Invited Article

WHAT, WHY AND HOW OF TRANSLATIONAL RESEARCH IN VETERINARY SCIENCES – A SMALL BEGINNING AT TANUVAS

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In 2100, the global population is expected to cross 10.1 billion, almost 50% more than the present 7 billion. India would replace China as the most populous country in the world. This increasing population puts tremendous pressure on our agricultural systems to produce more food, feed and fibre on limited and decreasing land area, reducing water resources and deprived soils. In this context, the role of animal sector assumes greater significance to support and complement the agricultural productivity to feed the growing millions.

To achieve this target, the technologies to be developed should be aimed at

- Producing more with less inputs
- Labour saving production methods
- Reducing environmental and biotic stressors
- Increasing trade through regulatory compliance
- Improving nutritional and safety of animal produce

Basic, Applied or Translational Research

The word research is derived from the old French word "cerchier" meaning to seek or search

Research is motivated by two things:

- Understanding (Basic research)
- Applications (Applied and translational research)

Basic (or fundamental) research is experimental or theoretical work undertaken primarily to acquire new knowledge of the underlying foundation of phenomena and observable facts, without any particular application or use in view.

Applied research is also original investigation undertaken in order to acquire knowledge. It is, however, directed primarily towards a specific practical aim or objective.

Both basic and applied research, work together and is in continuum. If a scientific research does not end up in a product or technology, it only means that the research was not continued towards that goal! Hence without research towards basic aspects of how things work, it can be difficult to bridge the gap with the improvements that applied scientists are looking to make. Thus basic research ensures that applied researchers do not need to reinvent the wheel every time they start on a new project, because the groundwork has been done.

The Center for Disease Control (CDC) characterizes translational research as

- the sequences of events by which a proven scientific discovery (e.g., an evidence-based intervention) is successfully institutionalized or seamlessly integrated into established practice and policy (CDC, 2007).

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Translational research, "transforms scientific discoveries arising from the laboratory, clinical, or population studies into clinical applications…"

(Source: National Cancer Institute, National Institutes of Health)

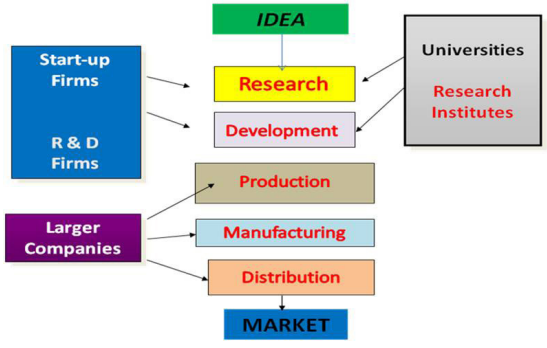
Translation refers to the application of results of basic biomedical research to the practice of medicine. More specifically, it describes the process of converting laboratory discoveries into clinical interventions that provide a direct benefit to animal / human health. It often refers to research that facilitates rapid and effective transition of results of basic research toward large scale evaluation and validation for ultimate use in improvement of health and increase productivity of animals.

In India, several institutions are engaged in animal science research that invariably ends in development of products and processes, leads or candidate proteins for vaccines or diagnostic reagents. However, ultimately these leads / candidates are not converted in to viable products / processes to the desired levels that are either marketable or available in the market shelves for the stake holders and farmers. This means that Science is not converted in to Technology or knowledge in to wealth. Translatability of the advances made in research projects and findings into tangible benefits for the farmers seems to be lacking to the extent desired. This responsibility lies with the Academia, Government and Industry. The so called 'rhyming phrases' of lab to land, field to fork, bench to bedside, mind to market etc. seems to suffer from a 'translational disconnect'. Translational research need to focus on two major aspects namely, converting research in to technology and the other is to disseminate the technology among the stake holders. This is more clearly defined in the human medicine sector as follows:

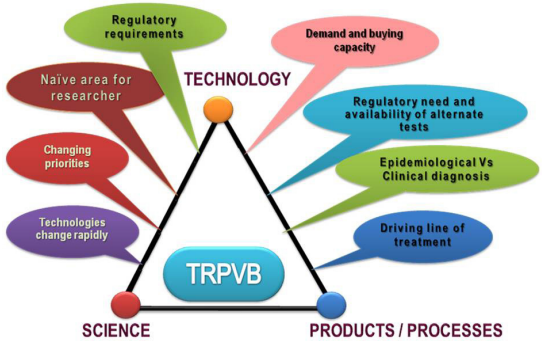
- T1 is described as "the transfer of new understandings of disease mechanisms gained in the laboratory into the development of new methods for diagnosis, therapy, and prevention and their first testing in humans."
- T2 is "the translation of results from clinical studies into everyday clinical practice and health decision making."

