. as well as ~~how what one~~ special measures for some subjects who may have mental status abnormalities due to brain infection HIV

(4) ONCE a promising agent like AZT is found ~~it is likely that~~ new ATEU studies will ~~entail~~ be of a preventive nature, e.g. can we modify rate of progression to full blown AIDS in asymptomatic ab ⊕ subject. ~~To reduce~~ ~~risks vs benefit~~ It ~~will be~~ necessary to use placebos for longer periods up to 2 yrs. since the incubation period is measured in yrs. RISK OF A ~~DRUG ACCELERATING~~ PROGRESSION
F ~~Data~~ IN these studies external data safety monitoring boards, will have responsibility for early termination. as IN OUR 1st AZT trial

(5) ISSUES OF ACCESS to those trials FOR ~~minority risk groups~~ unimmuned or unimmunable
(1) WOMEN ~~with~~ and pediatric
(2) ~~children~~ populations.
(3) ~~hemophiliacs & tx recipients~~

~~Despite these problems the ATEU's~~

In conc. While I have focused on Problems FOR PURPOSES OF ~~discussion~~ our discussion today, the ATEU's represent an important oppty FOR US at UC to contribute further to ~~control of~~ improved management of HIV infections.

① placebo
② randomized trials in a hosp sett
③ ongoing care precedents drawn from ATEV
④ informed consent & injuries during trials

SAMPLE BIBLIOGRAPHY
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IB — VR — JR — Persian Guy

6/83 — 12/83 — 1/84 — 3/83 — 1/84 — 6/83 — 1/84 — 1/84

HTLV I
p61
p24
HTLV II
ANTI LAV
QIS's
beta-2
acid labile IFN
thymosin α1
CMV
IgM
IgG.
EBV.
T subsets
OKT 4/8
CBC

Felix Goldberger

Immunohistology of LN in

PGT, MG, JWaltz, Rudnick, Deutsch, Medici, Haverkos

1. recent time V.R.
2. VR serology needed.
3. was it the same CMV by restriction typing

A. intro

B. 3 cases described

C. Table (2)

Imm	viral data and culture

D. Discussion

1. restate message of Francis paper re Koch's
2. describe cases (add Rosario) in more detail; clinical aspects and laboratory aspects
   a. immunology
   b. serology
   c. virology
3. unusual in that virus (CMV) isolated from blood

HTLV III antibody

4. incubation period (12–34
   severe immunologic abnormalities shortly after infusion of donor blood

5. serial specimens of semen time 6 mos vs post-[illegible] and what about titers

[illegible] of CMV from donor to recip
[illegible] of CMV latent.

6. pathogenesis
   a. Donor blood potent hi titer virus potently immunosuppressive just prior to clinical AIDS – post-infectious has not been established for [illegible]
   - presence laboratory HTLV III/LAV
   - b. did CMV [illegible]

7. Stress.
   Co-recipients – only case to date –

JR
24 yo homo ♂

12/82 DOE, FEVER, 10 lb ↓, oral thrush, cough

1/9/83 UCLA bilat INFil, cerv + ax nodes

~~Hxelicited~~ TBBx → PcP Rx success ∈ PENT

WBC 1.9 17 %0L

anaysic

CMV CF ⊖, αHBs ⊕, HbsAg ⊖, α EBV 1:320

IgA 568 (366) G (1426) 1313 M 134 (271)

	1/21/83	3/17	5/23	7/27	9/13		1/19
L1	60 (276)	64 (324)	48 (205)	44 (201)	36	(104)	46
2	43 (198)	44 (223)	2 (154)	47 (215)	27	(76)	43
3	8 (37)	6 (30)	3 (25)	3 (13)	1	2	1
	.19	.14		0.06	0.04		T10 70%

1/12/83 phg 1/1000 7.4 1/100 117,000

9/13 CMV ~~isolated~~

↓ PWM system → min Ig

B cells Nl amts 4:1

Blood reqs.

IMREG-2

Week	-6	-4	-2	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27
History * Physical	X		X	X		X		X		X		X		X		X		X		X		X		X		X		X		+	+
HTLV III	X																														
Skin Test 4 antigens w/ Tetanus Tox. 7°, 24°, 48°	*		*					X				X								*								X			*
Chest X-ray		X																													X
Hematology SMA-12 Immunoglobulins	X	X	X			X		X		X		X				X				X								X			+
Urinalysis	X																														X
Serum Sample	X		X			X		X				X				X				X				+				X			X
T-cell sub sets	X	X	X			X		X				X				X				X								X			X
Cellular Immune Studies				X		X		X				X				X				X				X				X			X
Treatment				X		X		X		X		X		X		X		X		X		X		X		X		X		X	

X Complete at ~~Week~~ -2

Screening at -6 otherwise pertinent interval