Investigational Therapeutics in CJD

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UCSF Memory & Aging Center
Outline

• Therapeutic Treatment of CJD
  – Quinacrine experience
    • Observational human data
    • UCSF mouse data
  – Other potential therapeutic compounds
  – Identifying lead compounds - Screening assays
  – Rational Drug Design

• UCSF Diagnostic Studies
  – Diagnostic utility of MRI
  – First Symptom
  – If time, Conformation Dependent Immunoassay (CDI)
Diagnostic Breakdown of UCSF Potential CJD Contacts Over past 4+ Years

- iCJD: 0.4%
- fCJD: 8%
- GSS: 7%
- Potential sCJD: 27%
- sCJD: 41%
- vCJD: 2%
- FFI: 1%
- Not CJD: 14%
- F:M = 0.9:1

85% from USA
UCSF referred ~1 potential case every 3-4 days

N = ~479
Conformational Changes Feature in Prion Replication

Prion models courtesy of Fred Cohen

Secondary Structure (%)

42 α-helix
3 β-sheet
30 Negative
39 Scrapie infectivity
43 Positive

Prion models courtesy of Fred Cohen
A Model of Prion Replication
More Detailed Model of Prion Propagation

Native PrP<sub>C</sub> → PrP* → PrP<sub>Sc</sub> multimers
Mechanisms of Treatment of Prion Diseases

• General Mechanisms
  – Prevention of accumulation of PrP$^\text{Sc}$
  – Promote clearance of PrP$^\text{Sc}$
  – Combination

• Specific Treatment Mechanisms
  – Mimicking PrP$^\text{C}$ Protective Sites
  – Blocking binding of Protein X (PrP$^\text{C}$ & PrP$^\text{Sc}$)
  – Promoting lysosomal clearance?
<table>
<thead>
<tr>
<th>Some Anti-prion Agents</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dextran sulphate 5</td>
<td>Ehlers &amp; Diringer (1984)</td>
</tr>
<tr>
<td>Amphotericin B</td>
<td>Pocchiari et al. (1989); Demaimay et al (1997)</td>
</tr>
<tr>
<td>Congo red</td>
<td>Caughey &amp; Race (1992), Caspi et al. (1998)</td>
</tr>
<tr>
<td>Anthracycline</td>
<td>Tagliavini et al. (1997)</td>
</tr>
<tr>
<td>Branched polyamines (poly amidoamide dendrimers, Polupropyleneimine, polyethyleneimine)</td>
<td>Supattapone et al. (1999)</td>
</tr>
<tr>
<td>Porphyrin and Phthalocyanine</td>
<td>Priola et al. (2000)</td>
</tr>
<tr>
<td>Cp-60</td>
<td>Perrier et al. (2000)</td>
</tr>
<tr>
<td>E-64d</td>
<td>Doh-Ura et al. (2000)</td>
</tr>
<tr>
<td>Bis-quinacrine</td>
<td>May et al. (2003)</td>
</tr>
</tbody>
</table>
Quinacrine & Chlorpromazine effective *in vitro*

Korth C, May BC, Cohen FE, Prusiner SB. Acridine and phenothiazine derivatives as pharmacotherapeutics for prion disease. PNAS. 98(17):9836-41
French Quinacrine Observational Data

- 8/01-12/02
- 1000 mg po over 30 hours then 100 tid po
- Followed monthly with Rankin (& toxicity)
- 9 patients > 30 days of treatment
- Trend toward improved survival, but not significant (8.8 vs 7 months)*
- No difference in pathology
- Side effects
  - 6 pts - Transaminase elevation
  - 2 pts - skin eruption
  - 1 pt - digestive intolerance
  - 1 pt - leukopenia in one.

<table>
<thead>
<tr>
<th></th>
<th>Treated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total sCJD</td>
<td>30</td>
</tr>
<tr>
<td>N alive (6/03)</td>
<td>9</td>
</tr>
<tr>
<td>Time from Onset to Quinacrine</td>
<td>6.4 mo (1-17)</td>
</tr>
<tr>
<td>Mean Treatment Duration (range)</td>
<td>36 d (1-265)</td>
</tr>
<tr>
<td>Mean Survival From Stop Quinacrine to Death</td>
<td>40d (range 0-176)</td>
</tr>
</tbody>
</table>

* N.B. different codon 129 ratios between groups

Haik 2004 Neurology
UCSF Observations of sCJD Patients on Quinacrine

• It appears sCJD patients who contacted UCSF who started quinacrine (on a compassionate basis by their local physician), may have survived slightly longer than those who patients who did not take quinacrine.