The funding agencies try to concentrate more on T1 while T2 is also equally important and State Universities such as TANUVAS have an edge in T2. The Veterinary Universities with its teaching hospitals and peripheral centres can act as a link between field and research labs bi-directionally, taking the research to the field and also to 'flag' the field problems to undertake research solutions.

Mind to Market pathway



The Sojourn from Science to Technology to Business



The conversion of a research lead in to a viable product and dissemination of the product among users is a long and cumbersome journey. However, the sojourn is only complete only when the purpose of the research undertaken is fulfilled.

The pathways can be either from 'mind to market' or from 'market to mind'!

Thus a field requirement or a problem can be solved through appropriate science or an idea which can also be converted to a product for field use. Both approaches can be successful only if the technology addresses an unmet need or brings an incremental improvement in the existing technology.

What makes this sojourn challenging is the fact that there are many hurdles to overcome as listed in the figure. The conversion of the technology in to product and selling the same is fraught with hurdles which can only be overcome by working in collaboration with a marketing person or a business analytic.

Since this transition from research laboratory to industry is so complex, it is expected that a via-media such as a translational platform would be a viable alternative to take care of the "transition needs" under a single roof and to foster better academia-industry partnerships.

Challenges of translational research

- Lack of zeal and drive on the part of the inventors
- Limited ability to study complex and dynamic biological systems in health or disease
- Need for multi-disciplinary and trans-disciplinary approach towards problem solving
- Interventions should be relevant, feasible, effective and sustainable
- Complex regulatory environment
- Naive area for the researchers
- Infrastructure and funding
- Difficulty developing and sustaining collaborations
- Differences in culture and mindset between basic and clinical researchers

Benefit to Universities / Institutions by fostering translational research

- Create a new dimension for the researchers to continue their research in to application
- Facilitating affordable access to expensive equipment and facilities
- Providing unique training opportunities for undergraduates, graduate students, and post doctorates and encouraging new talent to enter biomedical research
- Make students more 'industry-ready' and increase their 'employability quotient'
- Enhance the status of universities by promoting the development of new vaccines, diagnostics, devices and other therapeutic interventions which advances their research missions
- Gaining access to new funding opportunities supporting both institutional and industry projects
- Create 'spin-offs' from inventions arising out of Universities
- Source of income in terms of technology transfer and royalty fees
- Provide an conducive eco-system for entrepreneurship for the fresh graduates/start-ups

Benefit to scientists for fostering translational research

- Job satisfaction for having participated and contributed to develop solutions for veterinary and public health problems and hence a source of intellectual inspiration and stimulation.
- Providing opportunities for new linkages, funding and creation of fresh leads and fresh directions for existing projects

- Promoting trans-disciplinary collaborations across human doctors, vets, engineers, chemists, information technology experts, business analytics etc that can ignite shared passion, provide exposure to new areas of science, and generate new ideas / solutions to existing problems.
- Providing opportunities to mentor clinical colleagues in basic science methods
- Broaden the horizon of knowledge of the academic researcher

Why is it most needed now?

The quantifiable indictors for assessing the science and its impact have evolved over the years. From slogans like 'publish or perish' it has now moved to 'patent or perish'. It may further move towards to 'commercialize and contribute'.

From number of publications the evaluation has moved towards number of citations, impact factors, Hirsch index, patents filed and granted, Indian or international patents, technology commercialized, technology transfer fees and royalty generated etc. The impact of research institutions in India is being questioned and compared to institutions such as Massachusetts Institute of Technology or Harvard which has generated several game-changing technologies that has changed the course of everyday life. The day is not far when veterinary institutions will also need to 'stand up and deliver' in this aspect.

Added dimension to veterinary translational research

Veterinary translational research is no doubt needed to be done, on priority, to improve animal health and productivity through designing novel animal vaccines, diagnostics and therapeutics; it can also act as a prelude to human health. Further, with the "One Health Mission" gaining importance worldwide, translational veterinary research has the potential to foster and integrate the effort on animal and human health.

