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The Prediction and Prevention of Cancer: An Evolutionary Approach

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Abstract

Darwin's Theory of Evolution is widely known as one of the most important aspects of biology among scientists and researchers. The relationship between evolution and medicine is a critical phenomenon which can lead to the innovation of newly implemented models and techniques, in hopes of suppressing life-threatening diseases in humans such as cancer. This paper aims to discover and understand how evolution can predict and prevent cancer in humans. A major topic that this paper delves deep into is understanding the connection between evolution and medicine. Additionally, it looks to gain insight on how cancer has evolved and what scientists have learned from its progression over past generations. Lastly, this paper identifies and explains the various models that exist to aid in the prediction of cancer. Evolutionary medicine is a modern tool that can be used to further develop today's medicine. Predicting evolution can allow scientists to implement advanced technological tools in the field of medicine, such as antibiotics and vaccines, which can prevent and treat diseases including cancer before the onset of severe outcomes. Evolution is a fundamental principle that has the potential to improve the field of medicine.

Keywords: Evolution, cancer, Medicine, Disease, Prediction, Prevention

Darwin's Fundamental Theory of Evolution and Medicine

Darwin's Theory of Evolution is a broad topic that has played a major role in all of biology. It has cultivated scientists and researchers to be able to better understand the world we live in. Evolution, as proposed by Charles Darwin in his book titled "On the Origin of Species", is essentially described as changes in the heritable traits of an organism over generations (Than et al., 2021). The changes in traits and characteristics were discovered by Darwin to be driven by natural selection, which is a term he chose in contrast to artificial selection (Than et al., 2021). This idea of natural selection, being one of the main mechanisms of evolution, is popularly described as "descent with modification" and sometimes referred to as "survival of the fittest" among scientists and researchers (Than et al., 2021). In terms of evolutionary biology, an organism's fitness is deemed to be measured by their ability to survive and reproduce. As natural selection drives evolution in particular environments, this process can lead to an entirely new species, when given enough time, that is better suited for the environment and is able to survive and reproduce more efficiently (Than et al., 2021). In terms of evolutionary biology, the main focus is on the longevity of a species and their success in passing their genes to the next generation, however one critical component of evolution that seems to affect this process predominantly in humans is disease—specifically cancer.

Disease is a major component of evolutionary biology considering its effect on the fitness of organisms—particularly humans. The relationship between evolution and disease is an important stepping stone in modern medicine and public health, which works to effectively prevent and treat various diseases when they occur within the human population. Evolution is broadly known for its ability to not only predict science as a whole, but to allow scientists and

researchers to gain critical insight into the future of generations of species to come. As scientists and researchers use Darwin's Theory of Evolution to gain knowledge about the longevity and future well-being of various species, the main goal is to assess whether evolution can be used to predict and treat diseases such as cancer in humans (Casás-Selves & DeGregori, 2011). Some key components that this paper looks to address is the fundamental relationship between evolution and medicine, the evolution of cancer over time, and the identification of various models which can allow scientists and researchers to predict and treat cancer in humans. The idea of using evolution to aid in advancing medicine has been widely acknowledged by scientists and researchers since the principles of evolutionary medicine would allow for a better understanding of why diseases arise in humans, which is the ultimate goal.

Evolutionary medicine is a key phenomenon which can allow scientists and researchers to successfully predict and treat life-threatening diseases such as cancer. Gaining knowledge on the effect of evolution on the field of medicine is an important aspect regarding future medical advancements (Gluckman et al., 2011). The ability to connect evolutionary principles to medicine would allow scientists and researchers to further develop preventive strategies to suppress cancer in the human population. Another important stepping stone in using evolutionary medicine to prevent and treat cancer is to firstly understand how the disease has evolved, not only through the human race, but through other species in various environments as well, which can ultimately allow scientists and researchers to determine the specific environmental factors that increase an organism’s susceptibility to cancer and its driving factors (Grigorios, 2022). Lastly, using evolutionary models to predict cancer is one of the most efficient ways of suppression in regards to diseases such as cancer, which aid in the prevention aspect of evolutionary medicine. Having the ability to predict any disease has implications including the early implementation of

antibiotics, vaccines, and targeted therapies before the onset of the disease. The ability to forecast the risk of developing cancer in humans would be a significant step forward in the ultimate fight against this life-threatening disease.

Principles of Evolutionary Medicine

Evolutionary medicine, or sometimes referred to as Darwinian Medicine, is a growing field in the realm of biology which specifically deals with the prevention and treatment of diseases with the support of Darwin's Theory of Evolution. One of the core principles of evolutionary medicine is that natural selection, being the driving force for all of evolution, acts directly on the fitness, rather than the health, of species (Gluckman et al., 2011). This principle demonstrates that disease is not a direct result of evolution, rather, the species' risk of developing a certain disease in a specific environment is the reason behind the evolutionary onset of a particular disease within a population (Gluckman et al., 2011). This idea leads to many discrepancies between physicians and scientists about the validity and emphasis of evolution in regards to medicine (Gluckman et al., 2011).

