DOI: 10.31703/gdddr.2018(III-I).02
URL: http://dx.doi.org/10.31703/gdddr.2018(III-I).02 Vol. III, No. I (2018) Pages: 6 – 15

Muhammad Saadullah Khan[a] Farwa Shahid[b] Arooj Shahid[c] Gul Shahnaz[d]

Translational Medicine and Drug Discovery: A Mini Review

Abstract

There are a very large number of drugs that enter in the clinical trial phase but only a fraction of them is able to get their place in market. For a drug to reach at a phase of clinical trial requires a huge effort of research and a very large investment. Translational medicine, a relatively new discipline, uses the novel techniques that not only lower the risk of investment failure, but also focuses on reducing the testing duration in different phases of clinical trials. Discussed in the article are advantages of translational medicines and various challenges faced by translational medicine as well the ways by which this discipline will face these challenges. This article also focuses on recent advances in therapeutic development for diabetes, bone disorders, neurosciences, and oncology and the failures of translational medicine due to high external risk factors.

Key Words: Clinical Trials, Biomarkers, Alzheimer's, Fucoidin, Preclinical Modes, Bone Disorders

Introduction

The term translational medicine, also called as Translational Medical Science, Clinical and Translational Medicine, and disease targeted research could not be clearly defined anyone(Lindahl 2020). Every group or every organization has their own definition and explanation of translational medicine. A journal, Clinical and Translational Medicine, in effort to define this term, says that it is the clinical potential and application of translational research and science that betters the understanding of mechanisms and therapies of human diseases (Abraham, Marincola et al. 2012). Pfizer explains translational medicines as collaborative utilization of modern pharmacological tools, biomarkers, clinical approaches and technologies and study guide to enhance the belief in human drug candidates, grasp the concept of therapeutic index (safety ratio) in humans, improve the economical decision-making in the investigational development, and increase favorable outcomes in phase 2 to maintain continuous pipeline of products (Littman 2011). Translational medicine is a relatively new field and is making its roots deeps very fast. The aim of the discipline is to speed the process of drug discovery and development, and diagnosis using highly collaborative techniques.

Translational Medicine is basically a fresh effort to interpret and apply extraordinary scientific innovations for the betterment of patient's health and is a very important part of biomedical research (Zerhouni 2005). It is a bidirectional process of knowledge sharing. It translates discoveries from laboratory into clinical application (also known as bench to bedside) the purpose of which is to increase the efficiency of clinical testing to be performed on new treatment approach. Translational medicine also translates the new clinical findings to understand the molecular mechanism of diseases the purpose of which is to provide regular feedback of the new therapeutic strategy applied back to the researchers (Marincola 2003).

There is continuous need to find the more economical and cost-effective solution for health issues. Lack of surrogate endpoints that are the measurable biological markers used to assess the effectiveness of drug in chronic diseases in clinical trials prolongs the duration of clinical trials up to decades. The use of translational medicine

[a]Department of Pharmacy, Faculty of Biological Sciences, Quaid-i-Azam University, Islamabad, Pakistan.
[b]Department of Pharmacy, Faculty of Biological Sciences, Quaid-i-Azam University, Islamabad, Pakistan.
[c]Department of Pharmacy, Faculty of Biological Sciences, Quaid-i-Azam University, Islamabad, Pakistan.
[d]Chairperson, Department of Pharmacy, Faculty of Biological Sciences, Quaid-i-Azam University, Islamabad, Pakistan. Email: gshahnaz@qau.edu.pk

accelerated the incorporation of novel endpoints thus accelerating the process of clinical trials and lowering the cost (Lindahl 2020). Moreover, there is always a greater number of compounds and medical devices to be tested on patients, while the number of patient available is significantly less. Also, there is limited predictive accuracy making the preclinical trials not so reliable. As translational medicine transfers the results of safety and efficacy of testable agents from clinic back to the researchers, thus it more rapidly validates the agents and lowers the cost of preclinical and clinical trials (Woolf 2008).

History

Translational science term was first introduced in 1990s in biology-based literature which further led its way to cardiology, strokes, psychiatry and pathology (Karp and McCaffrey 1994). National institute of health (NIH) marked translational science as important and prominent fundable area in its current demonstration (Zerhouni 2003). Thalidomide set back in was a commanding incidence. Newly chemical successions were begun to be trialed, strongly for such medical ailments for which no proper cures were present previously. Comprehension and degree of propulsion for additional prognostic analysis and novel hazardous trials were made. However, in the 1970s and 1980s there was a wide lapse between research and development and humans and animals, and it was default application for investigation. To be actually, logistically, ethically differentiated. The investigating scientist invented molecule which met pharmaceutical standard and handed it over to development sector for investigation. There was no chance of clearance and cooperation in nay department. Failure for similar causes was observed in Good laboratory practice toxicology. Co-kinetics analysis in phase-1 and was main hindrance in pharmaceutical preparations and synthetic step up processes (Curry 2008).

