EDITORIAL

Increasing Role of Nanomedicine and Nanotechnologies in Translational Medicine

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ABSTRACT

Translational Medicine (TM) is "an interdisciplinary branch of the biomedical field supported by three main pillars: benchside, bedside and community. The goal of TM is to combine disciplines resources, expertise and techniques within these pillars to promote enhancement in prevention, diagnosis and therapies"[1]. In spite of the above guidelines and help, the goals in TM have not been fully attained and have taken a slow and difficult road. Turning basic research into useful therapy for community treatment remains a problematic and difficult process. The goals in TM have not been fully attained and have taken a slow and difficult road. Nanomedicine and nanotechnology, at the same time, were becoming available for medical research with clear and quick direction towards attaining treatment goals in TM. At present, nanomedicine and nanotechnologies have been validated as essentially important approaches for the treatment of human diseases. Nanomedicine and nanotechnologies are presently being applied in TM for diagnosis, prevention and therapeutic use. Advances in nanotechnology propose effective, safe, diagnostic and therapeutic action for TM. Future success in TM will be obtained by enriching our knowledge through ongoing research; and by eliminating difficulties in translational research.

KEY WORDS

translational medicine, therapeutic use, nanomedicine, nanoparticles, nanotechnology

INTRODUCTION

Translational Medicine (TM) is "an interdisciplinary branch of the biomedical field supported by three main pillars: benchside, bedside and community. The goal of TM is to combine disciplines resources, expertise and techniques within these pillars to promote enhancement in prevention, diagnosis and therapies"[1]. Though TM is evolving rapidly, the process needs to be backed by 1. development of biomarkers, 2. predictivity, 3. development of needed bio-statistical methods, 4. accelerated early human study design and 5. availability of decision algorithms. Thus, strong and meaningful development of the above will reduce the basic (pre-clinical) and widening clinical gap between stages of research; and the research and development process will also be reduced[1-3,12,15]. For achieving the above goal, help has come from the National Institute of Health (NIH) and the FDA. FDA's critical path and re-orientation of NIH are described as a road map that has been very helpful in enhancing the pace of development and establishing TM departments in universities[2-7,12]. In spite of the above guidelines and help, the goals in TM have not been fully attained and have taken a slow and difficult road. Turning basic research into useful therapy for community treatment remains a problematic and difficult process.

Nanomedicine and nanotechnology, at the same time, were becoming available for medical research with clear and quick direction towards attaining treatment goals in TM. Thus, nanomedicine and nanotechnologies have become very attractive and helpful processes for TM utilization. At present, nanomedicine and nanotechnologies have been validated as essentially important approaches for the treatment of human diseases like cancer, cardiovascular disease, infection, metabolic disease, Alzheimer's Disease and so on[7-12,14,15].

Nanomedicine and nanotechnologies came into existence in 1959; when Nobel Laureate Professor Richard Feynman, in his famous lecture, rendered the advice that "there's plenty of room at the bottom"[10,11,13,14]. Since then, nanotechnologies have been captured and are used in various areas such medicine, energy, the environment, cosmetics and so on.

In medicine, nanomedicine and nanotechnologies have been successfully used for various human diseases as described above. The focus and clear goal for nanomedicine was established in 2000 by President Clinton's Science Advisor Mr. Neal Lane[16]. The six clear goals for nanomedicine were defined by Mr. Neal Lane as follows: 1. rapid, more efficient genome sequencing enabling a revolution in therapeutics, 2. effective and less expensive health care using remote and in-vivo devices, 3. new formulations and routes for drug delivery that enormously broaden their therapeutic potential by targeting the delivery of new types of medicine to previously inaccessible sites in the body, 4. more durable rejection-resistant artificial tissues and organs, 5. sensor system that detects emerging disease in the body which ultimately will shift the focus of patient care from disease treatment to early detection and prevention, and 6. devices that enable vision and hearing aids[16].

Some of the above materialized goals have been utilized in nanomedicine and nanotechnologies; which are presently being applied in TM for diagnosis, prevention and therapeutic use. The application has markedly increased in TM[20,22,27]. These treatments are used successfully from 'benchside to bedside' and finally in the 'community'[1,16,20,22,27].

DEVELOPMENT OF NANOPARTICLES

The discovery and development of nanoparticles has become essen-

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tial for nanomedicine and nanotechnology to expand rapidly and successfully in TM. The role of nanomedicine and nanotechnologies have been increasing of TM: 1. therapeutics, 2. diagnosis and 3. prevention. "Delivery vehicles" are used for transporting treatment to the target diseases; particularly those diseases which involve the blood brain barrier. Nanomedicine, nanotechnologies and nanoparticles perform a very satisfactory role in this process[4,10,22,24,27)]. The therapeutic uses of delivery strategies for treatment have enhanced new drug approvals. The clinical features of newly approved drugs are evolving rapidly for use in the nanomedicine landscape. In the past decade, regulatory bodies worldwide have approved nanoparticles for utilization in nanomedicine; and newer nanoparticles are in the process of being approved. In the recent decade, the nano-pharmacological industry has shown marked growth; and has been helped by pharmacokinetic efficacy and safety. Advances in genome sequencing and genotyping by nanotechnology has opened new doors for further therapeutic success.