• This was not scientific study. No controlled, randomized study was done; therefore we do not know if quinacrine improves, worsens, or has no effect on survival or quality of life in patients with sCJD.

• Only a randomized, double blinded, placebo controlled study can answer this question. This study will start in 5/05.
CJD Quinacrine Treatment Study

~ 60 sCJD Patients

Placebo tid

Quinacrine 100 mg tid

UCSF < 1 wk

Telephone Follow-up every 2 weeks 1st month

Month 2 – Follow-up @ UCSF
All patients offered quinacrine

Monthly Telephone Follow-up

Month 12 – Follow-up @ UCSF

Monthly Telephone Follow-up to end of study

NIH-funded
Outcomes of UCSF CJD Quinacrine Trial

- Primary
  - Median Survival (or time to feeding tube)

- Secondary
  - Change on neurologic exam, cognitive testing, and ADL scales
  - Change in
    - EEG scale
    - MRI (atrophy & DWI change)

- Potential Variables Affecting Efficacy of Treatment
  - Stage & rate of decline of disease
  - Dose tolerated/Toxicity
### Comparison of UCSF vs UK Quinacrine Prion Trials

<table>
<thead>
<tr>
<th></th>
<th>UCSF CJD Quinacrine</th>
<th>UK MRC PRION1</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cohort</strong></td>
<td>sCJD*</td>
<td>All prion</td>
</tr>
<tr>
<td><strong>N</strong></td>
<td>60</td>
<td>90</td>
</tr>
<tr>
<td><strong>1° Outcome</strong></td>
<td>Survival</td>
<td>Survival</td>
</tr>
<tr>
<td><strong>Duration</strong></td>
<td>~3 yrs</td>
<td>3 yrs</td>
</tr>
</tbody>
</table>
| **Method**     | Stratified, randomized, blinded, placebo controlled | 1. Similar (but no placebo)  
2. Open Treatment  
3. Open No Treatment |

*If PRNP mutation later found, will continue in trial*
CJD Quinacrine Study

• Toxicity
  – Liver – reversible elevated transaminases
  – Blood dyscrasias
  – Rashes
  – Behavior

• Benefits of Study
  – Scientifically evaluate quinacrine – survival, neurologic & other function
  – Prospectively follow course of CJD
In vivo experiments for evaluating quinacrine efficacy against prion disease

| Mouse strains: | Wild type (non-transgenic) strain; FVB, CD-1  
|               | Transgenic strain; Tg(MoPrP-A)FVB-B4053 |
| Inoculation:  | Intracerebral inoculation with RML prion |
| Drug          | Quinacrine (racemate and each enantiomer) |
| Delivery:     | Oral administration using drug mixed liquid diet |
### Treatment of RML-inoculated CD-1 mice (life long Rx with various doses)

<table>
<thead>
<tr>
<th>RML QC (mg/kg/day)</th>
<th>Incub. Time ± SEM (days)</th>
<th>No. Animal prion-sick/total</th>
</tr>
</thead>
<tbody>
<tr>
<td>- -</td>
<td>&gt;250</td>
<td>0/5</td>
</tr>
<tr>
<td>+ 75</td>
<td>126.8 ± 3.0</td>
<td>9/9</td>
</tr>
<tr>
<td>+ 75</td>
<td>121.3 ± 2.6</td>
<td>9/9</td>
</tr>
<tr>
<td>+ 37.5</td>
<td>120.9 ± 1.9</td>
<td>9/9</td>
</tr>
<tr>
<td>+ 37.5</td>
<td>121.4 ± 1.9</td>
<td>9/9</td>
</tr>
<tr>
<td>+ 18.75</td>
<td>121.0 ± 4.3</td>
<td>9/9</td>
</tr>
<tr>
<td>+ 18.75</td>
<td>124.8 ± 3.2</td>
<td>9/9</td>
</tr>
<tr>
<td>+ PBS</td>
<td>120.2 ± 3.2</td>
<td>10/10</td>
</tr>
</tbody>
</table>