The idea of diagnostic growth begun to turn up in last decade of 20th century. Initially, pre-formulation (analysis of bodily and synthetic features related to pharmaceutical science). Pharmacokinetics in pharmaceutical trial strains and investigational (Pre- Good Laboratory Practice) toxicology begun to be initiated in medicines finding procedure. Moreover, there were new implications by chemical analysis, depart of medicine and by the retainless in the procedure so that it would result in development of superior molecule taken into consideration for good laboratory procedure toxicology and then for the first phase. It was anticipated to lower decreasing figure and duration for availability of a drug to the group of patient for which it was prepared (Curry 2008).

Knowledge Management in Translational Medicine

The viable organization of information in translational investigate setting could be a major challenge and opportunity for pharmaceutical investigate and improvement corporations. The research institutes funded by EU Horizon 2020 program demand good data organization, practices, and coordination among various tools for a successful analysis of the data produced during the research. It is a hell of load to download the data from source records present in aggregated forms and coding them in a specific manner to achieve the results. This makes these sorts of revelations expensive and truth be told very uncommon. To tackle such issues at hand, data curation is the best method available for researchers (Szalma, Koka et al. 2010).

Ordinarily, curation of determined information bases of omics tests to make correlations for particular mining in light of explicit inquiries can be done such as development of various resources for the integration and analysis of gene expression and other data. However, they have a drawback that they can only limit the answers to specific questions and inhibit the deep study analysis and exploration of data. One such system software currently in use is tranSMART, which analyze samples efficiently after curing public information. This tranSMART system is facilitating translational researchers, clinicians, and innovation biologists to bring into line the genotypic and phenotypic data of individuals or organisms for a better and efficient clinical trial system. The tranSMART framework is under dynamic advancement including dynamic curation of extra examinations, actualizing new modalities, and adding novel work processes (Szalma, Koka et al. 2010).

The main purpose of this advancement in technology and organization of data is to enable the scientists for an effective testing of their specimens and generation of novel hypothesis using highly curated and enhanced knowledge in translational medicine. This will lead to better understanding of the complex biological processes and thus can help in the development of enhanced treatment strategies. Dynamic curation and undertaking information administration have demonstrated to be the basic parts of progress (Szalma, Koka et al. 2010).

Applications of Translational Medicine in Diabetes Drug Development

Diabetes Mellitus Type-II is amongst the largest burdens on health care. Only is USA, there 23.6 million active cases of diabetes, 95% of which have type –II diabetes (Riedel, Heien et al. 2007). Only half of the patients meet American Diabetes Association's standard of blood glucose with the use of single anti-diabetic agent, thus require an additional therapy or eventually insulin and suffer from adverse effects of these multiple medicines (Philippe and Raccah 2009). Microvascular and Macrovascular complications are the examples of complications of diabetes and its therapies. The concept of Translational Medicine can expedite the probability of success in anti-diabetic drug development and/or develop the biomarkers that can serve in testing the success of anti-diabetic drugs (Calle and Taylor 2011).

Efficacy: Glucose Lowering

Glucose lowering is primary goal of antidiabetic drugs so the usefulness of the new drug can only be explained by this parameter. But there are a few questions that are to be answered before: is the target modulated by the compound in required magnitude being efficacious at a safer dose (proof of mechanism)? is the blood glucose circulation lowered by the modulation, and what is the comparison of this effect with pre-existing therapies (proof of concept)? and does the compound has any clinical effect other than glucose lowering? (Calle and Taylor 2011).

Before moving to phase-III of clinical trials, phase-II results must prove the drug to be safe, tolerable, and efficacious. Also, the drug needs to be better than the extant drugs either in terms of glucose lowering or any other clinical application or both. HbA1c is the surrogate endpoint that is validated and accepted by regulatory agencies. Predicting drug efficacy by HbA1c as an endpoint reduces the risk of investment failure in drug development. However proper investigation of object drug with HbA1c requires at least a long study of 12 weeks and a larger sample size (Unnikrishnan, Anjana et al. 2012).

There is a unique characteristic that all the glucose lowering capability of antidiabetic drugs must be glucose dependent. They must stop lowering blood glucose beyond a lower limit. This limits the use of normal healthy patients in standard phase –I studies as glucose lowering cannot be measured directly early on, making the use of a glycemic target-related biomarkers must in acute studies. Additionally, glycemic endpoints other HbA1c may also be included. In phase I- two factors, the available knowledge of mechanism, and the fact that whether they have target specific biomarkers that can provide proof of mechanism, influence the selection of population, the duration, and endpoints of the study. Target or mechanistic biomarkers that do not depend on early efficacy signal of glucose lowering and that can be measured with significant variation in short term studies can be made part of phase –I studies to be performed on healthy subjects giving the proof of concept in early stages. Dipeptidyl peptidase-IV inhibitors (DPP-4i) developed for the use in type-II diabetes is an example of this approach being successfully applied (Hu, Yin et al. 2009).

