Original Inventions based on Chemical scaffolds and electro-physical activity-derived biosimilars interacting with specialties in biology yielding platforms for analysis in virology and antiviral compounds

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Background:

Original inventions in developing countries, in terms of number of patents filed, granted and that are taken to useful applications as well as in terms of publications of high impact remain relatively lower\textsuperscript{1,2} compared to that of developed nations. The reasons could be attributed to lack of importance given to basic research in funding, the number of institutes involved, limited technical support or expertise available etc\textsuperscript{3}. Though such initiatives may take a long time to yield fruits, one of the parallel steps we considered worth was to take the original inventions from Japan, born out of basic research in one field, taken through an application-oriented inter disciplinary interactive research in healthcare, thereby paving way for novel solutions. Thus was conceived, the Inventions- Inter-Disciplinary Interactions and Solutions (IIDIAS), an academic session as a part of the one-day International stem cell meet organized every year in the month of October by Nichi-In Centre for Regenerative Medicine (NCRM), an academic Institute based in Chennai, India. In the IIDIAS session, based on original invention(s) presented as a prelude in brief, original interdisciplinary interactive research work based on the original invention by NCRM and/or its collaborators are presented by the faculty of the relevant institute. That will be followed by an interactive session in which the potential solutions based on the above accomplishments would be discussed. The IIDIAS session 2014 was based on the following two inventions:

1. A bio-film-based biosimilar invented by an electro-physicist
2. A unique polymer invented by a chemical engineer

Inventions and Interdisciplinary Interactions:

Invention –I: The bio-film-based biosimilar invented by an electro-physicist:

An electro physicist with the Kyoto University, Japan, Dr Nobuyuki Yamaji observed during his experiments that plants and mammalian tissues secrete a layer of fluid after getting hit by lightning or electric current\textsuperscript{4}. The significance of the secretion was unknown to him. Later when he met his friend, Dr. Sunao Kubota, who was a physician and professor of General Surgery in St. Marianna University, he shared his work and Dr. Kubota began analyzing the nature of the secretions. Dr. Kubota hypothesized that the secretion's role may be to provide a temporary barrier to the entry of pathogens through the area of skin desiccation caused by the electrical damage, until healing process helps to cover the dehiscence. Then for the next decade Yamaji and Kubota worked to isolate the ingredients of the secretion and they together developed a citric acid-based biosimilar capable of killing a wide range of pathogens which are known to cause common as well as severe infections including nosocomial infections such as MRSA, VRE etc\textsuperscript{4} without having to use alcohol-based disinfectants. This biosimilar named as Clinister has not only been proven as a disinfectant but is also considered worth was to take the original inventions from Japan, born out of basic research in one field, taken through an application-oriented inter disciplinary interactive research in healthcare, thereby paving way for novel solutions. Thus was conceived, the Inventions- Inter-Disciplinary Interactions and Solutions (IIDIAS), an academic session as a part of the one-day International stem cell meet organized every year in the month of October by Nichi-In Centre for Regenerative Medicine (NCRM), an academic Institute based in Chennai, India.

Inter-Disciplinary-Interaction based on the Invention-I:

Evaluation of citric acid-based granules in controlling Chickungunya Virus:

Clinister has not only been proven as a disinfectant but is also...
also a powerful anti-bacterial and anti-fungal agent that strongly restricts the recurrence of the microbes for a long term. In the present study, Clinister was evaluated for its virostatic efficacy against Chikungunya virus (CHIKV) in vitro for the first time. It showed expressive effect on virus grown in BHK cell cultures by inhibiting the development of virus induced cytopathic effect at an effective concentration of 1.5mg/ml in comparison to 70% ethanol, a common disinfectant. The effects on the virus were further checked by Polymerase Chain Reaction (PCR) at different regular post infective intervals from 0 to 72 hrs. The observations suggested that, other than the anti-microbial activity, Clinister also have specific effect on viruses that may cater the need to prevent the spreading of contagious viruses during epidemics which may occur in the future. However it is essential to study the specific targets of Clinister in viruses at a molecular level, and the same is under progress.

