Paper DH09

Human BioGeography™: predicting clinical trials outcome using a 3D human body simulation and a GIS framework

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ABSTRACT

Due to the limited success rate in clinical trials, with less than 20% of drug candidates progressing through all phases for marketing approval, novel innovative approaches remain essential to improve these statistics. This paper proposes a novel system combining relevant databases from different Open Data sources with a Geographic Information System (GIS) that will contribute to confront this challenge. By integrating information from several biorepositories, including previous reports of drug development processes, into a 3D simulation of the human body our system aims to identify determinants restricting clinical trial success. We call this “Human BioGeography™” and is based on a hierarchy of anatomy => disease => therapeutic target => drug => chemical structure. This approach provides crucial insights for drug developers, offering data on aspects that influence drug approval rates, such as potential adverse events and drug viability and metabolism. This system is expected to improve both trial design and development processes, revolutionizing the clinical trial landscape

INTRODUCTION

In the field of developing new medicines and medical devices, a major challenge persists: clinical trials face very low success rates. Indeed, less than 20% of new drug candidates successfully accomplish all the necessary steps to be approved for public use (Figure 1) [1] [2] [3] [4]. This hurdle significantly slows down clinical progress, urging scientists and drug developers to find more effective strategies for achieving success in these clinical trials.

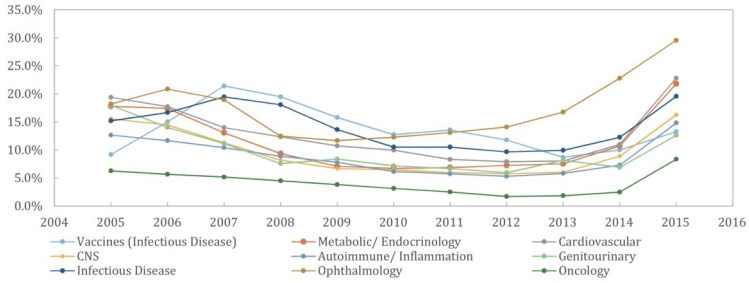

Figure 1. Evaluation of the clinical trials success between 2005 and 2015. In this study, Wong CH et al. included 406,038 of clinical trial data for over 21,143 compounds. Data are classified by the therapeutic area [1].

Both successful and unsuccessful clinical trials have generated a huge amount of incredibly useful information available through Open Data databases. The wise integration of these data can help us find the weak points leading to clinical trial failure. For example, the combination of these data could help us to predict how the human body reacts to different medications in order to prevent adverse events. Additionally, during the last few years with the development and combination of both omics and bioinformatic tools a huge amount of data has been generated. This information is invaluable because it provides the groundwork for creating new drugs tailored to meet the diverse needs of patients. However, this valuable data is spread out across many websites and databases and lacks organization in a way that researchers can easily cross-link such data. Therefore, there is a necessity for a comprehensive tool that can gather, integrate and present all of this Open Data information in a clear and practical manner.

A Geographic Information System (GIS) is defined as "An integrated collection of computer software and data used to view and manage information about geographic places, analyze spatial relationships and model spatial processes" [5]. GIS serve as an indispensable technology in the field of spatial data analysis. They are commonly used to analyze and visualize information related to locations on the Earth's surface. These technologies are designed to capture, store, manipulate, analyze, manage, and present all types of geographical data, helping users to better understand the complex relationships between various data points by mapping them onto geographical locations.

Imagine a scenario where all the data from past clinical trials as well as the information from previous preclinical research are acquired, aggregated, combined and presented within a 3D simulation of the human body. This is the essence of Human BioGeography™, which integrates data from various stages of drug development using Open Data databases and the analytical abilities of GIS, making this information much more understandable and accessible to all types of users.

Within the complex world of human biology, Human BioGeography™ creates a clearer picture, aiming to improve the landscape of clinical trials and contribute to advancements in medical research.