If there is not any specific biomarker available, the systemic mechanism of the drug effects the selection of population for phase I, its duration and the endpoints. Such mechanisms include the secretion of insulin by the secretagogues, increased insulin sensitivity in liver and periphery, effects on nutrient absorptions. If systemic mechanism brings changes quickly and steady state is achieved rapidly, the results of glycemic endpoints may be achieved by a single dose, or short-term studies of 7-14 days (González-Ortiz, Hernández-Salazar et al. 2005). Contrarily, if the mechanism requires a longer period of time, the study may be extended to 3-8 weeks (Rasouli, Raue et al. 2005).

Selection of non-diabetic patient having abnormal glucose metabolism (e.g., impaired glucose tolerance), and/or population in pre-diabetes or early diabetes states are the two options in early studies where pharmacodynamics measures farther than the target biomarkers. Oral Glucose Tolerance Tests (OGTTs) assess the response of glucose and insulin both, in population with impaired glucose tolerance (Johanson, Jansson et al. 2005).

Scientists and clinicians use static and dynamic tests to measure the endpoints. Static tests include fasting glucose, fructosamine, 5-α-glucitol, HbA1c, and proinsulin. While the dynamic tests include Glucose area under curve (Glu-AUC), insulin area under curve (Ins-AUC), Glucose infusion Rate (GIR) (Dominiczak, Smith et al. 1988), (Johnson, Metcalf et al. 1983).

Safety

Cardiovascular

Macrovascular and atherosclerosis problems are the major cause of deaths in patients with diabetes. The diabetic patients suffer with the large number of

different cardiovascular events (including myocardial infarction, heart failure and sudden death) (Juonala, Viikari et al. 2004). Scrutinizing the end points of new diabetic therapies on cardiovascular risks in phase-I and phase-II studies, requires the evaluation of numerous risk factors for different cardiovascular mechanisms. Endothelial functions such as flow-mediated dilation FMD predicts the cardiovascular hazards in some population. These Different cardiovascular studies exemplify as concealing for drug related cardiovascular risks. Measurement of FMD studies may be used as screening strategies. Heed should be taken in clarifying FMD data (Juonala, Viikari et al. 2004), (Yeboah, Crouse et al. 2007).

Hypoglycemia

The Action to Control Cardiovascular Risk in Diabetes (ACCORD) studies shows that patients with severe hypoglycemia can have high death rate than those without severe hypoglycemia (2008). More efficacious drug with less or no hypoglycemic risk are preferred the most. GLP-1 analogues and DPP-4i mechanisms are thought to provide more safety in developing hypoglycemic risks. Safely glucose lowering agents are being explored like glucagon antagonist and glucokinase agonists which interfere in the recovery of hypoglycemia. Hypoglycemic clamp is safely operational in which IV insulin is used to increase the circulation of insulin level in body. Clinical hypoglycemic data should be handled with great care. American Diabetes association ADA provides the instrument to gear the adverse events of hypoglycemia (Juonala, Viikari et al. 2004).

Applications of Translational Medicine in Neuroscience

The development and use of translational medicine in treating neurological disorders is currently one of the major scientific challenges faced by the professionals. With the increasing population of elderly people in the society because of improved average life expectancy in many countries, the progression of neuro-disorders is substantially growing. Hence, the need for identifying the cause of neurodegenerative disorders and treating them is also a major issue at hand. The developing scientific society is trying to evaluate and coordinate information which is not comparable by bringing into practice various computational and modeling approaches. Then, by comparing this information with phenotypic perceptions and information and employing Systems Biology technique to neuroscience, scientists are seeking solution for current neurological problems. As the society is growing old without the cure for neurological diseases and depending only on healthcare system, extra endeavors are required to create novel symptomatic and helpful approaches based on biomarkers and their use in the clinical zone (Gentile and Cavallaro 2019).

The most emerging and expanding neurological disorder is Alzheimer's disease (AD) with number of cases expected to increase every year worldwide. For the improvement in the analysis, prediction, and treatment of Alzheimer's disease, scientists are focusing on genome-based tests because of the strong genetic influence of Alzheimer's disease(Yu 2011). Different types of genes are found to be the root cause of Mendelian and non-Mendelian AD but only a small percent of population has Mendelian mode of transmission. Non-Mendelian AD is more complex and involve numerous vulnerable genes which interact with other genes, more specifically apolipoprotein E (APOE). As there is limited genetic testing opportunities available for non-Mendelian AD and APOE genotyping does not help in identifying the causes of transmission or medical diagnosis, widespread research is ongoing for the treatment, initial recognition, and avoidance of Alzheimer's disease (Mihaescu, Detmar et al. 2010).

