Supplementary Material

A Novel Approach to the Treatment and Prevention of Alzheimer's Disease Based on the Pathology and Microbiology

Pathway for Spirochetes in Alzheimer's Disease

Spirochetes have been demonstrated in AD brains by pathology [1-3].

Spirochetes have been cultured from AD brains by microbiology [1,2].

Those cultured spirochetes make A β and A β protein precursor simultaneously with making biofilms *in vitro* [4].

Biofilms have been demonstrated by pathology both intra and extracellularly in vivo [5,6].

A β has been demonstrated intracellularly *in vivo* by pathology [5].

A β plus ordinary tau protein has been shown to generate p-tau [7].

P-tau has been shown to eventuate in dendritic disintegration and neurofibrillary tangles [7].

Extracellular biofilms have attachment sites for TLR 2 which generates both NFkB and A β by known pathways [8].

Spirochetes may require up to two years to make a single biofilm [5].

Bacteria such as *porphyromonas* can make a biofilm in minutes [9].

Biofilms made by one organism have receptor sites for other organisms which are incorporated into the community. Their role, if any, is undetermined [8, 10].

Given the similarity by pathology, microbiology, and clinical findings of GP and AD, it seems reasonable to consider organisms similar to *T. pallidum* in the etiology of AD.

REFERENCES

- Miklossy J (2011) Alzheimer's disease a neurospirochetosis. Analysis of the evidence following Koch's and Hill's criteria. *J Neuroinflammation* 8, 90.
- [2] MacDonald AB (1986) Borrelia in the brains of patients dying with dementia. JAMA 256, 2195-2196.
- [3] Riviere GR, Riviere GH, Smith KS (2002) Molecular and immunological evidence of oral treponemes in the human brain and their association with Alzheimer's disease. *Oral Microbiol Immunol* 17, 113-118.
- [4] Miklossy J (2016) Bacterial amyloid and DNA are important constituents of senile plaques: further evidence of the spirochetal and biofilm nature of senile plaques. J Alzheimers Dis 53, 1459-1473.
- [5] Allen HB (2016) Alzheimer's disease: assessing the role of spirochetes, biofilms, the immune system, and beta amyloid with regard to potential treatment and prevention. J Alzheimers Dis 53, 1271-1276.
- [6] Allen HB, Allawh R, Touati A, Katsetos C, Joshi SG (2017) Alzheimer's disease: the novel finding of intracellular biofilms. *J Neuroinfect Dis* **8**, 247.
- [7] Iqbal K, Alonso AC, Chen S, Chohan MO, El-Akkad E, Gong C Khatoon S, Liu F,
 Rahman A, Tanimukai H, Grundke-Iqbal I (2005) Tau pathology in Alzheimer disease
 and other tauopathies. *Biochim Biophys Acta* 1739, 198-210.
- [8] Tukel C, Wilson RP, Nishimori M, Pezeshki M, Chromy BA, Baumier AG (2009) Responses to amyloids of microbial and host origin are mediated through toll-like receptor 2. *Cell Host Microbe* 6, 45-53.
- [9] Singhrao SK, Harding A, Poole S, Kesavalu L, Crean S (2015) *Porphyromonas gingivalis* periodontal infection and its putative links with Alzheimer's disease. *Mediators Inflamm* 2015, 137357.
- [10] Stewart PS, Camper AK, Handran SD, Huang C-T, Warnecke M (1997) Spatial distribution and coexistence of *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* in biofilms. *Microb Ecol* 33, 2–10.