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Analysis of outcomes following mesenchymal stem cell therapy in subjects with musculoskeletal conditions

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Musculoskeletal conditions are major public health problems and often associated with reduced function and pain. Musculoskeletal-related pain is affecting more than one third of the adult population worldwide. Pain reduction is one of the main outcomes to determine the success of therapy of subjects with most common orthopedic conditions. Inflammation plays an important role in the occurrence of acute and chronic musculoskeletal-related pain. Numerous investigations suggest that Mesenchymal Stem Cells (MSCs) represent a valuable tool for therapy of inflammation and regeneration of tissue damage. BHI Therapeutic Sciences offers a novel method of arthritis therapy using a patient's own stromal vascular fraction (SVF) cells including MSCs. The therapy is available at Malacky Hospital in Slovakia. Blue Horizon International Slovakia is licensed by the Ministry of Health of Slovak Republic to provide adipose stem cell therapies for orthopedic joint applications: Knees, hips, shoulders and ankles. Procedures utilize cutting-edge technology and adult stem cells only. Results from patients' follow-up examinations and MRI scans showed that stem cell therapy was safe for the patients. Follow-up examination results conducted 10 days, 3 and 6 months after therapy have shown significant improvement of clinical condition relating to pain relief, improved mobility, which was shown also on the follow-up MRI scans of the affected joints.

Biography

Brian M Mehling is a practicing American Orthopedic Trauma Surgeon, Researcher and Philanthropist. He started his path in medicine through undergraduate study at Harvard University, obtaining Bachelor of Arts and Master of Science degrees in Biochemistry from Ohio State University. Completing his degree of Medicine at Wright State University School of Medicine, he has received Post graduate education through Residencies and Fellowships at St. Joseph's Hospital in Paterson, NJ and the Graduate Hospital in Philadelphia, PA, while pursuing PhD in Chemistry. He operates his own practice, Mehling Orthopedics, in both West Islip, NY and Hackensack, NJ.

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ACL regeneration and osteointegration using a new silk fiber-based scaffold: Results from a study in sheep

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Introduction: Because of ongoing limitations with ACL reconstruction, new approaches in the treatment of ACL injuries, in particular strategies based on tissue engineering have gained increasing research interest. To allow ACL regeneration, a structured scaffold which provides the mechanical basis, cells from different sources and mechanical as well as biological factors are needed. The optimal scaffold for ACL regeneration is regarded to be biocompatible and biodegradable to allow tissue ingrowth, but also needs to have the right mechanical properties to provide immediate mechanical stability.

Hypothesis: A degradable silk-fiber based scaffold with mechanical properties similar to the native ACL is able to initiate ligament regeneration and osteointegration after ACL resection and reconstruction under *in vivo* conditions.

Methods: 33 mountain sheep underwent ACL resection and randomization to two experimental groups: ACL reconstruction with scaffold alone (SA) and ACL reconstruction with cell-seeded scaffold (CS). Histological evaluation of the intra-articular portion of the reconstructed/regenerated ligament was performed after 6 and 12 months. Additional bone histology was performed to assess osteointegration.

Results: After six months, connective tissue surrounded the silk scaffold with ingrowth in some areas. The cell seeded scaffolds had significant lower silk content compared to the unseeded scaffolds and demonstrated higher content of newly formed tissue. After 12 months, the density of the silk fibers decreased significantly and the ingrowth of newly formed tissue increased in both groups. No differences between the two groups regarding the silk fiber degradation as well as the regenerated tissue were detected anymore at 12 months. Bone histology revealed good osteointegration after 12 months.

Conclusions: The novel silk-fiber based scaffold was able to stimulate ACL regeneration as well as osteointegration under *in vivo* conditions. Additional cell seeding lead to increased tissue regeneration and decreased silk-fiber content after 6 months, whereas these differences diminished after 12 months.

Biography

Thomas Nau has completed his MD from Karl-Franzens University Graz, Austria and his Specialist Orthopedic Trauma training at the Medical University of Vienna, Austria. He is an Adjunct Professor at the LBI for Experimental and Clinical Traumatology, Austrian Cluster for Tissue Regeneration where he is directing the bone and ligament regeneration group.