An example of failure of translational medicine in the treatment of Alzheimer's disease is Flurizan. According to the research conducted to test the potency and efficacy of Flurizan in AD patients, it failed in phase III clinical trials, which is not a shocking fact for most of the researchers. After a thorough assessment of the evidence present before the start of the study, Flurizan had weak potency, it was unable to pass the blood-brain barrier, and it lacked target modulation in patients. These three parameters were the key to success in this study (Fripp, Bourgeat et al. 2008). Approximately 2,500 Alzheimer patients failed to show positive response to Flurizan because of the ineffective treatment in the clinical trials. This showed that the strategy employed was insufficient and it needed the use of biomarkers for the proper mitigation and effective treatment

(Wan, Jacobsen et al. 2009).

The main cause for the failure of development of novel therapies and use of translational medicine in treating neurological disorders is the blood-brain barrier. Blood-brain barrier allows only lipid substances to pass through it, therefore, the drugs to be made for CNS must be lipophilic in nature to reach their target. An example of this is the failure of

pharmacological action of duloxetine for treating depression (Marek 2011).

Applications of Translational Medicine in Oncology

It is now a proven fact that the molecular makeup of oncological diseases in the society vary from person to person because of their heterogeneous nature and similar is the case with their treatment sensitivity. Because of this reason, the available drugs for treatment become ineffective for most of the patients while they continue to pay the medical costs. It delays the effective treatment period for most of the cases (Goldblatt and Lee 2010). The development of new genetic techniques and translational medicine has enabled to target specific patients requiring systemic treatment and those can benefit from a targeted molecular therapy. Translational research has ended up imperative since society is thought to merit an unmistakable return in terms of wellbeing and quality of life on its speculation in essential biomedical discipline (Struss 2020).

An advancement in the field of oncology to diagnose and treat tumor cells is the improvement and swift growth of liquid biopsy. This has led to the ease of sample analysis which was previously done either by frozen tissue samples or FFPE (Struss 2020). The main focus of translational medicine in this field is to understand the basic underlying principles and mechanisms involved in disease origination and advancement. With the help of liquid biopsy, various nucleic acid sources of cancerous cells can be evaluated which include cfDNA (circulating cell-free DNA), ctDNA (circulating tumor DNA), cfRNA (circulating cell-free RNA), and CTCs (circulating tumor cells). As there is minimum invasion involved in performing liquid biopsy, so it has the benefit over tissue biopsy providing same genetic information (Struss 2020). Due to the development in translational research over the past few years in oncology, heterogeneity in tumor cells, diagnosis at molecular level, and systemic treatments have improved a lot. Along with the progress in translational medicine, new challenges are brought into light in the clinical practice (Ghoshal 2017).

Fucoidan is the translational medicine developed to treat cancerous cells. Not only anti-cancer properties, but it has also shown anti-inflammatory, anti-proliferation, and immuno-modulatory activity. After many clinical trials and research work, Fucoidan has constantly proved its efficacy against cancerous cells. Additionally, combining it with other therapeutic agents can provide beneficial results due to the limitations of pharmacological activity of Fucoidan. It can also aid in the advancement of current approaches to treat cancer (Hsu and Hwang 2019).

Applications of Translational Medicine in Osteoporosis

Osteoporosis is portrayed by low mineral bone content with skeletal delicacy that can be expanded with certain events of breaks (Stoch 2011). Ossein destruction takes place when there is no equilibrium between the bone formation and resorption. There are different treatments for it but most of the patients still are untreated. They are significant antiosteoporotic treatments incorporate bisphosphonates (alendronate [ALN], risedronate, ibandronate, and zoledronate), estrogens, specific estrogen receptor modulators (raloxifene, bazedoxifene), also, PTH. Other specialty medicines incorporate calcitonin, nutrient D subordinates, also, strontium (in certain nations) (Stoch 2011).

Biomarkers Considerations

Biomarkers anticipate clinical results and can be utilized to survey the adequacy of novel specialists. Biomarkers basically link the product target and the activity that is being performed. Bone turnover is portrayed both by bone resorption and bone arrangement which reflect osteoclast and osteoblast action, separately. Biomarkers are divided into two categories:

- Different types of enzymes and proteins secreted by osteoblast and osteoclast.
- Products of bone type 1 collagen.

