Annual Congress on

RARE DISEASES & ORPHAN DRUGS

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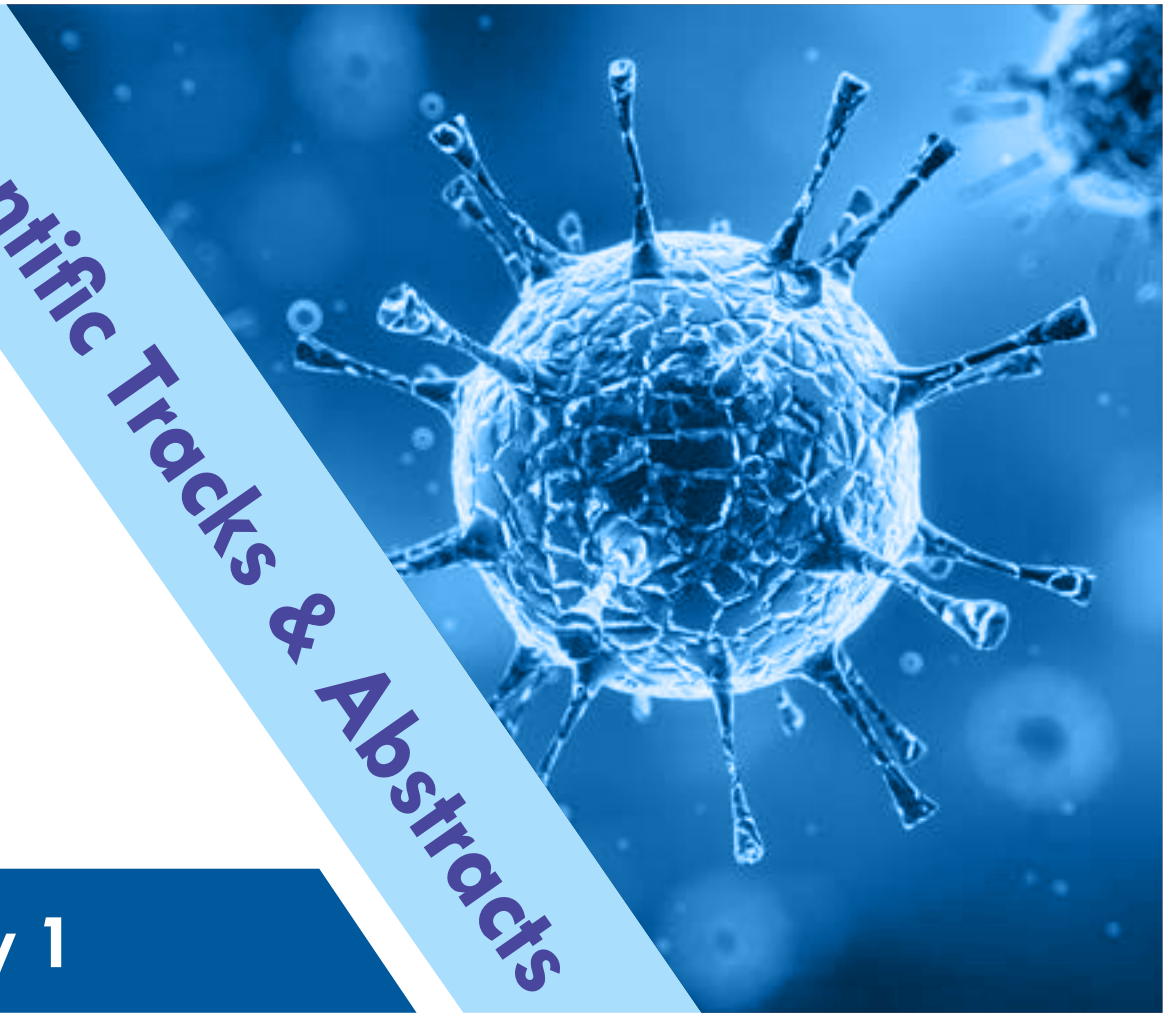
Scientific Tracks & Abstracts



Day 1

Rare Diseases 2016

Sahota A et al., J Genet Syndr Gene Ther 2016, 7:5 (Suppl)
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Tailored inhibition of cystine stone formation as a therapy for cystinuria

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Background & Aim: Cystinuria, caused by mutations in *SLC3A1* or *SLC7A9* is characterized by excessive excretion of cystine in the urine and cystine stones in the urinary tract. Cystine stones are difficult to treat surgically and medical treatments have major side effects. Previous studies from our group have demonstrated that cystine analogs such as cystine dimethyl ester (CDME) inhibit cystine crystallization *in vitro*. Here we show that this analog also inhibits cystine stone formation in *Slc3a1* knockout mice.