Postinoculation (days) 0 70 105 140

Legname, Ryou, Prusiner, et al.
Treatment of RML-inoculated CD-1 mice (Duration of Rx)

| RML (mg/kg/day) | QC | Incub. Time ± SEM (days) | No. Animal prion-sick/total |
|-----------------|--------------------------|----------------------------|
| -               | -                         | >250                       | 0/5                        |
| +               | -                         | 120.2 ± 3.1                | 10/10                      |
| + 37.5          |                           | 120.9 ± 1.9                | 9/9                        |
| + 37.5          |                           | 131.1 ± 4.5                | 9/9                        |
| + 37.5          |                           | 145.0 ± 4.6                | 8/9(1)                     |

Legname, Ryou, Prusiner, et al.
Survival curve for CD-1 mice treated for 30 days with quinacrine starting at 70 days post-inoculation.

Post-inoculation (days)

% survival

P = 0.0003

37.5 mg/kg/day for 30 days

Control (no QC)

Legname, Ryou, Prusiner, et al.
Survival curve for FVB mice treated for 30 days with quinacrine starting at 60 days postinoculation.

- **37.5 mg/kg/day for 30 days**
- **Control (no QC)**

Postinoculation (days)

% survival

P=0.00011

Legname, Ryou, ..., Prusiner
Survival curve of RML-inoculated FVB mice treated for 30 days with quinacrine enantiomers starting at 60 days postinoculation (18.75mg/kg/day)
Summary of in vivo quinacrine studies

• Treatment of prion-inoculated mice with quinacrine prolongs the incubation time, suggesting that quinacrine is effective in vivo for delaying the progress of the disease.

• Prolongation of the incubation time was statistically significant. (2.5-3.5 weeks of prolongation [16-20 % of the incubation time])

• Anti-prion drug effective even when the treatment begins long after the infection has occurred

• Treatment for a short period (30 days) is effective in delaying disease onset

• Questions: how to apply mouse data on time and dose window to people?!

Legname, Ryou, ...., Prusiner
Pentosan Polysulfate (PPS) as Treatment for Prion Disease

- Mice expressing hamster PrP inoculated with 263K prion hamster brain homogenate
- I.T. admin of PPS given 7, 10, 21, and 35 dpi x 4 weeks
- High dose PPS improved incubation 141% at 10 dpi and 71% at 35 dpi
- Decreased pathology also noted at side of infusion, but not contralaterally
- Subcutaneous infusion – no benefit
- Safety - 2/6 dogs on 345 g/kg/day and 3/4 dogs receiving 460 g/kg/day suffered seizures shortly after infusion (1/group survived)
- Also looked at I.T. quinacrine (no benefit) and amphotericin B (26% improvement only at early administration; no benefit at late administration)
- 5 UK vCJD patients; 2 US patients on compassionate use PPS

Dohura 2004 J Virol
Use of Flupirtine to treat CJD

- Flupirtine maleate –
  - centrally acting, non-opioid analgesic
  - In PrP infected cells (and AD models) reduces apoptotic cell death
  - Generally safe, well tolerated drug

- Study done in Germany
- Primary outcome – change in baseline cognitive scale (ADAS-cog); Secondary outcomes – survival
- Placebo controlled. 28 patients total
- MMSE 19-20
- Significantly less decline in ADAS-cog with flupirtine (p=0.02)
- No difference in survival (median 106 vs 107 d; mean 141 vs 97 d), although study not powered for survival
- One conclusion of authors: “It is clear the main challenge in CJD is early diagnosis”

Otto 2004 Neurology
Mechanisms of Treatment of Prion Diseases

• General Mechanisms
  – Prevention of accumulation of PrP\(^{Sc}\)
  – Promote clearance of PrP\(^{Sc}\)
  – Combination

• Specific Treatment Mechanisms
  – Mimicking PrP\(^{C}\) Protective Sites
  – Blocking binding of Protein X (PrP\(^{C}\) & PrP\(^{Sc}\))
  – Promoting lysosomal clearance?
  – Removal of PrP\(^{C}\)?
Drug screening using a cell model of prion infection

Chromically prion infected cells simulate a biologically relevant conversion of PrP<sup>C</sup> to PrP<sup>Sc</sup>

Use cell-based assays as initial screen for efficacy against prion activity

In vitro screens may also be effective

Courtesy of Barney May
Rational Drug Design: blocking prion conversion through small molecule mimicry of “protective” sites

A. 

