Hong Kong Student Science Project Competition 2023

Template of Extended Abstract (Investigation Design Proposal)
(Word Limit: 1,600 words, Pages: 3 pages only)

Team Number: JCBC160

Project Title: Theranostics of Prion Disease - A Disease that has currently No Known Ways to Cure

Project Type: Investigation Design Proposal

***To our best knowledge, there are similar works in the field*; related research links are as below:**

Langeveld JP, Wang JJ, Van de Wiel DF, Shih GC, Garssen GJ, Bossers A, Shih JC. Enzymatic degradation of prion protein in brain stem from infected cattle and sheep. J Infect Dis. 2003 Dec 1;188(11):1782-9. doi: 10.1086/379664. Epub 2003 Nov 18. PMID: 14639552. https://pubmed.ncbi.nlm.nih.gov/14639552/

The enhancement our project proposed / the difference with related research are:

Work [1] focuses on what degrades prion protein and how the method can help effectively sanitise related equipment. Work [2] discusses the possibilities of using bacterial keratinise produced by Bacillus licheniformis to fully degrade prion protein. However, both works do not mention the cure(s) of prion disease in brains. Our proposal aims to develop a way to cure prion disease in the brain.

Please delete if not applicable. The competition values the originality of works. Students must do enough literature research to ensure that their works are unique and list relevant reference materials before starting research or invention.

I. Background

Prion disease is a neurodegenerative disease caused by misshapen proteins in the brain. The disease is extremely rare but extensively fatal, having only 1-2 cases in a million contracting it every year [2]. This disease affects both humans and animals, and branches of it include *Kuru, Gerstmann-Sträussler-Scheinker syndrome, fatal familial insomnia*, and most commonly diagnosed, *Creutzfeldt-Jakob disease (CJD).* **Prion disease originates from the prion protein, which is found in many body tissues, including the brain.** The disease happens when proteins as such mutate from their original forms and form a clump, aggregating in brain tissue, hence becoming the cause of prion disease. This causes the brain to have a sponge-like form, damaging nerve cells and killing neurons. Currently, there are many different methods to diagnose and to slow the progression of disease, but there has been no cure discovered to heal this disease completely. Thus, this project aims to fill this research gap.

II. Objective(s)

We aim 1) to further our understanding regarding the prion disease(s) by obtaining detailed information about it; 2) to raise the public's awareness about the prion disease(s) through a website; and 3) to develop a possible cure for prion disease with two steps: 3a) to perform a surgery to open the skull and inject the attached destabilisation materials to GPR126 (G protein-coupled receptor 126 of prion), and 3b) repeat the same process but inject the attach degrading materials to GPR126 instead.

III. Hypothesis

It is hypothesised that Bacillus licheniformis can degrade prion proteins after pretreatment of heat in the presence of detergents and attachment to GPR126. Glycine will bind to GPR126 via its side chain and is able to destabilise prion's secondary structure, i.e. the beta sheet.

IV. Methodology

Materials:
Glycine (receptor of prion & used to destabilise prion)
Bacterial enzyme keratinase (to destabilise prion protein)—Bacillus licheniformis (to degrade prion)
GPR126 (receptor of prion)
microscope and laboratory tools
Sup35NM-His6, which has a chemical structure similar to that of a prion,[5]

Our cure method is proposed based on related works on toxin therapy that is used to treat cancer [4]. To test the applicability of our method, two experiments are designed.

Experimental protocol:
The first experiment is to test out whether GPR126 can bind to glycine via polypeptide side chains, and then test out whether it can destabilise Sup35NM-His6. As glycine has binding preferences, its receptor can be verified through "quantitative comparison of the identified peptides with a sample generated by a control probe [3]". The second experiment is to test out whether GPR126 can bind to bacterial enzyme keratinase after pretreatment of 100°C heat with the presence of detergents or other prion-degrading materials [1] via polypeptide side chains by examining the product's chemical structure, and whether it can degrade Sup35NM-His6.