There are different biomarkers used for bone formation and bone resorption. Bone formation biomarkers
are bone specific alkaline phosphatases, osteocalcin. Both of these products are released into the
circulation.NTx and CTx are the biomarkers of bone resorption (Stoch 2011).

Preclinical Models

Animal models of osteoporosis have been utilized to assess likely novel treatments preceding testing in people for target commitment and distal impacts. Animal models are basically used for the determination of the safety and efficacy of the drug and the initial dosing strategy.

Cat K Inhibitors

Cat K are bountiful cysteine protease communicated in the osteoclast which is accepted to be instrumental

in ossein grid debasement important for ossein resorption.Ensuing inhibitors bound reversibly yet needed sufficient selectivity (Mishra and Burke 2020). It was imagined that strong, profoundly specific, and reversible inhibitors of Cat K that contain less-responsive practical gatherings would be an alluring element of inhibitors proposed for constant use.24 Odanacatib (ODN), a strong, specific, nonpartisan Cat K inhibitor with an IC50 of 0.2 nM for human Cat K25 was created to address metabolic liabilities of other Cat K inhibitors. It has little movement on Cat L and roughly 400-overlay selectivity for Cat F and Cat V.25.

Bone Disorders

Benign Adobe-Osseous Lesions

Adobe-bony injuries are different neurotic gatherings, in which ordinary ossein is supplanted with stringy nexus and development of unpredictable, woven bone. Verifiably, sores in the tooth-relevance bones are noted to contain cementoid material. The incorporate formative, responsive, abnormalcy, cystic processes. Due to variable etiology and pathogenesis, exact arrangement stays like test (Mishra and Burke 2020).

Langerhans Disease

Recently it is called as histiocytosis X, Langerhans cell nephrology is portrayed by osteolytic ossein injuries and "macrophagic" invasion.

B cells, phagocytes, and white blood cells may invade variable organs. Different subjects may give one or various hard sores, ongoing dispersed structure. (Hand-Schuller-Christian illness) which includes cranium injuries, intense scattered structure (Letterer-Siwe), influencing numerous organs with pathetic visualization (Abraham, Marincola et al. 2012). Clinically, incendiary delicate tissue sores, including ulcerations, might be seen. Langerhans cells can be recognized from different histiocytes by electron microscopy, or more generally immuno-histochemical staining for histiocyte markers CD1a, S100, also, CD207 (langerin).

Clinical and Translational Medicine

The expression "Clinical and Translational Medicine" (CMT) is characterized here as "objective prospect and use of translational exploration and science to aid the comprehension systems or treatments of hominian infections''. It is an important idea for the advancement of illness explicit biomarkers and remedial methodologies to screen and fix sickness.

Translational science has been characterized as a bi-route cycle that decipher disclosures outside of seat into objective utilization and to boot the interpretation of objective discoveries to the comprehension of subatomic instruments. Clinical and translational medicine plays an essential role in defining the cause of disease, pharmacokinetic parameters and the translational medicine helps to find out the drug target and activity by using different biomarkers and animal models to ensure the safety and efficacy of the drug product (Fletcher CDM 2013).

Clinical and translational medication will play a significant and material job in observing and dealing with the rumpled between the development of exploration defrayment and the abatement in translational profitability (Fletcher CDM 2013).

Clinical and translational medication have to be moreover characterized as well as separated out of the comprehension of other "translational" ideas, including translational science, translational examination, translational medication, or clinical and translational science. As opposed to them more extensive methodologies, clinical and translational medication are required to focus on objective application-arranged translational science and exploration to aid the precision, productivity and adequacy of objective analyses, treatments, assurance of forecasts for sufferers. Clinical and translational medication plays a significant or material job in observing and dealing with the rumpled between the development in examination payment and the diminishing in translational efficiency, and called attention to as of late by Elias Zerhouni (2011).

Nanostructured conveyance frameworks (NDS) are unpredictable nano systems, which can be fundamentally separated into two sections, that is, the outside layer (shell), which might be functionalized with an assortment of little particles, proteins, metal particles, as well as polymers, and the inner layer (center), which is basically the focal bit of the NPs and synthetically made out of various materials.

NDS are found to be more useful because of their small sizes so they have high surface area and due to their chemical composition. The original of NPs was formed by a fundamental lattice, with little particles captured or just adsorbed onto their surface. Notwithstanding, likewise with any outside particles that enter the body, NDS face numerous safeguard frameworks pointed toward perceiving, killing, and disposing of unfamiliar substances, in this way

restricting the restorative methodology (Mendes, Sousa et al. 2018).