Methods: CDME (200 µg per mouse) or water was administered by stomach tube daily for four weeks; higher doses were administered to assess organ toxicity. Urinary amino acids and cystine stones were analyzed to assess drug efficacy using several analytical techniques.

Results: Treatment with CDME led to a significant decrease in stone size compared with the water group (p=0.0002), but the number of stones was greater (p=0.005). The change in stone size distribution between the two groups was evident by micro computed tomography. Scanning electron microscopy analysis of cystine stones from the CDME group demonstrated a change in crystal habit with numerous small crystals. L-cysteine methyl ester was detected by UPLC-MS in stones from the CDME group only, indicating that CDME is absorbed from the intestine and a metabolic product incorporated into the stone material. No pathological changes were observed at the doses tested.

Conclusions: These data demonstrate that CDME promotes formation of small stones but does not prevent stone formation, consistent with the hypothesis that CDME inhibits cystine crystal growth. Combined with the lack of observed adverse effects, our findings support the use of CDME as a viable treatment for cystine urolithiasis.

Biography

Sahota A is a Professor in the Department of Genetics, Director of Scientific Programs and Director of the Clinical Genomics Laboratory, RUCDR Infinite Biologics; Clinical Professor and Laboratory Director in the Department of Pathology and Laboratory Medicine, Robert Wood Johnson Medical School (RWJMS) and Clinical Professor in the Division of Urology, RWJMS.

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Notes:

Maite A Castro, J Genet Syndr Gene Ther 2016, 7:5 (Suppl)
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Failures in brain energy metabolism unveil therapeutic targets for Huntington's disease

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The brain makes up 2% of a person's weight. Despite this, even at rest, the brain consumes 25% of the body's energy. Most of the energy consumed in the brain is attributable to restoration of the membrane gradient following neuronal depolarization. Neurotransmitter recycling, intracellular signaling and dendritic and axonal transport also require energy. Even though neurons are responsible for massive energy consumption, the brain is made up of many cells, including neurons, glial and ependymal cells. Every brain cell has a specific function and thus every brain cell has different metabolic needs. Many of these specific functions are concerned with maintenance of neuronal transmission. Astrocytes play a central role in supporting neurons metabolically by producing lactate, through glycolysis and activation of glycogen catabolism. There have been several reports of metabolic impairment in a variety of neurodegenerative disorders such as Alzheimer's disease, Huntington's disease, amyotrophic lateral sclerosis and Parkinson's disease, among others. Moreover, deregulation of energy metabolism could be implicated in an increased production of oxidative species. During the last 10 years we have been making steady progress in the mechanisms of communication between neurons and glial cells, the way they regulate their metabolism and the use of ascorbic acid as inter cellular messenger. Here, we will describe the regulation of neuronal glucose, lactate and ascorbic acid transporters under synaptic activity in mice models of Huntington's disease. Experiments demonstrating a failure in astrocytic ascorbic acid recycling and ascorbic acid-dependent modulation on neuronal metabolism in Huntington's disease will be discuss. Brain is an expensive organ in energetic terms so disruptions in energy production may affect neuronal transmission and thus, neuronal survival.

Biography

Maite A Castro is a Professor in the Department of Biochemistry at the Universidad Austral de Chile since 2005. She has obtained her PhD in Biological Sciences at Universidad Austral de Chile in 2005. In 2009, she did a Postdoctoral training in Dr. Michael Levine's Laboratory at the University of California, Los Angeles, USA. During the last 15 years she has been making steady progress in the mechanisms of communication between neurons and glial cells and the way they regulate their metabolism. Presently, her interest is to study the correlation between failures in brain energy metabolism and the progression of Huntington disease.

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Notes:

Tyson E Dewsnup, J Genet Syndr Gene Ther 2016, 7:5 (Suppl)
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Epilepsy & rescue meds in schools

Tyson E Dewsnup
Epilepsy Association of Utah, USA

Statement of the Problem: While there are many other conditions, syndromes and diseases that both faculty & staff at public schools are comfortable and encouraged to administer rescue meds. Epilepsy remains a strange and scary thing. The over-all issue, especially in Utah is from school nurses not administering medications and not having enough nurses to cover schools.

