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Funding report: CJDSGN Memorial Grant in memory of Frank Burton, Bassil Gianniodis, Primo Monaci, Rhonda Sanders, Cesarina Stilla and Ross Glasscock and others lost to CJD

The above award covered a 0.55FTE salary for the recipient between 1/1/18 and 30/6/18. During this period, the following activities were undertaken:

- Negotiation of new international collaborations to enhance the competitiveness of prion grant applications within Australia.
- Submission of an NHMRC Project Grant application for funding from 2019–2021. Application ID: APP1163854. Title: "Spontaneously generated recombinant prions: a tool for understanding triggers of transmissible spongiform encephalopathies". Chief Investigators: Dr Simon Drew, Prof Jiyan Ma (USA). Associate investigators: Prof Oliver Kohlbacher (Germany), A/Prof Vicki Lawson, Dr Suzette Priola (USA).
- Assessors' reports for the above application were received and a rebuttal to those comments was submitted on 13/7/18.
- Preparation of substrate for generation of recombinant prions by PMCA, following the protocols of Jiyan Ma.
- Serial PMCA experiments to replicate the findings of Prof Ma, with the aim to spontaneously generate and study recombinant prions in Melbourne. Two independent experiments were conducted, the first comprising 4 replicate samples, the second comprising 3 replicate samples. In both experiments, serial PMCA was conducted over a period of 17–20 days, with replicate samples being diluted into tubes containing fresh substrate each day. In total, 130 individual sample tubes were subjected to PMCA.
- In the first experiment, a protease-resistant species with a molecular weight near 17kDa was generated in 1 of 4 replicates, as determined by proteinase K digestion followed western blotting. The species appeared after 4 rounds of PMCA and persisted up to 20 rounds. In the second experiment, none of the 3 replicates produced protease-resistant PrP.
- Practice in culture of RK13 cells (self-taught) in preparation for eventual screening of infectivity within PMCA-treated samples.

Future experiments to be conducted to obtain additional preliminary data in support of major funding:

- Test the ability of the above protease-resistant PrP samples to infect RK13 cells.
- Test the ability of Jiyan Ma's recombinant prions to infect RK13 cells (positive control).
- Test for the presence of RNA bound to protease-resistant PrP, to investigate the hypothesis that nucleic acid chemically-bonded to PrP creates a spontaneous infectious seed.

The support of the CJDSGN and the generosity of the donors is gratefully acknowledged for enabling the possibility to continue this research.

Simon Drew
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