Thesis Project Portfolio

Optimization of an SQL Database Towards Selective Targeting of Acute Myeloid Leukemia Cells

(Technical Report)

How Machine Learning and Artificial Intelligence Can Help Us Fight the Next Pandemic

(STS Research Paper)

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Introduction

Diseases, and humanity's struggle to control them, have been a defining part of human history. Malaria, which remains one of the deadliest diseases on the planet, has been responsible for the deaths of an estimated 4 to 5 percent of all people who have ever lived (Harford, 2013). While malaria still remains a very important issue, in the future the diseases that will pose the biggest threat to humanity will come in the form of pandemics. As evidenced by the global response to COVID-19, our increasingly globalized and interconnected world makes it very difficult to have a controlled response to new infectious diseases. This problem is important, considering another pandemic within our lifetimes is more likely than some people might like to admit (Marani et al., 2021). Given this challenge, we must use the best tools that we have at our disposal. Since these are problems that involve complex systems with many inputs and outputs, Artificial Intelligence (AI) and machine learning (ML) technologies have the potential to be very helpful. The STS research paper examines how humanity can use AI and ML to stop future pandemics. Aside from pandemics, it is also important to consider other, non-infectious diseases and how we can prevent the harm they cause, such as Acute Myeloid Leukemia. An examination of this disease and an attempt to find a novel therapeutic target is performed in the technical report.

Summary of Technical Report

Acute Myeloid Leukemia (AML) occurs when there is an accumulation of poorly differentiated cells in the blood and bone marrow (Meyers et al., 2013). AML is the most prevalent form of leukemia for adults, representing roughly 80% of cases, and follows a rapid clinical progression. In 2015, there were over 20,000 recorded cases of AML and over 10,000

recorded deaths in the US (De Kouchkovsky & Abdul-Hay, 2016). Despite advances in treatment, it is estimated that up to 70% of AML patients 65 years or older will die as a result of the disease within 1 year of their diagnosis (Döhner et al., 2015). There is a critical unmet need to identify new targets in order to improve standard-of-care therapy and increase overall survival. ZielBio, a clinical stage biotechnology company, has developed a novel drug discovery platform, which has been used to successfully identify targets that have been overlooked by comparable screening techniques. The platform integrates phage display technology in order to reverse engineer the discovery process, allowing unbiased screening to be coupled with bioinformatics and drive target identification (Brinton et al., 2016). By performing screening within the native context of the cell, the platform is able to identify mislocalized targets. Thus far, the platform has yet to be applied to hematological cancers. This capstone project aims to harness the platform to identify AML-selective targets for the future development of an anti-cancer targeted therapeutic. In addition, the platform's database is examined and refined in order to increase the efficiency of its search processes.

Summary of STS Research Paper

Due to their ability to process vast amounts of information and perform pattern recognition at superhuman speed, Artificial Intelligence (AI) and Machine Learning (ML) have the potential to kill the next pandemic in its crib. As demonstrated by COVID-19, the modern, globalized world can turn strange local phenomena into worldwide problems. This is especially true for pandemics, which have occurred at a relatively regular pace throughout human history and can now spread with relative ease due to increasing amounts of international travel and trade (Piret & Boivin, 2021). In this paper, the following research question is examined: How can humanity use AI and ML to prevent and minimize future pandemics? An analysis is performed

through a search of academic literature using relevant keywords such as “AI”, “Pandemic”, “COVID-19”, “Machine Learning”, and “Disease X”. This research results in a conclusion regarding the likely ways in which AI and ML may be used to prevent the spread of future deadly diseases. Using the frameworks of Political Technologies and Risk Analysis, the issue at hand is also examined through a Science, Technology, and Society (STS) lens. By grappling with the ramifications of AI before it becomes ubiquitous, STS scholars can better understand the societal changes that are still to come.

Conclusion

Working on these projects concurrently has added both perspective and depth to my understanding of diseases and how we as a society should address the challenges they present. By seeing and performing the lab techniques that make up the cutting edge of drug discovery, I have seen the remarkable levels of effort that are involved in the creation of new medicines that will save and improve lives. At the same time, diving into the science behind stopping a future pandemic has allowed me to see the future of drug discovery, vaccine development, and societal coordination. The same collective incentives that make cancer drug discovery a worthwhile endeavor are those that will bring us together to fight the next pandemic. Seeing this similarity and realizing that both areas are downstream of scientific research has made me more grateful for the people I have worked with and the degree I have pursued.

Works Cited

Brinton, L. T., Bauknight, D. K., Dasa, S. S. K., & Kelly, K. A. (2016). PHASTpep: Analysis Software for Discovery of Cell-Selective Peptides via Phage Display and Next-Generation Sequencing. *PLOS ONE*, *11*(5), 1–22. https://doi.org/10.1371/journal.pone.0155244

De Kouchkovsky, I., & Abdul-Hay, M. (2016). 'Acute myeloid leukemia: a comprehensive review and 2016 update'. Blood cancer journal, 6(7), e441. https://doi.org/10.1038/bcj.2016.50

Döhner, H., Weisdorf, D. J., & Bloomfield, C. D. (2015). Acute Myeloid Leukemia. *The New England journal of medicine*, *373*(12), 1136–1152. https://doi.org/10.1056/NEJMra1406184

Harford, T. (Host). (2013, October 5). Have Mosquitoes Killed Half the World? [Audio podcast episode]. In More or Less. BBC. https://www.bbc.co.uk/sounds/play/p01hnv98

Marani, M., Katul, G. G., Pan, W. K., & Parolari, A. J. (2021). Intensity and frequency of extreme novel epidemics. Proceedings of the National Academy of Sciences, 118(35), e2105482118. https://doi.org/10.1073/pnas.2105482118

Meyers, J., Yu, Y., Kaye, J. A., & Davis, K. L. (2013). Medicare fee-for-service enrollees with primary acute myeloid leukemia: an analysis of treatment patterns, survival, and healthcare resource utilization and costs. *Applied health economics and health policy*, *11*(3), 275–286. https://doi.org/10.1007/s40258-013-0032-2

Piret, J., & Boivin, G. (2021). Pandemics Throughout History. *Frontiers in microbiology*, *11*, 631736. https://doi.org/10.3389/fmicb.2020.631736