Methodology & Theoretical Orientation: By encouraging staff buy-in and advocating with school nurses, the Epilepsy Association of Utah hopes to make seizure med training the norm in schools, not just in Utah, but across the country.

Findings: This does not seem to be a local problem only affecting those with epilepsy in Utah, but other states as well. Epilepsy affects more people than multiple sclerosis, cerebral palsy. Muscular dystrophy and Parkinson's disease combined! Yet, epilepsy receives less funding than each of them individually. Just the use of the name "epilepsy & seizure disorders" creates a stigma for many people. Epilepsy still seems strange and foreign, even while 1 in 3 know someone with epilepsy. 1 in 10 will have a seizure in their lifetime. 1 in 26 will be diagnosed with epilepsy. By increasing public knowledge and awareness, through concerted efforts and outreach, we can show that not only are rescue meds important but also that failure to administer them endangers safety and violates various statutes and federal laws. Seizures can be scary for those who aren't used to seeing them and those who are used to it. With a little training, however, our public schools can be more seizure-friendly. No parent should have to worry that while at school, their child may have a medical need that won't be addressed.

Biography

Tyson E Dewsnup has served as the Chairman of the Board of the Epilepsy Association of Utah since July 2016. Earlier he has served as the Associate Vice President of Programs. Outside of his service with the Epilepsy Association of Utah, he has served on various other non-profit boards in the public and private sector. He has a Bachelor of Science in Human Resource Management and is currently working on both his MBA and MHA. Aside from his board service, he is a Practice Supervisor for Intermountain Medical Group, a Physician and medical practice subsidiary of Intermountain Healthcare.

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Thomas C Chen et al., J Genet Syndr Gene Ther 2016, 7:5 (Suppl)
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NEO212: A new drug for Temozolomide resistant malignant gliomas

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Although the alkylating agent temozolomide (TMZ) has become the standard of care in the treatment of malignant gliomas, its overall efficacy is still limited by development of drug resistance, limited blood brain barrier (BBB) penetrance and myelotoxicity. Recently, we have synthesized a TMZ analog by covalently linking the monoterpene perillyl alcohol (POH) to TMZ via a carbamate bond. This new compound (NEO212) has been tested in TMZ resistant malignant gliomas. U251 and U87 TMZ resistant gliomas were tested and implanted intracranially for *in vivo* model. NEO212 was administered subcutaneously using 10 day treatment, 7 day rest cycles; no significant toxicity on normal astrocytes and brain endothelial cells were detected. NEO212 revealed considerably greater therapeutic efficacy than TMZ, where a single cycle of treatment (10 days) extended median survival benefit from 6 days (in the case of TMZ) to 24 days with good tolerance. Pharmacokinetic analysis demonstrated that NEO212 has at least three times the brain concentration compared to TMZ when both agents are administered subcutaneously. Formal toxicity studies conducted at Charles Rivers (Montreal, Canada) demonstrated that it can be safely tolerated in both acute and chronic administration studies (up to 250 mg/kg). Long term toxicity appears to be myelotoxicity. NEO212 appears to be a promising well tolerated new agent with similar mechanism of cytotoxicity to TMZ. Its increased potency is most likely multi-factorial increased DNA damage, involving a broader scope of DNA repair mechanisms, linkage with POH, resulting in longer biological half-life and stability, increased lipophilicity, allowing for better penetration of the BBB and possibly cell membrane. This talk will emphasize the bench to bedside development in taking this drug to IND status.

Biography

Thomas C Chen has founded NEONC Technologies, Inc., in 2008 and serves as its Chairman, Chief Executive Officer and Chief Scientific Officer. He is an Executive Director at Cognos Therapeutics Inc., Co-Founder of Pharmaco-Kinesis Corporation and serves as its Chief Oncology Officer. He serves as a Scientific Advisor, Scientific Collaborator at Tocagen Inc. He serves as an Associate Professor of Neurological Surgery and Pathology at the University of Southern California (USC), Principal Investigator of an Independent Laboratory and Head of the Glioma Research Group at USC. He also serves as the Director of Surgical Neuro-Oncology at USC. He is a Member of Neurological Board, Member of Clinical Advisory Board at Magnetecs Corporation. He is a Physician and a board certified Neurosurgeon. He holds an MD from the University of California San Francisco, completed his Neurological Surgery Residency and PhD in Pathobiology at the University of Southern California. He has obtained Fellowship training in Spinal Surgery from the Medical College of Wisconsin and was graduated from the University of Illinois at Urbana-Champaign. He holds a Bronze Tablet Honors from University of Illinois at Urbana-Champaign and was inducted into the Phi Beta Kappa national academic honor society.