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Autologous stem cell transplantation in patients with idiopathic premature ovarian failure

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Background: Premature ovarian failure (POF) is defined as failure of the ovary to function adequately in its role either as an endocrine organ or as a reproductive organ in a woman younger than 40 years of age. It is characterized by amenorrhea, hypoestrogenism and elevated serum gonadotropin levels. This condition occurs in approximately 1% of women and it has major physical and psychological consequences/impact in those patients. Stem cell therapy is increasingly gaining grounds in the regeneration of damaged or failed tissues and organs.

Aim: The purpose of this study is to investigate the role of the transplantation of autologous bone marrow derived mesenchymal stem cells in amelioration of this condition.

Study Design: It is an open label single group safety/efficacy study. Primary outcome measures are cases will be followed using serum FSH, estrogen and anti-mullerian hormone levels. Secondary outcome measures are disappearance of menopausal symptoms e.g., hot flashes rise in serum AMH level, pregnancy rate within 1 year, miscarriage rate within one year of injection and long term follow-up for any adverse effect, assessed for one year from injection.

Subjects: 30 patients with POF were included. Inclusion Criteria: (1) Patients with normal karyotype spontaneous premature ovarian failure. (2) Patients between 18-40 years old. Exclusion Criteria: (1) Patients with secondary ovarian failure (e.g., hypothalamic causes). (2) Autoimmune diseases. (3) Those with major medical problems such as malignancy, hepatitis, etc and (4) Abnormal karyotyping (e.g., Turner syndrome)

Methods: After stimulation with G-CSF, 60 ml of bone marrow were aspirated from the posterior iliac spine and mesenchymal stem cells (MSCs) isolation was done under GMP conditions. Isolated MSCs were injected in one side as follows; 3-5 million in the ovarian tissue through laparoscope and 3-5 million in the ovarian artery through catheter.

Results & Conclusions: 26 out of the 30 patients included (86.7%) showed fall in FSH levels and rise in estrogen and AMH levels after 4 weeks of injection and this change was maintained throughout the 48 week follow-up period. 18 patients (60%) showed ovulation with ovum sizes ranging from 12-20 mm. Only one patient had spontaneous pregnancy, while three patients were subjected to IVF cycles. This study shows that autologous MSC may improve the conditions in patients with POF. Optimization of the cell dose and route of injection needs further experimentation.

Biography

Hala Gabr is a renowned Researcher in Stem Cell Biology and Therapy in Cairo University, Egypt. She is the Director of the Pediatric Bone Marrow Transplantation and Cellular Therapy Lab in Cairo University. She is the Co-Founder of the Egyptian Society for Progenitor Stem Cell Research, the leading stem cell research body in Egypt. She has published more than 30 papers in reputed journals and is an Editorial Board Member of a number of reputed journals. She has supervised nearly a hundred PhD and master thesis in stem cell research.

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Nanocarrier-directed targeted cell delivery for stem cell therapy

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Stem cell-based therapy has emerged as a promising treatment option in regenerative medicine. However, targeted systemic delivery of therapeutic cells to the dysfunctional tissues remains one formidable challenge. Herein, we present a targeted nanocarrier-mediated cell delivery method by coating the surface of the cell to be delivered with dendrimer nanocarriers modified with adhesion molecules. Infused nanocarrier-coated cells reach to destination via recognition and association with the counterpart adhesion molecules highly or selectively expressed on the activated endothelium in diseased tissues. Once anchored on the activated endothelium, nanocarriers-coated transporting cells undergo transendothelial migration, extravasation and homing to the targeted tissues to execute their therapeutic role. We now demonstrate feasibility, efficacy and safety of our targeted nanocarrier for delivery of bone marrow cells (BMC) to cutaneous wound tissues and grafted corneas and its advantages over conventional BMC transplantation in mouse models for wound healing and neovascularization. This versatile platform is suited for targeted systemic delivery of virtually any type of therapeutic cell.

Biography

Zhao-Jun Liu is an Associate Professor at University of Miami, Miller School of Medicine. His research interests span both vascular biology and cancer biology. He has published more than 60 research papers, review articles and book chapters.

