Mathematical modelling of immunotherapy treatments: interleukin-27 and anti-programmed cell death-1

Xander Bjornsson and Dr. Kang-Ling Liao

University of Manitoba

Background

Cancer is a leading cause of death. Checkpoint inhibitors and cytokines have been recently successful treatments, but lab results can take months. Mathematical modelling can accelerate the learning process.

Programmed cell death (PD-1)

- Binds to ligand (PD-L1)
- Inhibits T cell tumor response
- Expressed by tumor cells
- Anti-PD-1 treatment aims to prevent interaction

Interleukin-27 (IL27)

- Pro and anti-tumor effects
- Promotes PD-1 complex

Objectives & hypotheses

Objective

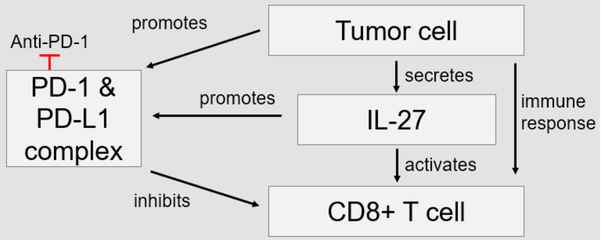
- Successfully simulate the interactions between IL-27 and anti-PD-1.
- Replicate experimental results
- Test for optimal dosage

Initial hypothesis

- The combination of these two treatments can enhance the efficacy

Methods & experimental design

1. An interaction model is created showing the various interactions of importance between the tumor and the treatment.

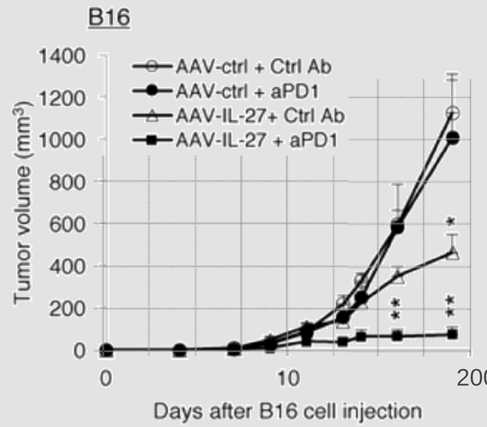


Interaction model for IL-27 and anti-PD-1 treatments

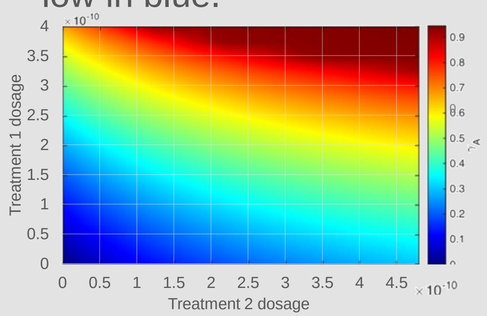
2. The interaction model is used in the creation of an equation.
3. A simulation using the equation is made to test if the model is accurate and will be compared to the results by Zhu et al. (2018); Fig 3.
4. Once the simulated model is confirmed tests on the effects of varied dosing can be done to determine an optimized dosage of both treatments.

Expected results

- Expect that the simulated model reflects experiment results by Zhu. et al (2017)



- Simulations provide a heatmap of the most efficient treatment prepared. Figure below shows the simulated efficacy of a combination treatment by Lai. et al. (2017). High efficacy in red, low in blue.



- We plan to create a similar heatmap but for the results of IL-27 and anti-PD-1 treatments.

Conclusion

Final hypothesis

- There is an optimal dosage for the combination of the IL-27 and anti-PD-1 treatments

When the heatmap gets created it will provide insight into how to provide the most effective treatment. This is important because researchers can design their future results with a more effective model. The researchers can also find a more cost-effective treatment as the prices for the treatments are expensive. Modelling also produces results much quicker than lab-based experiments whereas testing a treatment can take months.

Acknowledgments

I would like to thank cancer researchers for their continuous efforts in helping cancer patients. I would also like to thank Dr. Kang-Ling Liao, Dr. Jane Waterman, and the 2020 class of BIOL 3100 at the University of Manitoba for all the help, guidance, and advice.

References

- Lai, X., & Friedman, A. (2017). PLoS ONE, 12(5), 1–24. https://doi.org/10.1371/journal.pone.0178479.
- Zhu, J., Liu, J. Q., Shi, M., Cheng, X., Ding, M., Zhang, J. C., Davis, J. P., Varikuti, S., Satoskar, A. R., Lu, L., Pan, X., Zheng, P., Liu, Y., & Bai, X. F. (2018). JCI Insight, 3(7). https://doi.org/10.1172/jci.insight.98745