One of the primary principles of evolution is that natural selection, the main mechanism and driving force of evolution, acts directly on the fitness of an organism and nothing else (Gluckman et al., 2011). The point of natural selection acting on an organism's ability to survive is to pass on favorable traits to the next generation of offspring, which is known as descent with modification. This idea of descent with modification advocates for the belief that only the fittest species in a particular environment will survive to be able to pass on their genes. In regards to medicine and public health however, efforts to promote the well-being of a population typically revolve around preventing and treating diseases rather than directly applying the evolutionary

concept of "survival of the fittest" (Than et al., 2021). Since there seems to be a major difference on how evolution is perceived to act upon species compared to how medicine looks to act upon populations, some physicians tend to neglect many of the core principles of evolutionary medicine.

Another major principle of evolutionary medicine is that evolution, through natural selection, does not cause disease to occur in populations or individuals, but rather, evolution works to affect the susceptibility or probability that a specific population of species might develop a particular disease in the future (Gluckman et al., 2011). The final principle states that the environment which habitats the human population has drastically changed in comparison to hundreds of thousands of years ago when selection used to play a major role in human evolution (Gluckman et al., 2011).

A study by Grunspan et al. (2017) states that evolutionary medicine has grown to provide a deeper understanding of human health related topics including aging, immune function, and most importantly, cancer. This study went on to define the core principles of evolutionary medicine and asked several panelists made up of physicians, biologists, and experts in other fields whether they agree with the core principles that were listed. The results showed that out of the 27 core principles of evolutionary medicine that were provided for the panelists, 23 of those principles were agreed upon by more than 50% of the panelists (Grunspan et al., 2017). Some of the core principles of evolutionary medicine that had either 100% or close to 100% agreement between all panelists were that all evolutionary processes are important for understanding traits and diseases, several limitations exist that inhibit natural selection to shape traits that are optimal for health, and natural selection maximizes reproductive success at the expense of health and longevity

(Grunspan et al., 2017). The study goes on to state that evolutionary medicine is a rapidly growing field which needs more emphasis in the medical field due to its increasing potential to advance the field of medicine as a whole.

The Evolution and Origin of Cancer

Understanding the evolutionary history of cancer can allow scientists and researchers to gain a better insight into the overall prevention and treatment of the disease. Darwin's Theory of Evolution is typically labeled as “science about the past”, however having the ability to make the connection between the evolutionary history of cancer and its progression over time is a fundamental aspect in the fight against the disease (Nosil et al., 2020). The process of evolution, described as natural selection and mutations acting on a population and leading to the creation of a new species, can be directly compared to the process of cancer, which involves natural selection and mutations acting on cells and leading towards the creation of tumors (Casás-Selves & DeGregori, 2011). There are many known factors that are evident in promoting cancer evolution, in which having a good understanding of, can allow scientists and researchers to better understand why cancer occurs more commonly in certain social groups or environmental factors than others.

Cancer is known to have evolved over several generations and will continue to evolve over many future generations, however, this disease has been shown to be more prevalent in humans than any other species because of its evolutionary makeup and genetic inheritance factors (Gerstung & Jolly, 2020). There are billions of cells in the body that are subject to evolutionary processes through mutations and natural selection (Gerstung & Jolly, 2020). A research article by Aktipis (2021) based on a study explains how understanding the ecological and evolutionary perspective of cancer will highlight ways in which scientists and researchers can detect whether cells are willing to cooperate. The study describes how cells have a set of rules that they must

follow in order to successfully sustain life and survive. When cells end up breaking these rules, they are known as “cheating” cells as the study suggests (Aktipis, 2021). These “cheating" cells essentially divide when they shouldn’t, rob neighboring cells of their nutrients and supplies to benefit themselves, and ultimately pollute the extracellular space (Aktipis, 2021). As the evolution of cancer becomes more evident and new findings are discovered, this new perspective of the disease will allow scientists and researchers to gain further insight as to why cancer happens and why it doesn’t (Aktipis, 2021). The study goes on to discuss the role of cell cooperation in terms of evolution and how larger animals, such as elephants, rarely develop cancer compared to humans, despite having many more cells with the potential to essentially “cheat”. It was discovered that these larger animals are equipped with extra copies of cancer suppressor genes which primarily work to control cells that fail to cooperate, one of them being TP53 (Aktipis, 2021). The study concludes by stating that after many generations of evolution, humans and other species have evolved to acquire the tools necessary in preventing cancerous cells from taking over the cellular environment.