HUMAN BIOGEOGRAPHY™

By employing a geographical metaphor, Human Biogeography™ integrates anatomical, biological, and genetic data enabling the visualization of intricate spatial patterns and relationships inside the human body. Based on the concept of a *GeoReferencing*, used by GIS to link digital maps to real-world geographic coordinates, we propose the concept of "*BioReferencing". A BioReference* connects biological and medical data points within a standardized reference system of the human body. Similar to how GIS assists in precise Earth location, *BioReferencing* anchors all the information about the target in the specific body localization, where users can pinpoint the exact anatomical structures, diseases, or therapeutic targets that are linked by the specific *BioReference*. It will be visualized as a mapping system of the human body containing all the relevant biological information stored in different databases spatially interconnected by means of the corresponding *BioReference*. This system will integrate and contextualize biological data, such as anatomical structures, diseases, therapeutic targets, drugs, or chemical compositions, providing a standardized framework in which each data points will be accurately referenced and interconnected.

In essence, adopting a *BioReferencing* model will provide a wealth of benefits that facilitate drug development, enhance patient safety, and drive the pharmaceutical industry towards more targeted and effective therapies. This approach allows researchers and clinicians to explore biological data at different levels, from macroscopic organ systems to microscopic cellular interactions, fostering a profound comprehension of human physiology, and providing a complete depiction of the relevant aspect during drug development process. Users can delve into specific biological layers, such as metabolic pathways or genetic expressions, enhancing the depth of analysis and uncovering key points for drug development. By integrating historical and real-time data within the layers, predictive modeling becomes feasible for anticipating biological responses, adverse events, and drug interactions, allowing researchers to make data-driven decisions. *BioReferencing* will establish a standardized reference system, streamlining collaboration among researchers, pharmaceutical companies, and regulatory authorities. This common reference ensures consistent communication, leading to more efficient drug development processes and regulatory approvals.

HUMAN BIOGEOGRAPHY™ IN DRUG DEVELOPMENT

Human BioGeography™ is a novel approach to serve as a basis for drug and clinical trial development by integrating diverse elements into a geographical-like framework. At its core, data are meticulously organized in a hierarchical structure, ranging from fundamental anatomical structures to intricate chemical compositions. This arrangement offers a better understanding of the elements to be considered prior to starting a clinical trial.

A key strength of Human BioGeography™ lies in its ability to merge information from various Open Data databases. By exploiting this collective knowledge, the system provides a panoramic view of clinical trials, encompassing both new drugs and cutting-edge medical devices. This integration is foundational to its predictive capabilities, covering a spectrum of critical factors influencing clinical trial outcomes. From predicting adverse events to evaluating drug viability, metabolism intricacies, and age-dependent responses, Human BioGeography™ covers every facet essential for informed decision-making.

What sets Human BioGeography™ apart is its intuitive, Google Maps-like visual interface. Complex datasets are transformed into layered visualizations, each representing a specific aspect for the drug development process (Figure 2). This visual approach simplifies understanding, making the complex information easily accessible and facilitating precise analysis.

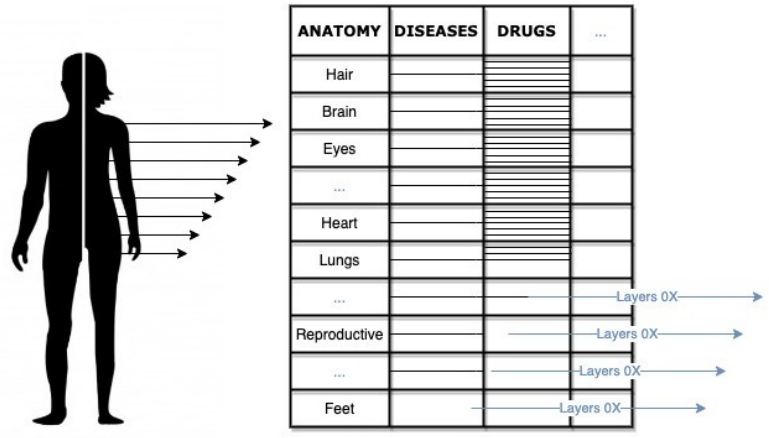

Figure 2. Scheme of the Human BioGeography ™, composed by layers hierarchically classified as shown, from a macroscopic to microscopy depiction.