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Allogenic bone marrow-derived mesenchymal stem therapy in Duchenne muscular dystrophy

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Background: Duchenne muscular dystrophy (DMD) is the commonest hereditary muscular dystrophy. It is characterized by progressive muscle leading loss of walking ability and complete wheelchair dependence. Further, disability leads to respiratory failure, which is the common cause of death.

Aim: The aim of the present work is to evaluate the safety and therapeutic efficacy of allogenic bone marrow derived mesenhymal stem cell therapy in Duchenne muscular dystrophy

Subjects & Methods: This study was conducted on 40 myopathic patients, ages ranging from 6-18 years. DMD was documented by family history, history of disease progression, laboratory investigations, muscle biopsy and genetic study. Patients with fixed deformities were excluded. The study group was randomly divided into patient and control groups. Both groups were given traditional treatment (physiotherapy & medical treatment drugs); while the patient group received additionally stem cell treatment. Stem cells were administered in 6 doses 4 weeks apart in a dose of 3×106 cells/kg suspended in 50 ml PBS. Cell suspension was injected locally in 0.5 ml doses intramuscularly. A single systemic injection in a dose of 3 X10 6 cells/kg was given with the sixth intramuscular dose. Follow-up was done using North Star Ambulatory Assessment CHAQ (Child Health Assessment Questionnaire), manual muscle strength testing using Medical Research Council strength scores and functional outcome measures. Scoring was done before and after every month for 12 months. Any complications or adverse effect were recorded.

Results & Conclusions: During the one year follow-up, no serious complications were recorded. Self-limited pain and mild fever were reported for 48 hours after injection. Significant improvement in assessment scores and quality of life questionnaire was seen in the treatment group. This was translated into substantial improvement in ambulation.

Biography

Wael Abo Elkheir has completed his PhD from Cairo University, Egypt. He is the Co-Founder and Board Member of the Egyptian Society for Progenitor Stem Cell Research, a society initiated with the mission of enhancing scientific research and cooperation in the field of stem cell research and regenerative medicine. He is the Director of a number of registered clinical trials in the field of stem cell therapy, especially for neuro-regeneration and musculoskeletal disorders. He has published more than 20 papers in reputed journals.

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3D intestinal co-culture analysis of the interaction of secreted proteins from intestinal nematode parasites with the mucosal habitat

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Intestinal nematodes represent multicellular organisms within the gut microbiota, which colonize their habitat for years and which sustain tolerance mechanisms, thereby containing inflammatory host responses to prevent their expulsion. Of major relevance, concurrently this parasite's influence attenuates adverse inflammatory responses associated with autoimmune diseases like Crohn's disease and ulcerative colitis. The major effect is attributed to excretory/secretory (E/S) products released from the parasite affecting and modulating host local immune system. We are investigating E/S proteins from the intestinal *Strongyloides ratti* and *Trichuris suis* for immunomodulatory effects. We here report our preliminary characterization of the two *S. ratti* proteins, secreted protein acidic and rich-in-cysteine (Sr-SPARC) and thioredoxin-like protein (Sr-Trx-lp) and the *T. suis* E/S protein Ts-Trx-lp. The genes of these proteins were identified, cloned and recombinantly expressed under optimized conditions. The effect of the secreted parasite proteins on host cells were studied applying a novel *in vitro* 3D mucosal model that mimics the *in vivo* natural intestinal microenvironment. In the 3D co-cultures which comprise human intestinal epithelial and dendritic cells growing on a collagen scaffold, an initial pro-inflammatory response (TNF-α) after 24 hours was followed by an increased anti-inflammatory response after 48-72 hours detecting the Th2-type-related cytokines IL-22, IL-10 and TSLP. Thus, Sr-SPARC, Sr-Trx-lp and Ts-Trx-lp can contribute in the reported immunoregulatory potential of intestinal helminth infection. 3D intestinal mucosal co-cultures represent a novel appropriate model to investigate the interaction of intestinal parasites and their released products with the host tissue habitat.

Biography

Emmanuela Maria Anandarajah is currently a PhD student from the Westphalian Wilhelms-University of Munster, Germany and finalizing her thesis at the Bernhard Nocht Institute for Tropical Medicine in Hamburg, Germany. She has completed her BSc in 2011 and MSc in 2013 at the Westphalian Wilhelms-University of Munster.

