Nevada Consortium on Dementia Research | Friday, March 31, 2017, 12:00PM-1:00PM

Attendance: Mary Johlfs; Dr. Ronald Fiscus ; Merrill Landers; Charles Bernick; LeeAnn Mandarino; Kat Hartley-Mack; Isaac Santa Ana. (listened in) Peter Reid; Cheyenne Pasquale.

Meeting Notes:

1. Dr. Bernick Welcome
2. Dr. Ronald Fiscus & Mary Johlfs Presentation
    a. Introduction to Capillary Electrophoresis.
    b. New technologies for identifying/quantifying biomarkers in Alzheimer's, Parkinson's, & Lewy body dementia. Discovery of the molecular mechanisms (e.g. nitric oxide (NO) & PKG-Ialpha) of Abeta neurotoxicity, sAPPalpha neuroprotection & therapeutic effects of PDE5/PDE9 inhibitors & memantine.
    c. Dr. Fiscus predicts a combination of PD inhibitors with memantine should be an effective therapy for animal models.
        i. Endothelial Cell: Signaling pathway in blood vessels. Nitrates lower blood pressure. Identified protein kinase, PKG for vasodilation. Human body is producing its own nitric oxide, keeping our blood pressure low. If any step in the pathway is blocked, it causes hypertension.
        ii. Parasympathetic Neuron: Penile erection and erectile dysfunction utilizes the nitric oxide pathway. Viagra, Cialis, Levitra are enhancing the pathway. Drop in blood pressure, vasodilatation.
        iii. Neuronal PKG (hippocampal neurons). Confocal microscopy identified PKG cholinergic neuronal cell to co-localized with tubulin.
    d. NanoPro1000, capillary electrophoresis. Looking at cell survival proteins. sAPP alpha, secreted form of APP has the opposite effects, neurotrophic factors. Phosphorylates transcription factors, e.g. CREB. Phospho-BAD are in neural cells part of neuroprotective mechanism.
    e. PKG is the cell survival protein. PKG 1 alpha, Dr. Fiscus' Lab separated the iso-forms using NanoPro 1000. Separates all the proteins, so we can look for off-target effects of the anti-body.
    f. How to use this new technology?
        i. Abeta 1-40, Abeta 1-42, sAPPalpha, sAPP beta, tau protein (total), phosphorylated tau protein, alpha-synuclein.
        ii. Post-translational modifications? Acetylation, glycosylation, Nanopro1000 can use a single antibody and separate them using PI value and have ability to measure what percent is in each post-translational modification form.
    g. Nitric oxide at toxic level, Stuart Lipton. Blocking NMDA receptor, results in a mass release of Glutamate and nitric oxide, toxic to the neurons. Macrophages, neutrophils, use nitric oxide to produce toxic nitric acid.
    h. Memantine shifts the balance of nitric oxide to safer physiological protective levels.
    i. PD5 & PD9 are especially protective. Pfizer has a PD9 inhibitor, which synergistically enhances protective effects. PD9 in humans are neuroprotective. Bayer has their own, showing protective effects in neuron cells. Dr. Fiscus suspect low levels of neuroprotective pathways.
3. NCDR Website:
    a. Website is designed to facilitate collaboration between researchers and provide a pathway for patients to participate in clinical trials.

b. Introduced clinicaltrials.gov registry for linking website to clinical study information, which eliminates duplicating work. However, ClinicalTrials.Gov is not all that we do. There is academic research and sociological research, as well. It is not required that all researchers conducting human studies (clinical trials or observational studies) to register their study in clinicaltrials.gov. But it is in their best interest to post their clinical studies and keep them up to date for recruitment purposes.
    i. The following types of studies are generally excluded from the registration and results submission requirements of FDAAA 801 (see note). This is not a complete list.
        1. Phase 1 drug trials, including studies in which investigational drugs are used as research tools to explore biological phenomena or disease processes (see note)
        2. Small clinical trials to determine the feasibility of a device or a clinical trial to test prototype devices, where the primary outcome measure relates to feasibility and not to health outcomes (see note)
        3. Trials that do not include drugs, biologics, or devices (such as behavioral interventions)
        4. Noninterventional (observational) clinical research (such as cohort or case-control studies)
        5. Trials that were ongoing as of September 27, 2007, and reached the Completion Date (see Primary Completion Date data element on ClinicalTrials.gov) before December 26, 2007 (see note)
        6. Note: Trial may be subject to the Voluntary Submissions provision of FDAAA 801. See the statutory provision for Voluntary Submissions (PDF) for more information.
        7. For complete statutory definitions and more information on the meaning of Applicable Clinical Trial, see Elaboration of Definitions of Responsible Party and Applicable Clinical Trial (PDF).

c. There's been a suggestion to create a link for current research in Las Vegas and Reno, then another link to clinicaltrials.gov. Third link "Would you like to participate in any of the clinical trials occurring in Reno and Las Vegas?"
    i. To include what trials are available; basic demographics; menu of different studies. HealthyBrains.org offers an educational component and opportunity to opt-in to participate in clinical trials using Healthy Brains website. However, how will other site recruit their subject?

d. Cheyenne
    i. We have to be cognizant of the language used in the website. What is the bare minimum that physicians and patients need to know to participate in the clinical study? Inclusion and Exclusion criteria.
    ii. "Recommend" button brings up a form to email someone, a link to the trial information.
    iii. Is it the responsibility of the researcher to update the information in the website?
    iv. Two options for website design:
        1. Trials as a listing. Access is given to each research to register their own clinical study listings. Pros: they have easy access to editing. Con: is having to relying on researchers to keep their study information up to

date. Yet, again, it is in the researcher's best interest to maintain their study information up to date for recruitment purposes.

2. Central person. Central person captures all clinical studies from clinicaltrials.gov occurring in Nevada, which requires researchers to keep clinicaltrials.gov up to date. We can send out reminders every quarter or half year for central person to post all clinical studies occurring in Nevada. Pros: research does not have to post study in website. Con: clinicaltrials.gov is not always up to date, especially for recruitment purposes.

v. Consensus: NCDR members decided researchers will manage their own listings. And have a "recommend" and "participate" button.

vi. LeeAnn and Isaac will schedule a meeting next week.

4. Bylaws
    a. Review for later.
    b. Include mission statement.
5. Who's willing to present next time?
6. Next meeting. Quarterly. December 2nd.