



UNLOCKING THE SECRETS OF BRAIN DISEASE®

Areas of Research Focus for CurePSP in 2016-17

CurePSP has five core areas of *Research Focus* that top our list of priorities again in 2016-17. In addition, there are two new areas that we believe deserve added attention from the community of researchers and clinicians who focus on prime-of-life neurodegenerative disorders: *investigating the potential of cell therapy and regenerative medicine* and *iPS cells & gene editing research*.

1. **Etiology/Pathogenesis of PSP/CBD and related disorders.** This is a very broad category of interest that would include identification of genetic risk or susceptibility factors, environmental contributions to disease risk (exposures to chemicals, viral or other pathogens, diet etc.) and identification of potential protective genetic or environmental factors.
2. **Development of validated models of PSP and related disorders.** Again, this is a broad category that encompasses both cell culture and animal models of neurodegeneration.
3. **Identification and validation of disease-specific biomarkers.** This category recognizes the value of biomarkers to aid in early (and definitive) diagnosis of PSP and related disorders (or to accurately classify specific Tauopathies). In addition to diagnostic utility, biomarkers are expected to be useful in the context of clinical trials as indicators of biologic activity (and perhaps, early indications of disease modification).
4. **Leverage existing and emerging genetic risk alleles to validate new targets for drug development.** Several risk alleles have now been identified through GWAS and sequencing efforts. While great strides have been made developing novel therapeutics targeting Tau, less is known about the biology of other risk alleles. Successful disease modification for patients with PSP and related disorders may ultimately require combination therapy with a Tau-targeted agent, plus drugs targeting other processes such as inflammation, protein turnover, or susceptibility to

apoptosis. We need more insight into the function of other risk alleles, and how the specific changes associated with increased disease risk impact that function.

5. **Clinical studies focused on obtaining ‘proof of concept’ for novel therapeutics, or that introduce important advances in symptom management or palliative care for patients with PSP and related disorders.** Small clinical studies have the potential to provide initial clinical data needed to gather the (significant) resources required for definitive studies leading to approval of new therapeutics. These might include testing of a new indication for a previously approved drug, or picking up development of a clinical stage asset that failed for another indication, but for which there is a strong rationale for testing in patients with PSP or related disorders. Symptomatic management of patients with PSP and related disorders could be significantly improved even with agents that are not disease modifying.
6. ***Investigating the potential of cell therapy and regenerative medicine.*** Thus far, we are aware of few preclinical or clinical studies that focus on cell replacement, whether through stimulation of endogenous neuronal precursors or introduction of exogenous cells. We believe that regenerative medicine approaches should be explored now to lay the groundwork for potential therapeutic application in the coming decade.
7. ***iPS cells and gene editing.*** Rapid advances in these distinct scientific realms open the possibility to create novel models of disease that encompass parts of points 2, 3 and 4 above. The ability to generate patient specific cell lines (“disease in a dish”), and to create isogenic lines with specific risk alleles incorporated or corrected via gene editing opens up many possibilities for disease modeling, generation of cell lines for drug screening, and phenotypic characterization of novel disease-associated DNA variants.

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