Darwin's Theory of Evolution is widely known to act on the fitness of an organism, rather than the direct health of a species. In terms of cancer, evolution by natural selection is known to have conflicting effects with multicellular individuals and is known to favor proliferating cells which act as promoters for the disease (Aktipis, 2021). As generations have progressed, humans and other species have evolved to develop suppressors that work to limit cancer. Even though natural selection is seen to act on the development of cancerous cells, there are many other environmental factors that are known to drive the evolution of cancer (Casás-Selves & DeGregori, 2011). Factors including aging and carcinogens are found to make healthy cells more vulnerable to DNA damage and mutations, which are both known to promote

the development of tumors, eventually leading to cancer (Casás-Selves & DeGregori, 2011). The environmental factors that drive the evolution of cancer are the reasons why scientists and researchers cannot solely focus on the principles of evolution to discuss the prevention and treatment of this disease. Scientists and researchers must consider the surrounding environment as a way of maintaining fitness and preventing cancerous cells from outcompeting cooperating healthy cells.

Evolutionary Models to Predict Cancer

Darwin's Theory of Evolution has always been acknowledged as a form of historical science that gives insight into the past, however due to recent studies, this seems to be deemed as a misinterpretation. The predictability of evolution is an important strategy that can be implemented to further develop the field of medicine. The ability to predict science and evolutionary change, specifically in humans, has major implications regarding medicine, including the development of antibiotics and vaccines to aid in the fight against various diseases (Nosil et al., 2020). In the realm of evolution, predicting is essentially forecasting allele changes which might lead to evolutionary change in an organism. The ultimate goal, in terms of medical advancements, is to have the ability to forecast whether an individual will develop a certain disease so that prevention and treatment can be implemented early to improve the overall health outcomes of patients and prevent catastrophic events or outbreaks from occurring within a population (Barrick, 2020).

The ability to forecast evolutionary change is a major challenge—but not impossible. One study by Nosil et al. (2020) suggests that by using temporal data that spans several generations, we can essentially apply trends in data to predict what is to come. The study states that focusing on medium-term evolution will allow scientists and researchers to predict immediate evolutionary

responses to selection, as long as the trends are parallel with those that are discovered over large time scales (Nosil et al., 2020). Figure 1 shows that by using trends which have been witnessed over past generations, scientists and researchers can continue these same trends over future generations and come extremely close to the actual observed data.