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Re-imagining the ovary: Recent advances and technical hurdles in recapitulation of the human ovarian micro environment

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Stem cell-based strategies for improvement of female infertility harbor tremendous potential not only restoring or sustaining fertility via oocyte production and development but also minimizing severity of the health consequences that accompany the endocrine disruption that occurs at menopause. Recent advances from our work and others have convincingly demonstrated that viable oocytes can be generated from primitive stem cell sources, opening the door for new avenues of research centered on ovarian regeneration and tissue bioengineering. However, both the endocrine function of the ovary and our current ability to generate fertilizable eggs is dependent upon the ovarian follicle structure, which includes the germ cell surrounded by a highly specialized layer of somatic cells responsible for the synthesis of sex steroid hormones. These cells, termed granulosa cells are requisite for the maintenance of hormonal stasis with the hypothalamic-pituitary axis. With advancing age these cells decline in number and function, ultimately resulting in cessation of fertility and endocrine dysfunction. Accordingly, cell- or tissue-based strategies aimed at generating an 'artificial ovary' for fertility or endocrine purposes must take into account multiple cellular lineages that work together in a complex microenvironment, comprised of distinct biological matrices. Working towards this, we have evaluated human ovarian composition throughout development and adulthood via a comprehensive quantitative proteomic analysis and are directly applying this toward the development of an ovarian stem cell-based artificial ovary system.

Biography

Dori C Woods has completed her PhD at the University of Notre Dame, working on granulosa cell function and steroidogenesis. She is currently an Assistant Professor at Northeastern University in Boston, MA, with a research focus on ovarian stem cells and the decline in female fertility with age. She has published over 30 manuscripts and review articles on ovarian function.

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Tissue Regeneration in Wound : Possibility to reality

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A wound is a huge health problem across the globe. Special services are built across the globe for wound care. In the open wound after injury the vascularity is highly compromised .With the loss of skins the underlying exposed tissues such as muscles, tendons and bones, tends to undergo necro-sis.At times, co-morbidities such as diabetes; and presence of infections further leads to complexi-ties.The current solutions for such wound management essentially involve their urgent removal and further tissue losses, consuming huge resources and leading to morbidities.Sandeep's Technique for Assisted Regeneration of Skin (STARS) therapy has been developed by the authors as a solution for this complex wound problem. It is basically a mono-therapy based on regenerative medicine for wound healing with Platelet rich Plasma (PRP). With the help of this technique angiogenesis is in-duced, built up around & over these tissues, leading to the regeneration of such grossly dead/ dying tissues and eventually regeneration of skin, leading to complete wound healing. Till date in wounds the regeneration of tissues has never been achieved. Though its possibility have been predicted through regenerative medicine products. For the first time these possibilities are being converted into realities by the STARS technique. In this paper, we disclose evolution and clinical outcome of "STARS" therapy in these overtly very threatening situations.The STARS therapy is evolving with the intention of making the wound management safe, predictable and accessible across the globe including from primary care to tertiary care.

Biography

Sandeep Shrivastava has done his Masters and Diplomate of National Board in Orthopedic Surgery & Fellowship in Medical education, India. He is currently Professor of Orthopedics and DEAN of J.N.Medical College, Datta Meghe Institute of Medical Sciences, Wardha,India. He has published 2 books, 47 Papers and is Member of editorial boards of JDMIMS and JAOS. He also has a copyright & inventor for H_COIN, a research outcome measurement tool, "Pre-Yell" an emergency response Application. Self-assertive learning, academic appraisal program and Early Research Exposure Model.

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Health Care integrated biobanking, an important resource for precision medicine

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Biobanks are essential for biomedical research and, more specifically, for the discovery and development of novel diagnostic biomarkers in the context of personalized medicine. They represent a reservoir for future clinical studies, and thus, accelerate the development and validation of new biomarkers and therapies, while reducing the costs of clinical research. Despite recent methodological advances in "omics" technologies, the discovery of new biomarkers has been largely prevented by uncontrolled variability in the quality among and within existing Biospecimen collections. Therefore, state of the art technological Biobank infrastructure that enables researchers to meet the quality requirements of liquid samples is an indispensable precondition for the use of future analytical technologies, such as mass spectrometry. The Inselpital (University Hospital Bern) has implemented for its Liquid Biobank Bern an infrastructure, whose major focus is on sample quality. All pre-analytical processes are fully standardized and integrated into the clinical routine. Samples are being frozen only one hour after the blood draw with every step in the pre-analytical process being electronically monitored and documented. Such modern health-care integrated and automated biobanks provide an important resource of high quality samples for the application of modern omics-technologies in clinical research. In particular, the ability to document the quality of samples is an important precondition to identify and to account for potential sources of bias that have led to irreproducible published results during the "omics"-hype.