Native PrP^C → PrP^Sc → PrP^C:PrP^Sc .X Complex → PrP^Sc Oligomer

Auxiliary Molecule ‘X’

B. 

Helix B

T215

Q219

Q172

Q168

C. 

Cp-60

EC_{50}=20 \mu M

Courtesy of Barney May
Small molecule mimicry reduces PrP\textsuperscript{Sc} in cells!
Improving upon a lead compound

Lead compound, quinacrine, was the focus of study to improve potency in culture.

Dimeric analogs of quinacrine, “bis-acridines,” are 10-times more potent than quinacrine!

Courtesy of Barney May
Must diagnose CJD earlier!

- Earlier diagnosis, better chance of treatment
- Identify earliest symptoms
  - Prior studies, retrospective, autopsy
  - chart review
- Identify the very first symptoms
  - Pseudo-prospective, direct contact with patients and families
- On whom to use new diagnostic tests?
Classic MRI Findings in Sporadic CJD

Basal Ganglia Hyperintensities

Thalamic Hyperintensities
(less common)

Cortical Ribboning

T2 FLAIR DWI
Goals of UCSF CJD MRI Study

• What is the sensitivity and specificity of DWI and FLAIR MRI for CJD?

• Difference between electronic and film reading of MRIs?

• Spectrum of MRI involvement in CJD?
Methods - UCSF CJD MRI Study

- CJD cases - 40 serial pts 7/01-11/02 23 definite and 11 probable sCJD
  - 6 genetic CJD (4 E200K, 1 octapeptide repeat, 1 GSS)
- Controls - 53 patients, UCSF dementia clinic
- T1, DWI and FLAIR MRI
  - 12 CJD and 28 controls reviewed on a digital system
  - 28 CJD and 25 control cases viewed on film
- Two neuroradiologists read 93 MRIs blinded, random
  - Interpreted whether CJD or not CJD
  - Noted abnormal areas in each sequence

Young, Geschwind, et al AJNR 2005
### Combined Diagnostic Utility of FLAIR and DWI MRI in CJD* is High

<table>
<thead>
<tr>
<th>Image Display Technique</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Film</td>
<td>0.88</td>
<td>0.98</td>
<td>0.93</td>
</tr>
<tr>
<td>Digital</td>
<td>1.00</td>
<td>0.93</td>
<td>0.95</td>
</tr>
<tr>
<td>Combined</td>
<td>0.91</td>
<td>0.95</td>
<td>0.94</td>
</tr>
</tbody>
</table>

*Based on the average of both readers.

Young, Geschwind, et al AJNR 2005
MRI readings were reproducible

<table>
<thead>
<tr>
<th>Reproducibility of MRI Readings</th>
<th>Intra-Reader*</th>
<th>Inter-Reader</th>
</tr>
</thead>
<tbody>
<tr>
<td>Image Display Technique</td>
<td>Film</td>
<td>Film</td>
</tr>
<tr>
<td>Observed Agreement</td>
<td>0.93</td>
<td>0.92</td>
</tr>
<tr>
<td>Predicted Chance Agreement</td>
<td>0.53</td>
<td>0.50</td>
</tr>
<tr>
<td>Kappa</td>
<td>0.86</td>
<td>0.85</td>
</tr>
</tbody>
</table>