In neurodegenerative diseases like Alzheimer's Dementia, neurological diseases and some life-threatening diseases, the role of the delivery system (delivery vehicles) are gaining momentum[15,16,22,24,27-29,31,32)]. Experiences of past success confirms that the nanoparticle drug delivery system offers many advantages over the free drug delivery system. The clinical trials and the development of newer nanotechnologies, with the help of nanoparticles, are making breakthroughs for the improvement of the treatment path of human diseases. Examples include several successful ventures by Alnylam Pharmaceuticals. This company has used the LNP platform along with nucleic acid modification to produce ONPATTRO (patisiran) for TTR (transthyretin) which silences the specific gene which is responsible to produce hereditary transthyretin amyloidosis. Patisiran was approved as a first drug to be used as RAI therapy delivered by nanoparticles administered intravenously. Another breakthrough for vaccines has come through nanoparticles utilization in COVID-19 vaccine[9)]. In cancer areas, through the help of TM, nanotechnology has gained momentum and nano-bio interaction has become a fundamental area for cancer research[7,9-11)]. Nanoparticles can alter the function and effectiveness of drugs at the target site. At present, cancer therapeutics have become the most researched area of nanomedicine; with scientists now naming it Cancer-Nanomedicine. There are at least 15 approved Cancer-Nanomedicines and most of these are Liposomal formulations. Vyxeous is in Phase 3 trial for myeloid leukemia. This drug has improved survival rates for five to nine months[5,9-11,15,16,24,36-38)]. Doxorubicin is the standard first line treatment for patients suffering from soft tissue sarcoma[10,11,16,26)].

ROLE OF NANOMEDICINE IN DIAGNOSIS

In vitro diagnosis nanoparticles have become an established diagnostic device. In homogenous and heterogenous diagnostic assay for nano-IVD shows specificity, sensitivity and are compared well with traditional methods of IVP[10,21,25)]. Non-invasive MRI to diagnose AD has become more common. Synthetic nanoparticles of diverse surface character are generally used in contrast MRI. Nanoparticle Ferumoxytol is endorsed by the FDA to be used as first iron-oxide conjugate[10,16,21,23,24)]. Recent research has demonstrated that nanoparticles may be useful in variable ways in the diagnosis and treatment of AD[10,15-20,23,24)]. Further research is continuing for nanoparticles in CNS diseases.

Genome Sequencing: Nano technology has enabled less expensive genome sequencing than the present costly method. New sequencing and mapping techniques are replacing expensive reagents and these are based on long-read single DNA molecules. This single molecule genome mapping is at present used to help assemble genome to fill the information gap. The increasing role of nanomedicine and nanotechnology in regenerative medicine is beyond the scope of this paper and is not discussed here. However, in future the methods employed in regenerative medicine through nanotechnology can bring forth treatment from 'benchside to bedside, and into community' in TM[34-36)].

PREVENTION

One of the six goals of Mr. Neal Lane (described above) was to develop sensor systems by nanotechnology that detect emerging disease in the body; which ultimately, by these sensor systems, will shift the focus from treatment to early detection. Thus, preventing the occurrence of disease[16-19,21,22,24)].

TOXICITY

Nanoparticles use in medicine is increasing rapidly for various diseases and in TM. Therefore, there is always a need to evaluate the toxicity of nanoparticles and nanomaterials[40-42)]. Toxicity of nanoparticles depends on their physio-chemical properties[40-42)]. Hence, alterations in any parameters will have an impact on toxicity. Important toxicity seen in nanoparticles and nanomaterials include:1. biodegradation, 2. bio-accumulation, 3. genotoxicity, 4. cytotoxicity and 5. ecotoxicity. Enhanced research activities are desirable for studying toxicity of nanomaterials and nanoparticles because of expanding and therapeutic use in medicine[10,40-42)].

DISCUSSION

Advances in nanotechnology propose effective, safe, diagnostic and therapeutic action for TM.

These steps will cause less adverse reactions and safe processing systems of drug delivery in TM. Target delivery of therapeutics with increased visibility and controlled release of drugs is more helpful in enlarging success in TM. Future use will include the correction of defective DNA and genetic disorders; which will help in the treatment of cancer and the management of neurosurgery. At present, in spite of rapid advances in nanomedicine, much remains to be researched in future. Research in nano-bio interactions will be very exciting and will bring benefits to the field of medicine in general[10,20,21,24,40)]. Further, new phases of evolution and advances built on a solid base of nanomedicine, is desirable in TM[21,23,24)].

CONCLUSION

Translational Medicine (TM) needs to explore how to bring pre-clinical (benchside) research to the clinic (bedside) and further, to the community. TM has a difficult undertaking to solve the complexities of the above processes. These difficulties will not be solved until nano-bio interactions are fully understood. Nano-bio interactions, selection of ideal nano-formulations, and developing pre-clinical models that can translate to human disease models, are vital. Evidence-based information from research should help in translating basic research to successful clinical therapeutic use. In the recent decade, the nano-pharmacological industry has shown marked growth; and has been helped by pharmacokinetic efficacy and safety. Advances in genome sequencing and genotyping by nanotechnology has opened new doors for further therapeutic success. In spite of 30 years of research, much remains to be investigated and discovered to bring further success in the treatment of TM. The research format in TM should be simplified and the study design should be statistically powered so that results are easier to obtain. Future success in TM will be obtained by enriching our knowledge through ongoing research; and by eliminating difficulties in translational research.

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