Translational research is also often associated with clinical trials and acts as a first step in introducing a new intervention or technology aid to the market for use in the general population. Trials in laboratory animals which are maintained under very controlled settings or in client-owned pets / animals which share the food and environment as humans are not uncommon. However, prior to using animals as models for humans with comparable disease processes, it should be ensured that the safety of the 'leads' are proven unequivocally.

Studies in companion animals with clear parallels in disease pathogenesis, progression and symptoms, can be an effective intermediate step in screening for efficacy and complications of candidates that appear promising in induced rodent models, before committing them to human clinical trials *(http://research.vet.upenn.edu)*.

Translational success stories

When we need to 'lure' people into a particular field of enterprise one of the easiest and proven ways is to highlight success stories achieved by ordinary persons using technological interventions in that field. While we have many such 'successes' in information and communications technology, from Bill Gates, Steve Jobs, Sabeer Bhatia etc (to name only a few), it is essential we have a few pioneering success stories in translational veterinary research so that this field lures more entrepreneurs to undertake this arduous but potentially beneficial 'sojourn' in our country thereby demystifying this field.

A small start at TANUVAS

To bridge this gap, an autonomous institute named "Translational Health Science and Technology Institute (THSTI)" was set up in 2009 by the Department of Biotechnology, Ministry of Science and Technology, GoI. The mandate was to fast track health care solutions to meet the needs of a rapidly developing economy. On similar lines, the Department of Biotechnology, Ministry of Science and Technology, GoI also funded a programme, the

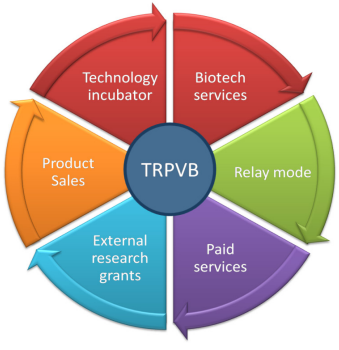
"Translational Research Platform for Veterinary Biologicals (TRPVB)" at TANUVAS with a vision to foster 'Productization' in the field of Veterinary Biologicals by converging the presently distant academic research, industry and pathways of regulatory compliance.

Some of the approaches undertaken by TRPVB-TANUVAS to bridge the existing gaps in the sojourn of 'Mind to Market' are depicted below.

TRPVB has brought together academia, industry and regulatory experts together who can leverage and assist clients in various stages of product development. Being housed in TANUVAS provides it the needed academic ambience, farm support, services and veterinary intervention support to achieve its mission

To facilitate seamless transfer of the technologies from the academia to industry, TRPVB-TANUVAS had created a state of art clean room facility meeting cGMP norms. The facility can be used for producing cGMP grade vaccine seeds and vaccine substrates (cell line) with the requisite QC testing and documentation as per the regulatory norms; cGMP grade test batches (intended for clinical trials); for process optimization at pilot scale and for manufacturing emergency vaccines.

TRPVB has evolved the following commercialization strategies for placing a research lead in the market



New products are being developed through in house development, co development and technology acquisition methods. If an industry has a lead or compound, they could get it validated through GLP-compliant studies for further development. Specific industry needs can also be met through in house expertise. Each strategy is uniquely placed for particular products / processes. For example, a diagnostic kit for wild life has limited market and a commercial company may not be keen to invest in development of a product line for a limited market size. However, this kit may be needed by the end-user, hence in such cases the direct sale option can be employed. Not all the research leads can be converted in to products and there could be process development that can be offered as a service, such as clinical services for diagnosis of Evans syndrome in dogs, canine parentage etc. TRPVB also serves as a Technology Incubator not only for research but also to support the small entrepreneurs in the early steps of the technology transfer process.

Generation of industry-ready manpower in the field of Animal Biotechnology is fostered through a unique DBT-funded Animal Biotechnology Career Enhancement programme (ABCEP) implemented at TRPVB as a six-month certificate course. This is aimed to bridge key skill shortages in Animal Biotech sector and to catalyze investment and growth of this emerging Animal Biotechnology sector.

TRPVB is a small step in the direction of Animal Sciences research commercialization taken by DBT and TANUVAS in partnership and hopefully this can be emulated by other veterinary institutions also.

The world-wide R and D spending has decreased dramatically. Translational research is also evolving as a new discipline and academia, Government and industry need to implement more innovative solutions. The departments should evolve into inter disciplinary research centres with

'fluid' environments to solve the problems with existing technologies and evolve disruptive ones.

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