*Digital not included due to 100% inter-reader agreement

Young, Geschwind, et al AJNR 2005
### Areas of Gray Matter Abnormality

<table>
<thead>
<tr>
<th>Region</th>
<th>Percent of Cases with Abnormality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neocortex (N)</td>
<td>CJD 88</td>
</tr>
<tr>
<td>Frontal</td>
<td>CJD 84</td>
</tr>
<tr>
<td>Rolandic</td>
<td>CJD 0</td>
</tr>
<tr>
<td>Parietal</td>
<td>CJD 72</td>
</tr>
<tr>
<td>Temporal</td>
<td>CJD 65</td>
</tr>
<tr>
<td>Primary Visual</td>
<td>CJD 9</td>
</tr>
<tr>
<td>Occipital</td>
<td>CJD 39</td>
</tr>
<tr>
<td>Limbic (L)</td>
<td>CJD 79</td>
</tr>
<tr>
<td>Striatum (S)</td>
<td>CJD 69</td>
</tr>
<tr>
<td>Thalamus (T)</td>
<td>CJD 34</td>
</tr>
<tr>
<td>Controls</td>
<td>Controls 17</td>
</tr>
<tr>
<td>Controls</td>
<td>Controls 9</td>
</tr>
<tr>
<td>Controls</td>
<td>Controls 1</td>
</tr>
<tr>
<td>Controls</td>
<td>Controls 3</td>
</tr>
<tr>
<td>Controls</td>
<td>Controls 11</td>
</tr>
<tr>
<td>Controls</td>
<td>Controls 1</td>
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<tr>
<td>Controls</td>
<td>Controls 2</td>
</tr>
<tr>
<td>Controls</td>
<td>Controls 25</td>
</tr>
<tr>
<td>Controls</td>
<td>Controls 4</td>
</tr>
<tr>
<td>Controls</td>
<td>Controls 0</td>
</tr>
</tbody>
</table>

Young, Geschwind, et al AJNR 2005
Patterns of Abnormality In CJD Cohort

- 68% had both cortical & subcortical (striatal +/- thalamic) abnormalities
- 24% had isolated cortical – “cortical ribboning” – without subcortical abnormalities
- 5% had only subcortical (striatal +/- thalamic) abnormalities
<table>
<thead>
<tr>
<th>Masters</th>
<th>WHO Revised*</th>
<th>UCSF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dementia w/ 1 of 5 following:</td>
<td>Dementia w/ 2 of 4 following:</td>
<td>Rapid cognitive decline w/ 2 of 6 following:</td>
</tr>
<tr>
<td>1. Myoclonus</td>
<td>1. Myoclonus</td>
<td>1. Myoclonus</td>
</tr>
<tr>
<td>5. Typical EEG</td>
<td><strong>AND</strong> Typical EEG or CSF 14-3-3 (if &lt; 2 year duration)*</td>
<td>5. Akinetic Mutism <strong>AND</strong> Typical EEG or <strong>MRI</strong></td>
</tr>
<tr>
<td>*<em>Typical EEG or CSF 14-3-3 (if &lt; 2 year duration)</em></td>
<td></td>
<td><strong>Other focal cortical sign</strong> (neglect, aphasia, apraxia)</td>
</tr>
</tbody>
</table>

* or MRI
First Symptom Study: Methods

- Reviewed relational database of UCSF “CJD” referrals for probable or definite sCJD cases
- Identified more than 100 potential symptoms/signs
- Records review; recorded in CJD database
- Scored quality of first symptom data (0-5)
  - Required clear identification of first symptom(s) by caregiver/patient and/or medical records
- 116 probable or definite sCJD cases with credible first symptom data
- Eliminated 2 patients with >4 first symptoms
- 114 cases for analysis
## Demographics of First Symptom Study

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total patients</strong></td>
<td>114</td>
</tr>
<tr>
<td><strong>Definite sCJD</strong></td>
<td>78 (67%)</td>
</tr>
<tr>
<td><strong>Probable sCJD</strong></td>
<td></td>
</tr>
<tr>
<td>Modified Revised WHO (MRI)</td>
<td>33 (92%)</td>
</tr>
<tr>
<td>Master’s</td>
<td>3 (8%)</td>
</tr>
<tr>
<td><strong>Mean Age</strong></td>
<td>62 +/- 10 (26-80)</td>
</tr>
<tr>
<td><strong>Men</strong></td>
<td>49%</td>
</tr>
<tr>
<td><strong>Women</strong></td>
<td>51%</td>
</tr>
</tbody>
</table>

Rabinovici et al AAN 2005
Distribution of First Symptoms
(Percentage of all First Symptoms)

- Visual: 5%
- Motor: 7%
- Sensory: 7%
- Cerebellar: 15%
- Behav/Psych: 16%
- Constitutional: 16%
- Cognitive: 34%

114 patients with 165 1st Symptoms

Rabinovici et al AAN 2005
## Comparison of Studies
(Percentage of Patients)