Challenges and Opportunities in Translational Medicine

- In the past 10 years, discovery of drugs has revolutionized, and many new challenges have arisen for the researchers and investors. Although there is much advancement in the technology, yet the quantity of drugs approved by the authorities is stationary, the rate of novel drug developmental process, and the price of bringing a specific drug into the market is very high. Humans are suffering so much because of the lethal diseases and currently there is no available treatment. To encounter such circumstances we have to remove several barriers that are slowing the growth of translational research (Fitzgerald 2005).
- The main challenge faced by research in translational medicine is the availability and consent of patients for their participation in research. Mostly, the studies are halted at phase III of clinical trials because of limited patients. Similarly, studies from different samples or methods cannot be compared to each other because of genetic variability and race differences among people (Fitzgerald 2005).
- When a drug is in the process of development, the backing and infrastructure required for moving that drug from phase I & II to phase III for marketing is huge. The expenses for this whole process are very high that they cannot be fulfilled from the public funding only. Therefore, different large pharmaceutical companies pay contractors and staff members for bringing a specific drug in the market. In Fact, it could be practically incomprehensible for academicians to secure adequate serious awards to carry a medication or a test to the center and follow all the testing important to meet administrative prerequisites. In any case, most scholastic organizations do not offer fitting administrative help or the offices to satisfy the guidelines for clinical item planning. At all the stages during the translational research, there are many barriers interfering with the progress, development, and pertinency of clinical tests (Hörig, Marincola et al. 2005).
- Additionally, the data provided by researchers can show non-compatibility with other formatted data and thus can prohibit the data set comparisons (Hörig, Marincola et al. 2005).
- For the perfect implementation of new technologies, translational researchers require special education to handle them. Researchers should be capable and ready to comprehend the moral impediments of exploration when managing individuals. Doctors should be sharpened to the confusions of planning and leading deductively legitimate clinical preliminaries (Hörig, Marincola et al. 2005).

In any case, the difficulties are the manner by which we can recognize the best restorative targets and how to convey the best medication to treat patients.

New Focuses of Clinical and Translational Medicine in 2020

Clinical Trans-Omics-Based Diagnosis

The basic purpose of clinical trans-omics is to recognize the trans-focuses or crossing-focuses among various omics layer organizations, particularly the ones incorporating clinical phenomena with atomic multi-omics (Dijkstra, Cattaneo et al. 2018). The focal point of clinical trans-omics is the situation of clinical phenomics to characterize sickness and phenome-explicit biomarkers and targets, also, advantage early conclusion and restorative procedures. Clinical trans omics have different approachable mechanisms by which drug resistance is prevented.

Human Gene Editing based Therapy

It is a very suggested therapy for the human diseases because of its safety profile. It is the most desired therapy for the treatment of human diseases. A new report recommends that prime altering is an adaptable and exact genome altering technique in human cells to accomplish the positive change in the predetermined DNA site. There is a special improvement in the formation of end products to prevent the off-targeting profile. The main issue in clinical use of quality altering is to indicate the clinical signs and patient populaces, guarantee the quality and soundness of the system, and build up the worldwide morals and guideline. It overcomes many barriers and is mostly used as the alternative therapy for cancer patients.

Artificial intelligence is the most useful research in the research studies. Advances in innovation in AI, particularly profound learning calculations and the designs preparing units (GPUs), add to a new and quickly expanding interest in clinical AI applications, including clinical diagnostics, and preparing enormous and complex genomic datasets (Cheng, Wu et al. 2020). It is incredible for calling variation, clarifying genome information, and connecting the information between aggregate furthermore, genotype. Along these lines, we expect the utilizations of AI in upgrading the comprehension of sicknesses and the profound learning systems for additional examination. All in all, clinical and translational medication pays extraordinary consideration from clinicians in 2020 for various themes, as clinical trans-omics-based analysis, human organoids–based medication screening, and human quality altering based treatment.

Conclusion

Translational medicine is a broad area of research in which preclinical research is done to improve the clinical studies and trials. It helps to remove the barriers in different diseases by improving the phase studies. It is a bidirectional concept in which bench to bedside factors are being used to improve the therapeutic strategy for the patient. It is a very rapidly growing field in the research studies and proved helpful in drug discovery and development process. The application of translational science had not progressed. Different challenges are faced by the researchers and the scientist during translational medicine research in the fields like neuroscience and oncology. First challenge in neuroscience is to overcome the blood brain barrier which requires a lot of research studies and investments. Secondly, most of the diseases are genetic which is difficult to treat as compared to the treatment at the organ level. Similarly, in cancer treatment mostly the patient is treated on genetic basis and every human being has a different genetic makeup. Systemic diseases are different in different populations and they require different approaches towards the treatment strategies. A single drug product is not enough to treat the variable systemic diseases so the drug can show an off-target response during the treatment. So translational medicine has many drawbacks in oncology. Translational medicine research requires a lot of investments in the novel drug discovery and thus it is not cost effective. Most of the laboratories use this research technique only for the diseases that are common in humans so that it would prove beneficial for the labs in the future and the people with a rare disease remain mostly untreated. Different types of software are used nowadays to check the efficacy and specific targets of the drugs which makes this research cost effective. In the bone disorders different types of biomarkers are used in the born turnover to specify the target site. Different types of animal models are used in the novel research to ensure the proper efficacy and safety of the drug product. Cat K inhibitors are mostly used for anti-osteoporotic therapy. Clinical and translational medicine has proved very useful to treat different disorders in humans. Nanostructured delivery systems are discovered with the help of basic research to improve the stability and easy application of the drug product.in 2020, different types of gene-based therapies are being used that come under translational medicine and clinical research which will prove very beneficial for mankind in future.