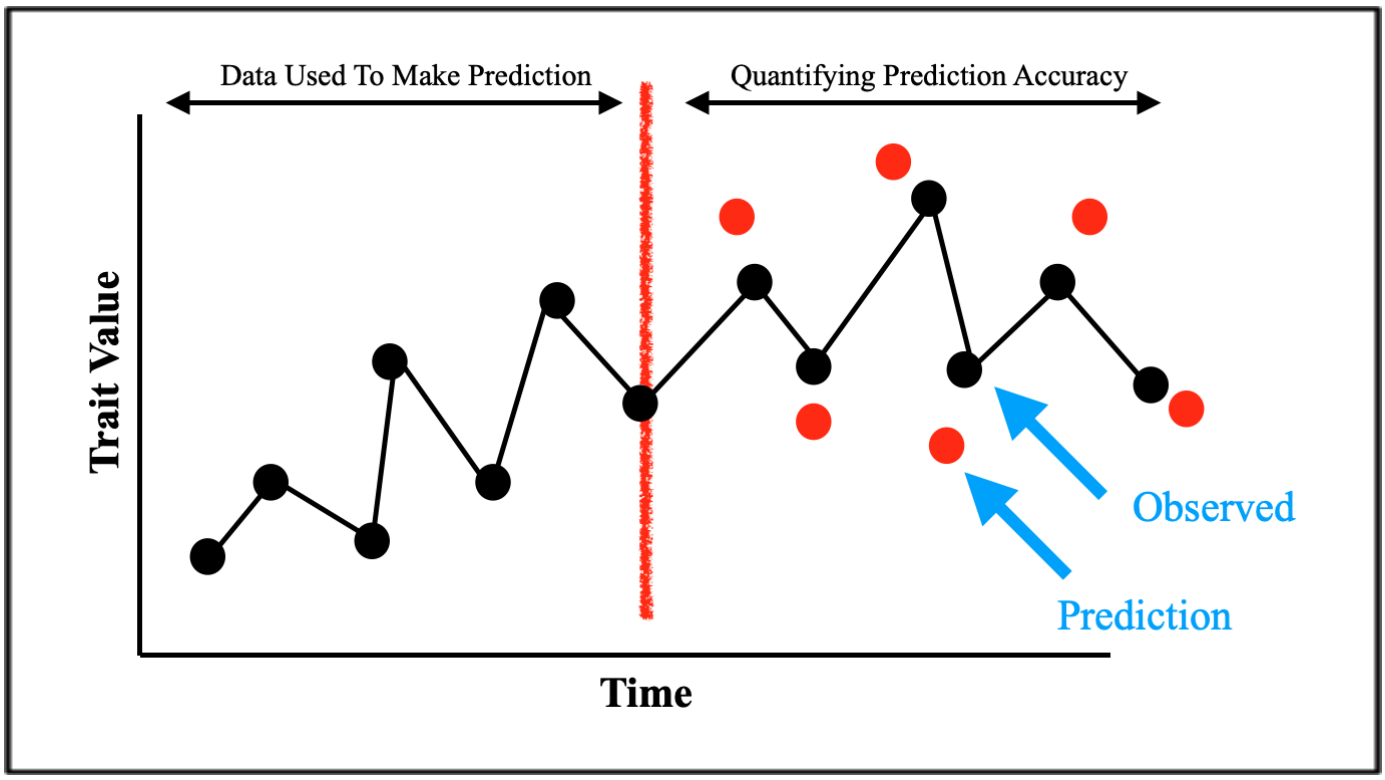

Figure 1. Quantifying predictability of evolution using time-series data. Data from previous generations can be used to predict future generation outcomes as depicted by the accuracy of the predicted values compared to the observed values. Adapted from Nosil et al. (2020).

Predicting evolution, in respect to medicine, is one of the most critical processes that can alter the ability to treat and prevent cancer. In a recent study, Diaz-Colunga & Diaz-Uriarte (2021) explain how evolution can be used to create prediction models, which can then be implemented to predict tumor progression. The study suggests that long term prediction is very limited in terms of

evolution due to random mutations and the unavailability of adequate data sets (Diaz-Colunga & Diaz-Uriarte, 2021). The research article states that models used to predict short-term evolutionary progression in tumors are more beneficial in a clinical aspect (Diaz-Colunga & Diaz-Uriarte, 2021). The study included 13 various methods that could be used to successfully predict 25 million tumor simulations and 25 real cancer cases (Diaz-Colunga & Diaz-Uriarte, 2021). Cancer Progression Models (CPMs) have been created to predict evolutionary changes in tumors by taking into account all possible mutation trajectories and providing probabilities for various evolutionary pathways, which gives insight and knowledge as to how the tumor can be assessed and treated early on. This method of predicting evolutionary pathways is a suitable counter to the limiting factors, including the randomness and unequal likelihood of mutations occurring at any nucleotide, which may suppress the ability to predict evolution in terms of medicine (Lind et al., 2019). Even though predicting evolution comes with many limitations, the process is still ongoing and continued research will ultimately allow scientists and researchers to further enhance their ability to prevent and treat life-threatening diseases such as cancer in humans.

Limitations to Cancer Prediction

The idea of using Darwin's Theory of Evolution to predict complex diseases in humans such as cancer is a major advancement in regards to today’s medicine, however, there are a few limitations that exist, which subdue the ability to forecast evolution. One article by Nosil et al. (2020) looks to classify these limitations using two distinct hypotheses; The Random Limits Hypothesis and The Data Limits Hypothesis.

According to the study, the Random Limits Hypothesis states that the ability to forecast

and predict evolution in today's world is bounded by complete randomness (Nosil et al., 2020). Some of the main driving forces of evolution, being mutations and genetic drift, are completely random processes and are almost always impossible to predict at times. For this reason, scientists and researchers have implemented a way to bypass this limitation—by implementing tumor and mutational progression pathways, rather than using direct predictions (Nosil et al., 2020). These prediction pathways provide various probabilities and chances of a specific progression pathway to be taken by a specific mutation or tumor, which may be more beneficial when direct predictions are not as feasible due to the randomness in mutations and genetic drift (Nosil et al., 2020). The second limitation, known as the Data Limits Hypothesis, states that sufficient data and proper analysis is required in order to make predictions regarding complex diseases such as cancer (Nosil et al., 2020). Since many of these forecasting methods use cross-sectional data, the criteria states that these data sets must be properly analyzed and free of any errors before making these forecasts (Nosil et al., 2020). Adequate data sets meeting the criteria of the Data Limits Hypothesis are usually difficult to obtain, thus leading to the limitation of the ability to forecast evolution.

Conclusion

Darwin's Theory of Evolution is one of the most important and fundamental aspects of biology. This idea of using evolution and medicine to prevent and treat life-threatening diseases such as cancer is only going to further develop and advance the field of medicine. Evolutionary medicine will allow for the use of evolution to make predictions and implement advancements in treatment options for life-threatening diseases. Models can be used to aid in the prediction of disease progression and health outcomes. By obtaining insight on the evolution of diseases in

humans such as cancer, it can allow physicians to effectively create plans to treat such diseases and prevent further negative health effects. Evolution is one of the most innovative ideologies that can help shape the future of medicine.

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