APPLICATIONS AND BENEFITS OF HUMAN BIOGEOGRAPHY™

By offering a global view of the human body's responses to existing drugs, this approach will aid in designing more targeted and efficient clinical trials. It will enable the prediction of potential adverse events, optimize drug formulations, and enhance overall trial outcomes. Moreover, Human BioGeography™ will facilitate data-driven decision-making, leading to improved success rates in clinical trials.

ADDRESSING LIMITATIONS OF EXISTING APPROACHES

While various tools and methodologies exist in the field of drug development and clinical trials, many of them grapple with inherent limitations. Traditional methods often lack a unified approach, resulting in fragmented data and incomplete insights. Moreover, some existing tools struggle with the integration of diverse datasets, hindering a comprehensive understanding of complex biological interactions, which results inefficient and time consuming (Figure 3).

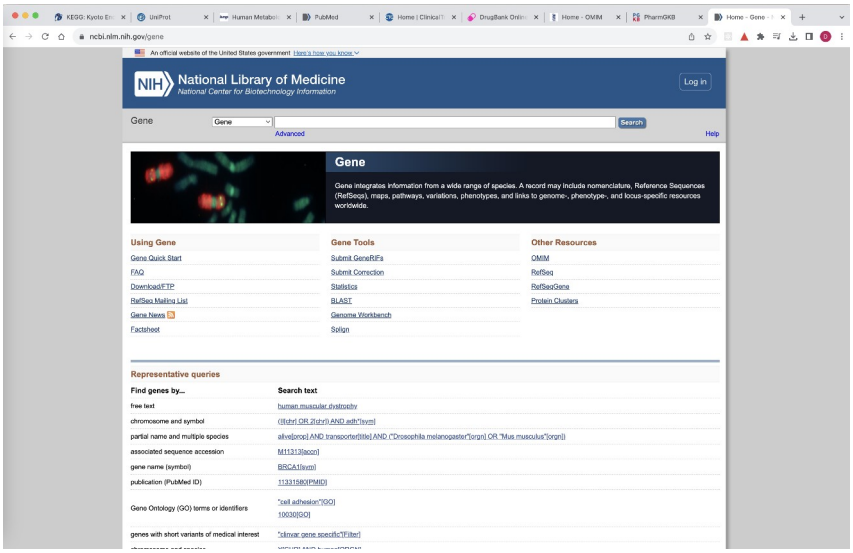

Figure 3. This screenshot shows a habitual investigator display searching for information about the existing information related drugs, clinical trials, among others.

Human BioGeography™, in contrast, bridges these gaps. Its unique approach organizes data hierarchically in a 3D, location-centric structure of the human body. By integrating information from various Open Data databases, users of Human BioGeography™ will uncover relevant information for clinical trials, new drug development, and the use of advanced medical devices, by predicting adverse events, drug viability and metabolism, and even considering age-dependent responses.

OPTIMIZING DRUG FORMULATIONS FOR TARGETED THERAPIES

Human BioGeography™ aims to improve the development of novel targeted drug formulations by increasing their effectiveness and reducing adverse events by analyzing data on therapeutic targets within specific anatomical structures

The integration of data on disease-specific responses and therapeutic targets within the human body refines the art of drug formulation, enhancing treatment effectiveness and fostering heightened patient compliance.

PREDICTING ADVERSE EVENTS

By delving into historical data on adverse reactions within the specific anatomical contexts, this innovative approach will equip drug developers with the foresight to anticipate and mitigate potential adverse events, ensuring better drug safety profiles, not only diminishing risks during clinical trials but also strengthening the safety standards in post-market usage.

USE OF DATA STANDARDS GOVERNOR TOOL FOR OPEN SOURCE DATA MANAGEMENT

We have employed the cutting-edge Data Standards Governor tool from NIHPO, a robust and sophisticated platform designed to manage vast volumes of Open Data efficiently [6]. This innovative tool serves as the backbone of our research methodology, providing a structured and secure environment to store, organize, and analyze extensive datasets related to the human body.