References

Abraham, E. F. M., Marincola, Z., Chen & X. Wang (2012). "Clinical and translational medicine: Integrative and practical science." Clinical and Translational Medicine 1(1), 1.

Calle, R. A., & Taylor, A. E. (2011). TRANSLATIONAL MEDICINE AND ITS IMPACT ON DIABETES DRUG DEVELOPMENT. Translational Medicine and Drug Discovery. B. H. Littman and R. Krishna. Cambridge, *Cambridge University Press*: 35-61.

Cheng, X. D., Wu, Y., Cheng, T. Q., & Wang, X. (2020). "New focuses of clinical and translational medicine in 2020." *10*(1), 17-19.

Curry, S. H. (2008). "Translational science: past, present, and future." *44*(2S), ii-viii.

Dijkstra, K. K. C. M., Cattaneo, F., Weeber, M., Chalabi, J., van de Haar, L. F., Fanchi, M., Slagter, D. L., van der Velden, S., Kaing, S., Kelderman, N., van Rooij, M. E., van Leerdam, A., Depla, E. F., Smit, K. J., Hartemink, R., de Groot, M. C., Wolkers, N., Sachs, P., Snaebjornsson, K., Monkhorst, J., Haanen, H., Clevers, T. N., Schumacher & Voest, E. E. (2018). "Generation of Tumor-Reactive T Cells by Co-culture of Peripheral Blood Lymphocytes and Tumor Organoids." Cell *174*(6), 1586-1598.e1512.

Dominiczak, M. H. L. A., Smith, J. M., & Paterson, K. R. (1988). "Assessment of Past Glycemic Control: Measure Fructosamine, Hemoglobin A₁, or Both?" 11(4): 359-360.

Fitzgerald, G. A. (2005). "Opinion: anticipating change in drug development: the emerging era of translational medicine and therapeutics." Nat Rev Drug Discov 4(10): 815-818.

Fletcher CDM, B. J., Hogendoorn PCW, Mertens F (2013). WHO Classification of Tumours of Soft Tissue and Bone, International Agency for Research on Cancer.

Fripp, J., P. Bourgeat, O. Acosta, P. Raniga, M. Modat, K. E. Pike, G. Jones, G. O'Keefe, C. L. Masters, D. Ames, K. A. Ellis, P. Maruff, J. Currie, V. L. Villemagne, C. C. Rowe, O. Salvado and S. Ourselin (2008). "Appearance modeling of 11C PiB PET images: characterizing amyloid deposition in Alzheimer's disease, mild cognitive impairment and healthy aging." NeuroImage 43(3): 430-439.

Gentile, G. and S. Cavallaro (2019). "Translational Medicine in Neurological Disorders: A Genomic Perspective." Current genomics 20(3): 151-153.

Ghoshal, A. (2017). "Translational Research in Oncology: Implications for Palliative Care." Indian J Palliat Care 23(4): 462-467.

Goldblatt, E. M. and W.-H. Lee (2010). "From bench to bedside: the growing use of translational research in cancer medicine." American journal of translational research 2(1): 1-18.

González-Ortiz, M., E. Hernández-Salazar and E. Martínez-Abundis (2005). "Effect of the administration of a single dose of nateglinide on insulin secretion at two different concentrations of glucose in healthy individuals." J Diabetes Complications 19(6): 356-360.

Hörig, H., E. Marincola and F. Marincola (2005). "Obstacles and Opportunities in Translational Research." Nature medicine 11: 705-708.

Hsu, H. Y. and P. A. Hwang (2019). "Clinical applications of fucoidan in translational medicine for adjuvant cancer therapy." Clin Transl Med 8(1): 15.

Hu, P., Q. Yin, F. Deckert, J. Jiang, D. Liu, L. Kjems, W. P. Dole and Y. L. He (2009). "Pharmacokinetics and pharmacodynamics of vildagliptin in healthy Chinese volunteers." J Clin Pharmacol 49(1): 39-49.