Biography

Carlo R. Largiadèr is a molecular population geneticist. He is currently vice director of the University Institute of Clinical Chemistry (UKC) at the Inselspital and the academic head of the Liquid Biobank Bern (LBB). He also heads a research group in Pharmacogenomics and drug metabolism at the UK. His current research focuses on genetic and non-genetic factors or mechanisms underlying inter-individual variation in drug response with a strong interest in translational aspects.

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Endotoxin detection in full blood plasma in a theranostic approach to combat sepsis

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Annually, an estimated 750, 000 individuals are affected by sepsis in the United States (similar incidence is reported in Europe and around the world), with approximately 200, 000 casualties. The pathogenesis of sepsis are relatively well known, one of the most potent immuno-activators being bacterial lipopolysaccharide (LPS) also known as 'endotoxin' – which is a major constituent of the outer membrane of Gram-negative bacteria. Clinical tests, such as the 'Limulus amebocyte lysate' (LAL) assay or the more recent 'endotoxin activity assay' (EAA), are available to detect endotoxin. However, these methods are expensive, relatively fastidious to implement and (may) require reporter molecules. In the present paper, we introduce a biosensor-based approach for detection of LPS in blood plasma. A qualitative, cut-off (mid pg mL-1) biosensor assay alternative for bacterial endotoxin is described. Detection is based on the acoustic wave physics of the highly sensitive, ultra-high frequency 'electromagnetic piezoelectric acoustic sensor' (EMPAS) transducing device. The biosensing platform features dual-functional, binary organosiloxane adlayer surface chemistry (on quartz resonator discs) combining high binding affinity for the target analytewith pronounced antifouling properties against biological matrix sample interference. Unlike current clinical tests, measurements are performed in a realtime and label-free advanced fashion, using full human blood plasma microsamples (50 mL). Another highlight of this work is the rapidity with which analysis is completed (approximately 35 min per replicate). Underway is an attempt to validate this assay with a statistically relevant number of blood sources. Next in line is the actual assessment of clinical testing performance with real-life samples drawn from hospitalized patient donors.

Biography

Michael Thompson has obtained his PhD from McMaster University in Hamilton, Ontario. He is Professor of Bioanalytical Chemistry in both the Department of Chemistry and Institute for Biomedical Engineering at the University of Toronto. He has published close to 300 papers in international journals and has received many prestigious awards for his research. He served on the Editorial Boards of major journals and is currently Editor in Chief of the Royal Society of Chemistry book series on Detection Science. He was made a Fellow of the Royal Society of Canada in 1999.

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Biocompatibility and biodegradation response of synthesized Mg-Zn-Ca alloys on viability of adipose derived mesenchymal stem cells

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Magnesium (Mg) based alloys have been extensively considered for their use as biodegradable implant materials. However, controlling their corrosion rate in the physiological environment of the human body is still a significant challenge. One of the most effective approaches to address this challenge is to carefully select alloying compositions with enhanced corrosion resistance when designing the Mg alloys. In this study ternary Mg-2 wt.% Zn-xCa (x=1, 2 and 3 wt.%) alloys as biodegradable magnesium alloys were studied. The microstructures of the alloys were examined with optical microscopy, Scanning Electron Microscopy (SEM), X-ray diffraction (XRD) examinations as well as potentiodynamic polarization (PDP). Biocompatibility of mentioned alloys performed with indirect MTT viability test according to ISO 10993-5:2009 standard. The microstructural examinations demonstrated that by addition of 1, 2 and 3 wt.% Ca, the grain size reduced from 807 μm for Mg-2Zn to 86, 36 and 17 μm, respectively. Mg-2Zn has the least corrosion potential and current density among all groups (E_{corr}=-1.56 and i_{corr}=152 μA cm^2) due to well solubility of Zn; however, among Mg alloys which contain Ca content, the best corrosion properties related to Mg-2Zn-1Ca alloy (E_{corr}=-1.57 and i_{corr}=195 μA/cm^2). The viability results indicate that Mg alloys extract have no significant toxicity effect on adipose derived mesenchymal stem cells (ASCs) viability; however the viability increased in Mg-2Zn-1Ca group. Also, direct ASCs culturing on the surface of Mg alloys represented good attachment and proliferation.