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Notes:

Philippe Jouvet, J Genet Syndr Gene Ther 2016, 7:5 (Suppl)
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Management of life threatening hyperammonemia in children

Philippe Jouvet
University of Montreal, Canada

Hyperammonemia is an acute life threatening situation encountered in the pediatric intensive care unit (PICU). Reduction in hepatocyte number or function in liver failure (LF) and inhibition or primary defect of urea cycle enzymes in inborn errors of metabolism (urea cycle defect UCD) are the main causes of hyperammonemia in children. Ammonia has been shown to affect brain function to modulate both excitatory and inhibitory neurotransmission and to contribute to cerebral edema. Ammonia direct neuronal toxicity coupled with an increase of cerebral blood flow can lead to cerebral edema. There are several demonstrations of a link between hyperammonemia and death or encephalopathy in either LF or UCD with threshold for risk of toxicity around 200-350 µmol/L. Targeting gut production of ammonia may be too slow and ineffective in lowering ammonia level and modulating its cerebral effects, in patients sufficiently ill to require PICU admission. The use of antibiotics remains controversial in the management of hepatic encephalopathy. Furthermore, there is no high-quality evidence to support the use of non-absorbable disaccharides. Ammonia scavengers are now widely used in patients with UCD and seem to improve outcome by efficient lowering of ammonia levels. The literature shows that few molecules have been tested in hyperammonemia. Possible treatment could include oral sodium benzoate, L-ornithine used in combination with L-aspartate, and phenylacetate, carglumic acid. When hyperammonemia is very high, an extracorporeal removal therapy is recommended. Recent advances in treating hyperammonemia suggest using synergistic combination treatments, broadening the indication of orphan drugs and developing novel approaches to regenerate functional liver tissue.

Biography

Philippe Jouvet has obtained his MD in 1989 at Paris V University and MD specialty in Pediatrics and MD subspecialty in Intensive Care at Paris V University. He has completed his PhD in Pathophysiology of Human Nutrition and Metabolism in 2001 at Paris VII University and joined the Pediatric Intensive Care Unit of Sainte Justine Hospital-University of Montreal in 2004. He is the Director of the Pediatric Intensive Care Unit and Scientific Director of the Health Technology Assessment Unit of the Sainte Justine Hospital-University of Montreal. He has a salary award for research from the Quebec Public Research Agency (FRQS). He currently conducts a research program on computerized decision support systems for health providers. He has published more than 130 papers in peer reviewed journals and gave more than 100 lectures in congresses.

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Notes:

Laura K Sunderlin, J Genet Syndr Gene Ther 2016, 7:5 (Suppl)
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Defending the dream; perils beyond science and finance

Laura K Sunderlin
Beazley, USA

Statement of the Problem: Scientists, medical researchers and their financial backers, particularly in the field of rare diseases and particularly with orphan drug development are entirely focused on the efficacy of the science and the impact of their work on the mitigation and cure of disease. Successful development however can come to grief because of alienation of affiliate groups, difficult or misunderstood clinical trials, public and legislator perception, unexpected lawsuits.

Methodology & Theoretical Orientation: A discussion of the cultural pitfalls surrounding drug development from 15 years of insuring life sciences companies. A discussion of growing distrust of clinical trials (from Constant Gardiner to distrust of results), perceptions on pricing and availability of product and alienation of orphan drug affinity groups, a tidal wave of public antipathy towards the drug industry and the critical role of a well-constructed informed consent, insurance and risk-management tactics and a look at what has put potentially successful companies out of business and ended promising research.

Conclusion & Significance: Attention must be paid to the cultural, social and legislative environment of drug development. Informed consents and monitoring in clinical trials, open and extensive communication with disease sufferers and their families, sensitivity to public perception and the use of insurance and risk management can assure that the focus can remain on the science.

Biography

Laura K Sunderlin has 30 years of experience in the Insurance Industry; the last 15 of them insuring life sciences. She has insured biotech start-ups and some of the largest biotechs in the country, for clinical trials and products liability. She brings the experience of a decade and a half of defending against claims, analyzing risk, discussing exposures with risk managers and scientists.