<table>
<thead>
<tr>
<th>Symptom /Study</th>
<th>1st Symptom</th>
<th>Early Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>UCSF ‘00-04</td>
<td>France ‘68-82</td>
</tr>
<tr>
<td></td>
<td>N=114</td>
<td>N=230</td>
</tr>
<tr>
<td>Cognitive</td>
<td>49%</td>
<td>46%</td>
</tr>
<tr>
<td>Constitutional</td>
<td>24%</td>
<td>17%</td>
</tr>
<tr>
<td>Behavioral</td>
<td>24%</td>
<td>29%</td>
</tr>
<tr>
<td>Cerebellar</td>
<td>21%</td>
<td>34%</td>
</tr>
<tr>
<td>Sensory</td>
<td>11%</td>
<td>5%</td>
</tr>
<tr>
<td>Motor</td>
<td>10%</td>
<td>5%</td>
</tr>
<tr>
<td>Visual</td>
<td>7%</td>
<td>17%</td>
</tr>
</tbody>
</table>
Distribution of Cognitive Symptoms

- Memory: 45%
- Language: 14%
- Memory and Aging Center
- Frontal/executive: 14%
- Confusion: 11%
- Other: 16%
- Unspecified
- Visuospatial
- Apraxia

N = 56
Rabinovici et al AAN 2005
Distribution of Constitutional Symptoms

- Dizziness: 39%
- Sleep disorder: 14%
- Fatigue: 18%
- Other: 29%

Other symptoms:
- Headache
- GI
- Palpitation/Syncope
- Urinary incontinence
- Weight loss

N = 27
Rabinovici et al AAN 2005
Distribution of Behavioral/Psychiatric Symptoms

- Depression: 15%
- Irritable: 29%
- Unspecified: 19%
- Other: 37%

N = 27

Rabinovici et al AAN 2005
Distribution of Cerebellar Symptoms

Unspecified 8%
Limb 12%
Gait/Balance 80%

N = 24
Rabinovici et al. AAN 2005
Distribution of Motor Symptoms

- **Pyramidal**
  - 27%
- **Extra-pyramidal**
  - 28%
- **Other**
  - 45%

- Fasciculations
- Tremor
- Cramps
- Handwriting changes
- Myoclonus

N = 11
Rabinovici et al AAN 2005
Conformation Dependent Immunoassay (CDI) as diagnostic test

- CDI is an Elisa-based assay for detection of the prion
- It has been shown to be more sensitive and specific than any existing technique for detecting prions in brain tissue
- Work is being done to see if it can detect prions in bodily fluids
CDI is better than gold standard of bioassay in Tg mice

3 sCJD cases

fCJD case

Safar et al. PNAS 2005
Can CDI differentiate prion from non-prion disease brain tissue?

Safar et al. PNAS 2005
Distribution of PrP$^\text{Sc}$ in 24 anatomical areas of 24 sCJD brains determined by CDI

Safar et al. PNAS 2005
Imaging & CDI beat gold standard - pathology

sCJD MV2  sCJD MM1 Bx  sCJD MM1 Ax#1  sCJD MM1 Ax#2

A  B  C  D

E  F  G  H

Courtesy of Steve DeArmond
Safar et al PNAS 2005
Memory & Aging Center (MAC)
Bruce Miller, Joel Kramer, Julene Johnson, Jill Goldman, Jennifer Martindale, Gil Rabinovici, Johannes Levin, Lisa Cook, Genevieve Yu, Jonathan Davis, Mary Konyavko, Andy Josephson, Carrie Meer, Rosalie Gearhart, Christina Wyss-Coray, Kathy Yule, Aissa Haman

Institute for Neurodegenerative Diseases
Stan Prusiner, Jiri Safar, Steve DeArmond, Giuseppe Legname, Chongsuk Ryou, Sam Barillas, Pierre Lessard, Patrick Culhane, Fred Cohen, Barney May

Other UCSF Groups
Neurology – Paul Garcia, Cathy Lomen-Hoerth
Infection Control – John Conte, Kathy Mathews, Anthony Kakis
GCRC – Joel Palefsky, Deanna Sheeley, Nursing staff, etc..
Pharmacy – Joe Guglielmo, Ron Finley
Cancer Center - Clinical Trials Group
Medicine – Bob Wachter & hospitalists
Ophthalmology – Jacque Duncan

Other
NPDPSC (CDC)
CA State Health Dept/CDC
CJD Foundation