Scientific theories behind the proposal of our cure:
Aza-amino acids can destabilise prion protein by disrupting beta-sheet structure. If GPR126 successfully binds to aza-amino acids via polypeptide side chains, the new "product" will then be able to bind to prion protein and destabilise it by disrupting the beta-sheet structure. Other GPR126 to bind to bacterial enzyme keratinase or other prion-degrading material via polypeptide side chains. The heat pretreatment and disinfection will then promote enzymatic degradation of prions [1]. The second "product" will then be able to bind to prion protein and degrade it.

V. Expected Results and Impact of research

已註解 [1]: In my opinion, this is actually not a limitation but can be an advantage, because similar method has been proven to work on cancer cells to treat cancer. Revise if I didn't understand you correctly.

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Expected results:
The prions, GPR126 and aza-amino acids are expected to bind with one another and the prions and GPR126 will be destabilised and degraded respectively.

Limitations:

1. Patients suffering from severe prion disease may not be able to be cured
2. Some nerve cells may be slightly damaged from the heat pretreatment of keratinase but it does little damage to the patient's nerve cells that are mostly dead already.

~~There are some existing related works such as Toxin therapy used on cancer cells [4].~~

Importance and impact of research:

- This research can raise the public awareness of important information of this deadly disease, such as disease trends, risk factors, outcome of treatment, and most importantly the possible cure. Since this disease currently has no known ways to cure, our proposed cure provides a new direction for investigation. If successful, this method may be applicable to other types of degenerative and neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, Cystic fibrosis, which are also caused by protein misfolding.

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VI. If your team will compete for the Sustainable Development Award, please indicate the specific sustainable development goal the project is related to, and provide justification for competing for this award. ***(Word limit: 300 words)***

The project is aiming to achieve SDG3 — Good Health and Well-being. SDG3 is about ensuring healthy lives and promoting well-being for all at all ages. The value behind aligns with our project aim. Our proposal is designed to find out a possible cure to a disastrous kind of brain disease, and promote it on a website to raise people's awareness on food hygiene and disease prevention. This group hopes that through competing for this award, the message will be exposed to the public, reminding everyone to take care of their physical well-being.

VII. If your team will compete for the Social Innovation Award, please list the target group or social issue the project focuses on, and provide justification for competing for this award. ***(Word limit: 300 words)***

N/A

VIII. Conclusion

Our proposal aims to develop a possible cure for prion disease with two steps - (1) attaching destabilisation materials to GPR126 and (2) attaching degrading materials to GPR126 (receptor of prion). We also hope to raise public awareness of this disease.

VIV. References

[1] Langeveld JP, Wang JJ, Van de Wiel DF, et al. Enzymatic degradation of prion protein in brain stem from infected cattle and sheep. J Infect Dis. 2003;188(11):1782-1789. doi:10.1086/379664 https://pubmed.ncbi.nlm.nih.gov/14639552/

[2] Occurrence and Transmission | Creutzfeldt-Jakob Disease, Classic (CJD) | Prion Disease | CDC. www.cdc.gov. Published November 14, 2022. https://www.cdc.gov/prions/cjd/occurrence-

transmission.html#:~:text=The%20majority%20of%20cases%20of

[3] Frei AP, Moest H, Novy K, Wollscheid B. Ligand-based receptor identification on living cells and tissues using TRICEPS. Nat Protoc. 2013;8(7):1321-1336. doi:10.1038/nprot.2013.072 https://pubmed.ncbi.nlm.nih.gov/23764939/

[4] Grenda T, Grenda A, Krawczyk P, Kwiatek K. Botulinum toxin in cancer therapy—current perspectives and limitations. Applied Microbiology and Biotechnology. 2021;106(2):485-495. doi:https://doi.org/10.1007/s00253-021-11741-w https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8763801/#__ffn_sectitle

[5]1. Wang JJ, Borwornpinyo R, Odetallah N, Shih JCH. Enzymatic degradation of a prion-like protein, Sup35NM-His6. Enzyme and Microbial Technology. 2005;36(5-6):758-765. doi:https://doi.org/10.1016/j.enzmictec.2004.12.023 https://www.sciencedirect.com/science/article/abs/pii/S0141022904004077