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Notes:

Megan O'Boyle, J Genet Syndr Gene Ther 2016, 7:5 (Suppl)
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Engaging families in research to drive progress: Phelan-McDermid Syndrome International Registry (PMSIR) and the Phelan-McDermid Foundation Data Network (PMS_DN)

Megan O'Boyle
Phelan-McDermid Syndrome Foundation, USA

Phelan-McDermid Syndrome (PMS) is a rare genetic condition associated with autism spectrum disorder, seizure disorders and severe to profound intellectual disability. Today, there is no cure for PMS and patient interaction with health care and research is for the most part navigated by parents and caregivers. In 2011, the PMS Foundation launched the PMS International Registry (PMSIR), centralizing data about the PMS community and removing barriers for researchers studying the condition and its associated interventions. The PMSIR has been family-led since its inception. In 2013, the Foundation was awarded a PCORI contract to participate in PCORnet as a Patient Powered Research Network and establish the PMS Data Network (PMS_DN), integrating patient-reported outcomes from the PMSIR with concepts extracted from electronic health records of PMS patients. The PMS_DN, a collaboration between the PMS Foundation, Harvard Medical School Center for Biomedical Informatics and Boston Children's Hospital, advances knowledge, care and treatment of PMS and related conditions by integrating diverse, complex data sources into a richly populated, high quality and centralized database to facilitate patient-centered research. The PMS_DN technical infrastructure is an i2b2/tranSMART data warehouse and web interface, which integrates patient reported outcomes (PROs), curated genetic testing results and knowledge extracted from clinical notes. The PMS_DN excels in engaging families in data sharing activities and prioritizing research questions, facilitating family communication and promoting transparency of patient data use in research, through the leadership of exceptional parents and the authentic engagement of patients and caregivers as champions for their families.

Biography

Megan O'Boyle is the Principal Investigator for the Phelan-McDermid Syndrome Data Network (PMS_DN, PCORnet) and the Phelan-McDermid Syndrome International Registry (PMSIR). She is passionate about the value of the patient's voice in research, drug development, clinical trial design, development of related legislation and quality of life decisions. She advocates for data sharing, collaborating with other advocacy groups, sharing resources and streamlining IRB practices and policies.

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Notes:

Yusuf Hovsep Eken, J Genet Syndr Gene Ther 2016, 7:5 (Suppl)
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Fever of unknown origin: Case study

Yusuf Hovsep Eken
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Adult onset Still's disease (AOSD) is a rare disease in adults, in children also known as systemic juvenile idiopathic arthritis. We describe two patients with intermittent fevers without unknown origin. Patients were from Twenteborg Hospital Almelo affiliated with Academic Center Radboud Medical Center in Nijmegen and Catharina Hospital in Eindhoven affiliated with Maastricht Medical Center. 27 years man and 75 years old woman, who presented with lymphadenopathy and recurrent fevers, there has been used intensive serologic, radiologic, laboratory investigation to exclude infectious diseases and malignancy. All the investigation showed no diagnosis. The clinical disease described for the first time 105 years ago by Dr Still is finally diagnosed. Both patients received Anakinra with rapid response in hematologic, biochemical and cytokine markers with reduction of systemic and local inflammation.

Biography

Yusuf Hovsep Eken has completed his Medical education in Utrecht University, Netherlands.

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Notes:

Marise Abdou, J Genet Syndr Gene Ther 2016, 7:5 (Suppl)
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A 20 days old patient with genital asymmetry

Marise Abdou
Abo El-Rish Children's Hospital, Egypt

A 20 days old patient reared as male was brought by his parents to Diabetes, Endocrine and Metabolism Pediatric clinic for atypical genitalia and bilateral undescended testis. On genital examination, the patient had underdeveloped right scrotal compartment, genital asymmetry, bifid scrotum, penoscrotal hypospadias and a phallus length of 3 cm. The left gonad could be felt at the medial end of the inguinal and it could be brought down to the scrotal sac and was of normal size and texture while the right gonad could not be felt along its course. The following investigations were ordered: Karyotyping, Basal hormones (17 (OH) progesterone, progesterone, DHEA, androstendione, testosterone, DHT, cortisol and ACTH) & Anti-Mullerian hormone and Abdominopelvic Ultrasonography. The result of the Karyotyping came back to show 45X0/46XY. Abdominal ultrasonography done revealed the presence of normal infantile uterus behind the urinary bladder, the vaginal canal was mildly dilated with fluid contents, a gonad mostly testis was seen on the left side measuring 12×7.2 mm and no gonad could be detected on the right side along its path of descent. The patient was prepared for laparoscopy at the department of Pediatric Surgery, Cairo University. During laparoscopy, specimens were obtained for histopathological examination and mullerian structures could be detected. The results of the histopathological examination revealed the presence of streak testis with male type ductal system which confirmed the diagnosis of mixed gonadal dysgenesis which is a variant of Turner Syndrome (Turner Syndrome with Y cell line)