DATA AGGREGATION AND CENTRALIZATION

The Data Standards Governor tool acts as a centralized repository, aggregating diverse Open Data sources from multiple databases and reliable sources. By consolidating this information, research teams gain a comprehensive perspective, spanning from anatomical structures to chemical compositions, creating a holistic dataset crucial for the Human BioGeography™ analysis.

ORGANIZED HIERARCHICAL FRAMEWORK

One of the key features of the Data Standards Governor tool is its ability to organize data hierarchically. Through an intuitive interface, users can navigate through anatomy, diseases, therapeutic targets, drugs, and chemical structures seamlessly. This hierarchical arrangement facilitates efficient data retrieval, ensuring that specific queries and research objectives are organized with precision.

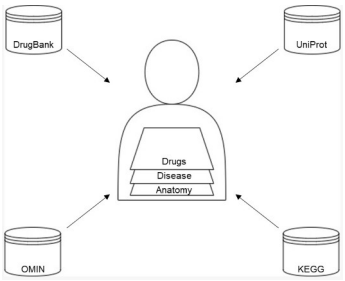

Figure 4. Example scheme of the Human BioGeography ™ data and layers representation (only a part of the data sources and layers have been included).

ADVANCED SEARCH AND ANALYSIS CAPABILITIES

The tool empowers users with advanced search functionalities, enabling them to perform intricate queries and analyses on the stored data. Researchers can filter information based on specific criteria, allowing them to identify correlations, patterns, and outliers essential for drawing meaningful conclusions.

ENHANCING CLINICAL TRIAL DESIGN AND OUTCOME

By unraveling comprehensive insights into the human body's responses to drugs, this approach offers a paradigm shift in trial design and outcomes. Through the integration of Human BioGeography™ data, researchers can meticulously design trials that are not only more targeted but also more efficient, capable of yielding meaningful results. This approach aims to accelerate the drug development process, heralding a future where trials are streamlined, outcomes are optimized, and both patients and pharmaceutical companies reap the benefits of pioneering medical research.

VALUE WE OFFER TODAY

At present, we offer a curated compilation of extensive data from multiple Open Data sources, meticulously integrated into our Data Standards Governor tool. This tool not only centralizes this wealth of information but also provides a user-friendly interface, enabling researchers to delve into complex datasets effortlessly. Its connectivity capabilities ensure seamless access to a plethora of integrated data points. While our groundbreaking 3D GIS Human Body system is in initial development, our current proposal provides immediate access to invaluable data, laying the groundwork for future innovations in drug development.

DATA SOURCES

Certainly, our approach leverages a wealth of data from diverse and reputable sources, forming the foundation for informed drug development and clinical trials. Below are the key data sources integrated into our system: PubMed, ClinicalTrials.gov, DrugBank, OMIN, UniProt, KEGG, NCBI Gene, among others [7] [8] [9] [10] [11] [12] [13].

These sources, when amalgamated, create a comprehensive knowledge essential for the drug development process. Their integration ensures the robustness and reliability of the data utilized in our approach, fostering innovation and advancements in the field of medicine.

LOOKING FOR COLLABORATORS

In our mission to transform drug development, we invite collaborators, including CROs and pharmaceutical companies to join our initiative. With our robust foundation of curated data and the advanced capabilities of our Data Standards Governor tool, we offer a unique opportunity for partners to actively engage in shaping the future of medical research. Collaborators stand to benefit from our existing data resources, coupled with the ongoing development of our innovative 3D GIS Human Body system. By joining forces with us, collaborators can influence the direction of our groundbreaking solutions while harnessing the power of our platform to accelerate their research initiatives. Together, we can pioneer a new era of clinical trials, driving unparalleled advancements in the pharmaceutical landscape.

CONCLUSION

In conclusion, Human BioGeography™ aims to enhance the success rates of clinical trials. By leveraging Open Data databases and GIS frameworks, this system aims to provide drug developers with invaluable insights into the human body's complexities. Predicting adverse events, optimizing drug formulations, and fostering data-driven decision-making, Human BioGeography™ reshapes the landscape of drug development. Its innovative perspective and 3D simulations offer a transformative pathway toward more effective and efficient clinical trials.

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