Invention – II : A unique polymer invented by a chemical engineer

A chemical engineer Prof. Yuichi Mori jointly with polymer scientist Dr Hiroshi Yoshioka developed a thermoreversible polymer (TGP) hydrogel composed of thermo-responsive polymer block [poly (N-isopropylacrylamide- co-n-butyl methacrylate)] (poly NIPAAm-co-BMA]) and the hydrophilic polymer block [polyethylene glycol (PEG)] (commercial name :Mebiol gel) [8]. This Mebiol gel provides a suitable in vitro environment enabling culture expansion of cells in the lab without the use of biological components such as amniotic membrane or feeder layers. TGP has been earlier employed for the three-dimensional culture of many cell types like corneal limbal stem cells [6], chondrocytes[7], embryonic stem cells [8], hepatocytes [9], induced pluripotent stem (iPS) cells [10] and bone marrow mononuclear cells [11]. TGP has been used for transportation of corneal endothelial precursor cells over long distances without cool preservation[11], for micro-encapsulation of islet cells [12] and as a wound dressing [13]. TGP has been intraresionally applied along with stem cells in an animal model of spinal cord in injury [10]. TGP is a unique polymer capable of maintaining stem cells in an undifferentiated manner for a longer period of time [14]. It does not affect the gene expression profile [15] and the karyotype of the cells is maintained even after long term culture [16]. The safety and efficacy of TGP as a valuable scaffold material has been established in the various in vitro and translational studies [8].

Inter-Disciplinary-Interaction based on the Invention-I: Mebiol Gel as a 3D scaffold for hepatocytes and viral replication

Mebiol Gel was used as a 3D scaffold for growing hepatocyte cell line. Mebiol Gel based hepatocytes had better differentiation and the cells were susceptible to hepatitis C virus replication. The Mebiol Gel based 3D culture system can be used as a better cell culture system for viral studies.

Potential Solutions:

The works presented in the IIDIAS session have portrayed that original invention in any field when subjected to multi-disciplinary interaction after carefully evaluating the potentials can lead to novel solutions. Though the experts in various disciplines in the reported work have got to interact by chance or due to geographical proximity to each other, when a networking platform to throw such ideas to a forum with mutually rewarding opportunities given for discussion and planning of interactive researches is made possible, novel solutions may not be impossible, if the target platform is well understood within the limitations of each stake holder. Creation of a niche or a suitable environment for such multi-disciplinary interaction may prevail and work to its best in a physical state of interaction but advances in information technology has broken the need for such physical interaction among peers to bring out novel solutions. Interactions across specialties in the IIDIAS session help in identifying roles for the invention in other fields which may not be directly related to healthcare. The probable solutions and advantages by combining the electro-physical activity-derived biosimilar and the chemically synthesized polymer described in the study include:

1. A novel platform for in vitro culture of HCV having been described, similar platforms for not so easily cultivable viruses can also be developed. The 3D viral culture technology can be exploited to study the replication process and other intricacies of the virus in vitro culture.
2. When in vitro expansion of viruses in an appropriate manner becomes feasible, anti-viral agents, either virostatic or virucidal, herbal or synthetic biosimilars can be analysed to come out with effective anti-viral agents.
3. A biosimilar-based compound having been proven against Chickungunya virus, the same could be tried against life threatening viruses in appropriate and safe environments.
4. Clinister being a food additive-based material, is considered to be safe to human beings [15] and hence its inclusion as an additive to cell culture medium could be studied further in order to check whether the use of common antibiotics and anti-fungals which may be detrimental to cell growth can be avoided yielding safer anti-bacterial and anti-viral agents for cell culture.

Conclusion:

Multidisciplinary interaction within and across various domains of science has several potentials in bringing out novel solutions and this has been proven by this study of interaction among physicists, chemists and biologists. The authors recommend that establishment of barrier-free interaction platforms within and among institutes and various specialties at varied stages of research activities as portrayed here like the IIDIAS session to bring about novel solutions such as the ones described in this article.
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