The Big Picture of FTD Research: Funding, Collaboration and the Scoop on Participation

1st Annual FTD Caregiver Conference
Raleigh, NC    July 12, 2011
Our objectives today

• Snapshot of medical research process
• Types of research and traditional funders
• Key challenges in FTD research
• New collaborations
• Opportunities for patient and family involvement
Momentum is growing

# of Papers with "FTD" or "FTLD"
# Types of research

<table>
<thead>
<tr>
<th>Type of Research</th>
<th>Objective</th>
<th>Examples</th>
<th>Traditional Funding sources</th>
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<tbody>
<tr>
<td><strong>Basic science</strong></td>
<td>Expand knowledge of normal vs. different</td>
<td>Normal development, structure and function of neurons, proteins and genes that code for proteins, How differ in FTD and other neurodegenerative diseases</td>
<td>Government - NIH via competitive grants, Academia, Private – Foundations, Family initiatives</td>
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<td></td>
<td>Does not create or invent anything new</td>
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<td>No commercial value to discoveries</td>
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<td><strong>Pre-clinical</strong></td>
<td>Knowledge applied to specific problems</td>
<td>Development of and testing in animal models; IPS cells</td>
<td>Traditionally few funders, Increasingly- Public / private initiatives</td>
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<td>Identify targets related to disease process for possible intervention</td>
<td>Identification of specific receptor sites</td>
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<td>Proof of concept</td>
<td>Medicinal chemistry (toxicity, passing blood brain barrier, etc.)</td>
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<td>Test for safety and effectiveness</td>
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<td><strong>Clinical</strong></td>
<td>Determine safety and effectiveness of medications, devices, diagnostic tests, and treatments intended for human use</td>
<td>Diagnostic tests, Biomarkers, Investigational treatments, Investigational drugs</td>
<td>Pharmaceutical or biotech industry, Private</td>
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<td>Potential for commercial value to industry</td>
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Drug discovery process

Generalized Schematic Overview of the Drug Discovery and Development process

Drug discovery process

The Funding Gap or The Valley of Death:

Government tends to fund basic research

A technology may have passed that stage and be too “applied” for further funding

The private sector will not yet pick up technology because it is too risky (has not been fully “applied” yet)

Source: Robert C. Bast, Jr, MD, University of Texas M.D. Anderson Cancer Center
From: The PDMA ToolBook 1 for New Product Development
Representation of attrition rate of compounds through the drug development process over time, [PhRMA, 2008]. 0.001% of compounds that enter the drug development pipeline are approved for marketing which can take up to 15 years and cost $1.3-1.7B; only 2-3 out of every 10 approved drugs recoup their R & D costs.
FTD research funding

Strategic Analysis of Research Funding 1998-2008

$432 million to FTD-related grants

- 10% of funding to Alzheimer’s research

NIH provided 83% of funding (NINDS and NIA)

- 74% toward basic disease research
- 10% toward pre-clinical development, clinical evaluation of tx or diagnostic technologies

NIH funding diminished over time; only partially offset by increase in foundation funding

FTD research challenges

- Clinical heterogeneity: behavior, language and motor
- Pathologic heterogeneity: tau, TDP-43, FUS
- Diagnostic challenges
- Rare disease: numbers are small for studies, recruitment is challenging
Challenges = Opportunities

Clinical heterogeneity “Degeneration” encompasses all clinical presentations; unites and focuses efforts

Pathologic heterogeneity suggests key partners for drug discovery
  - Tau: Alzheimer’s
  - TDP-43: ALS
Challenges = Opportunities

Rare disease confers Orphan Drug Status

FDA allows accommodations in clinical trial design
• Smaller number of patients
• Shorter trial
• Surrogate endpoints
• No current treatment taken into account

Rare disease communities have a voice
AFTD: Promote and fund research

Understand challenges (scientific, financial, etc.)

• Strategic Analysis of Research Funding 1998 – 2008
• Talk to academic researchers, pharma and biotech companies
• Talk to peer organizations

Identify where in drug development process we can make a difference

Identify key partners
AFTD: Promote and fund research

Basic research:
- Pilot grants
- Postdoctoral Fellowship

Pre-clinical (translational) research:
- FTD Drug Discovery grants
  - Partner ADDF matches donations 2:1
  - $1.6 million granted in four years
- iPSC Consortium: PD, ALS, HD, FTD
Clinical research:

- National patient database (NACC FTD Module)
- Posting research opportunities on AFTD website
- Host meetings to bring scientists and clinicians, academics and pharmaceutical industry together
AFTD: Promote and fund research

Nurture key relationships
- Scientists, ADDF, NINDS and NIA, pharma and biotech companies, FDA

Advocate for and represent most important partners in research

FTD patients and families
Clinical research opportunities

Key aspects of clinical research

• Informed consent – people have right to decide to participate or not participate.
• Randomization – assigned to experimental or control randomly
• Blinding – investigators not aware of assignment
• Placebo controls -
• Statistical and clinical significance
Ways to participate in research

Observational studies

• Follow individual patients to document natural progression of disease
• Gather data from neuropsych tests, brain imaging, etc
• Provides comparison in intervention studies

Considerations:

• Eligibility criteria; logistics of participation (distance, frequency, tolerance of tests)
• Major centers on AFTD website
Ways to participate in research

Brain autopsy / brain donation

• Examines brain tissue after death
• Only way to determine pathological diagnosis
• Can pursue definitive diagnosis via autopsy outside research program
• Greatest benefit to scientists is correlating pathology results with clinical history during life
• Brain donation for research requires enrollment in observational study
Ways to participate in research

Considerations:

• Can be emotionally difficult to consider
• Most often requires prior participation in observational study
• Requires early planning and coordination with research center, funeral home
• Gather information early; allow ample opportunities to discuss
Ways to participate in research

FTD Caregivers and Researchers: Partnering for Brain Donation

- AFTD /IUADC study to explore obstacles to brain donation; funded by NIH
- Found many families interested in brain donation, but lack knowledge about opportunities
- Ineffective communication and misunderstanding between researchers and caregivers is notable (when, how raised, by whom, what is involved, etc)
Ways to participate in research

Clinical drug trials

• Tests new compounds in patients and controls
• Number of trials of existing drugs in FTD population (ie: Memantine)
• Earliest trials of FTD disease modifying drugs starting
• Two Phase II trials underway in PSP (Noscira-tideglusib and Davunetide)
Ways to participate in research

Considerations:

• Strict eligibility criteria and adherence to protocol needed to ensure rigorous science
• Randomization doesn’t guarantee patient will get experimental drug
• May be unpleasant, serious or even life-threatening side effects to experimental treatment.
• The experimental treatment may not be effective
Ways to participate in research

**Phase I trials** - researchers test an experimental drug or treatment in a small group of healthy people (20-80) to evaluate its safety, determine a safe dosage range, and identify side effects.

**Phase II trials** - experimental study drug or treatment is given to a larger group of people (100-300) to see if it is effective and to further evaluate its safety.

**Phase III trials** - experimental study drug or treatment is given to large groups of people (1,000-3,000) to confirm its effectiveness, monitor side effects, compare it to commonly used treatments, and collect information that will allow the experimental drug or treatment to be used safely.

**Phase IV trials** - post marketing studies delineate additional information including the drug's risks, benefits, and optimal use.

Source: Clinicaltrials.gov
Momentum is growing

You can keep the momentum going.

• Register with AFTD for updates on research
• Investigate opportunities that may interest you
• Connect with a local academic research center
• Scan listings on www.ClinicalTrials.gov
• Donate to AFTD research or drug discovery efforts