Biography

Kobra Tahermanesh has completed her Medical degree from Shiraz University of Medical Sciences and graduated first Fellowship of Minimally Invasive Gynecology Surgery from Tehran University of Medical Sciences, Iran. She is an Assistant Professor of Iran University of Medical Sciences and Director of a research team focusing on bio-instruments and biodegradable implants for tissue engineering. She has a knowledge-based company in field of biomedical and tissue engineering. She is interested to work on interdisciplinary basic sciences and bio-engineering researches and do her best to connect the medical and engineering scientists to each other.

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Co-clustering of multidimensional big data with biomedical applications

Hong Yan
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In many biomedical applications, such as gene expression data analysis, we are interested in coherent patterns that consist of subsets of features and subsets of samples. To extract these patterns, we need clustering analysis in both feature and sample directions simultaneously using a biclustering method for two-dimensional (2D) data. When this process extends to three-dimensional (3D) data, we then need to perform triclustering. Biclustering and triclustering are examples of co-clustering, and they are naturally more complicated than the traditionally used clustering procedures. Recently, our research group has developed an effective co-clustering method for coherent pattern detection in multidimensional big data based on hyperplane detection in singular vector spaces. In our method, each subset of coherent features or samples corresponds to a linear structure after spectral decomposition of the input data. We have applied the method to gene expression data analysis and lung cancer drug effectiveness assessment with good results. The coherent patterns extracted in these applications are useful for Biomolecular data analysis, disease diagnosis and personalized treatment planning.

Biography

Hong Yan received his PhD degree from Yale University. He was Professor of Imaging Science at the University of Sydney and is currently Professor of Computer Engineering at City University of Hong Kong. His research interests include image processing, pattern recognition and Bioinformatics, and he has over 300 journal and conference publications in these areas. He is an IAPR Fellow and an IEEE Fellow. He was a Distinguished Lecturer of IEEE SMC Society during 2000 to 2015. He received the 2016 Norbert Wiener Award from IEEE SMC Society for contributions to image and bimolecular pattern recognition techniques.

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Developing a regulatory framework for precision medicine products: A Singaporean point of view

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Precision medicine is a robust field in health care that is distinguished by its reliance on genomic technology to deliver customizable preventive and curative treatments to a group of individuals. Like many other countries, Singapore is exploring ways to effectively facilitate the entry of precision medical products into its market. At present, these products are still subject to the same licensing procedures and standards as their "non-precision" counterparts. However, there are compelling reasons to believe that current legislations may not be ideal to effectively regulate this group of products. Firstly, as precision medical products are rarely used in solitaire, licensure of one product may inadvertently rely on the licensure of others it is bundled with. Secondly, this licensure interdependence may delay bringing innovative products into the market. Finally, in the backdrop of a lengthened premarket phase, industry may opt to "personalize" products at the clinical setting instead to escape from licensure requirements. This presentation serves as a systematic appraisal of Singapore's regulatory preparedness in ushering the era of precision medicine, specifically in terms of its ability to: keep up with technological advancements, adequately cover a diverse range of products, nurture innovation, and safeguard public health.

Biography

Andrew Green obtained his Medical Degree from Duke-NUS Graduate Medical School Singapore in 2012. He has also held a Masters of Science from the Max Planck Institute Tuebingen, Germany and a Masters of Public Health from the National University of Singapore. He is currently a senior resident in Preventive Medicine and concurrently holds the position of assistant director-equivalent at the Health Sciences Authority Singapore. His current portfolio includes the development of a national regulatory framework for advanced therapeutic products and precision medicine. Furthermore, he is also actively involved in Pharmacovigilance, health product compliance, and regulatory impact analysis.

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