Johanson, E. H., P. A. Jansson, B. Gustafson, M. Sandqvist, M. R. Taskinen, U. Smith and M. Axelsen (2005). "No acute effect of nateglinide on postprandial lipid and lipoprotein responses in subjects at risk for type 2 diabetes." Diabetes Metab Res Rev 21(4): 376-381.

Johnson, R. N., P. A. Metcalf and J. R. Baker (1983). "Fructosamine: a new approach to the estimation of serum glycosylprotein. An index of diabetic control." Clin Chim Acta 127(1): 87-95.

Juonala, M., J. S. Viikari, T. Laitinen, J. Marniemi, H. Helenius, T. Rönnemaa and O. T. Raitakari (2004). "Interrelations between brachial endothelial function and carotid intima-media thickness in young adults: the cardiovascular risk in young Finns study." Circulation 110(18): 2918-2923.

Karp, J. E. and R. P. McCaffrey (1994). "New avenues of translational research in leukemia and lymphoma: outgrowth of a Leukemia Society of America-National Cancer Institute workshop." J Natl Cancer Inst 86(16): 1196-1201.

Lindahl, S. A. M., F. (2020). "Translational Medicine." Encyclopedia Britannica, 2020.

Littman, B. (2011). "Translational medicine: Definition, history, and strategies." Translational Medicine and Drug Discovery: 3-34.

Marek, G., J. (2011). Translational Medicine and Drug Discovery.

Marincola, F. M. (2003). "Translational Medicine: A two-way road." Journal of Translational Medicine 1(1): 1.

Mendes, M., J. Sousa, A. Pais and C. Vitorino (2018). 4 - Clinical applications of nanostructured drug delivery systems: From basic research to translational medicine. Core-Shell Nanostructures for Drug Delivery and Theranostics. M. L. Focarete and A. Tampieri, Woodhead Publishing: 43-116.

Mihaescu, R., S. B. Detmar, M. C. Cornel, W. M. van der Flier, P. Heutink, E. M. Hol, M. G. M. O. Rikkert, C. M. van Duijn and A. C. J. W. Janssens (2010). "Translational research in genomics of Alzheimer's disease: a review of current practice and future perspectives." Journal of Alzheimer's disease : JAD 20(4): 967-980.

Mishra, R. and A. Burke (2020). Bone translational medicine: 283-309.

Philippe, J. and D. Raccah (2009). "Treating type 2 diabetes: how safe are current therapeutic agents?" 63(2): 321-332.

Rasouli, N., U. Raue, L. M. Miles, T. Lu, G. B. Di Gregorio, S. C. Elbein and P. A. Kern (2005). "Pioglitazone improves insulin sensitivity through reduction in muscle lipid and redistribution of lipid into adipose tissue." Am J Physiol Endocrinol Metab 288(5): E930-934.

Riedel, A. A., H. Heien, J. Wogen and C. A. Plauschinat (2007). "Loss of glycemic control in patients with type 2 diabetes mellitus who were receiving initial metformin, sulfonylurea, or thiazolidinedione monotherapy." Pharmacotherapy 27(8): 1102-1110.

Stoch, S. A. (2011). BONE DISORDERS: TRANSLATIONAL MEDICINE CASE STUDIES. Translational Medicine and Drug Discovery. B. H. Littman and R. Krishna. Cambridge, Cambridge University Press: 115-167.

Struss, W. J. (2020). "Implication and clinical application of translational medicine in the management of common urologic cancers."

Szalma, S., V. Koka, T. Khasanova and E. D. Perakslis (2010). "Effective knowledge management in translational medicine." Journal of Translational Medicine 8(1): 68.

Unnikrishnan, R., R. Anjana and V. Mohan (2012). "Drugs affecting HbA1c levels." 16(4): 528-531.

Wan, H. I., J. S. Jacobsen, J. L. Rutkowski and G. Z. Feuerstein (2009). "Translational medicine lessons from flurizan's failure in Alzheimer's disease (AD) trial: Implication for future drug discovery and development for AD." Clin Transl Sci 2(3): 242-247.

Woolf, S. H. (2008). "The meaning of translational research and why it matters." Jama 299(2): 211-213.

Yeboah, J., J. R. Crouse, F. C. Hsu, G. L. Burke and D. M. Herrington (2007). "Brachial flow-mediated dilation predicts incident cardiovascular events in older adults: the Cardiovascular Health Study." Circulation 115(18): 2390-2397.

Yu, D. (2011). "Translational research: current status, challenges and future strategies." Am J Transl Res 3(5): 422-433.

Zerhouni, E. (2003). "The NIH Roadmap." 302(5642): 63-72.

Zerhouni, E. A. (2005). "Translational and clinical science--time for a new vision." N Engl J Med 353(15): 1621-1623.