Biography

Marise Abdou has joined Diabetes, Endocrine and Metabolism Pediatric Unit (DEMPU) in 2010 and has completed her MD from Cairo University. She is an active Member of DEMPU which was founded in 1980 by Prof. Dr, Isis Ghaly. She is actively involved in many research studies that are carried out in DEMPU. She has one publication in the field of endocrinology.

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Ramune Sepetiene, J Genet Syndr Gene Ther 2016, 7:5 (Suppl)
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Association between *FBN1* polymorphisms and TGF-β1 concentration within aneurysms and dissections of ascending thoracic aorta

Ramune Sepetiene
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Transforming growth factor β1 (TGF-β1) is a cytokine that participates in a broad range of cellular regulatory processes and is associated with various diseases including aortic aneurysm. An increased TGF-β1 level is associated with Marfan syndrome (MFS) caused by fibrillin-1 (*FBN1*) mutations and subsequent defects in signaling system. *FBN1* single nucleotide polymorphisms (SNPs) rs2118181 and rs1059177 do not cause MFS but are associated with dilatative pathology of ascending aorta. A purpose of the investigation was to test hypothesis does an association between *FBN1* SNPs (rs2118181, rs1059177) and TGF-β1 level in human blood plasma exist among sporadic cases of dilatative pathology of ascending aorta. A study group was recruited from 312 patients who had undergone aortic reconstruction surgery due to dilatative pathology of ascending aorta and 741 healthy control subjects of Kaunas population (N=269) without cardiovascular disorders, except hypertension. Genomic DNA was isolated from potassium EDTA blood. Genotyping of *FBN1* SNPs was carried out by using ABI 7900HT Real-time PCR Thermocycler with commercially available kits from Applied Biosystems. TGF-β1 quantitated detection was tested with eBioscience Platinum human TGF- β1 ELISA commercially available kit based on standard sandwich enzyme-linked immune-sorbent assay technology according manufacturers' instructions. Non-parametric Kruskal-Wallis test was used for data analysis. The results showed a quantitative dependence of SNP genotype and TGF-β1 concentration. A presence of a single rs2118181 minor allele (G) increased the median amount of TGF-β1 level. Two copies of *FBN1* rs1059177 minor allele (G) were required to give a significant rise of TGF-β1 level in blood plasma. We also found higher TGF-β1 concentrations in men compared to women (p=0.001). The results are indicating that presence of minor allele of *FBN1* SNPs rs2118181 or presence of homozygous genotype of minor alleles of rs1059177 is associated with the significant increase in TGF-β1 blood plasma level but the mechanism of this association is still unknown.

Biography

Ramune Sepetiene is currently a PhD Student at Lithuanian University of Health Sciences. She has obtained her MD with medical laboratory specialization in 1999 from Lithuanian University of Health Sciences, Medicine Academy. She has more than 15 years of clinical work experience within immunology, hematology and genetics. She is a Junior Researcher in Laboratory of Molecular Cardiology, Institute of Cardiology, LUHS and part time laboratory MD position in patients' clinic. Recently she has published 4 papers within PhD dissertation subject in reputed journals of cardiac surgery and genetics.

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Notes:

Shin'ichi Takeda, J Genet Syndr Gene Ther 2016, 7:5 (Suppl)
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On-going exon 53 skipping clinical trial for Duchenne muscular dystrophy

Shin'ichi Takeda
National Center of Neurology and Psychiatry, Japan

Duchenne muscular dystrophy (DMD) is the most common childhood genetic disease, affecting one among 3500-5000 newborn boys, causing progressive muscle weakness, heart and respiratory failure and premature death. This disease is caused by the mutations of the DMD gene and there is no cure exists for this disease but a number of promising new molecular therapies are being intensively studied. Exon skipping by antisense oligonucleotides (AOs) is a novel method to restore the reading frame of the mutated DMD gene and rescue dystrophin expression. We have reported that systemic delivery of AOs targeting exon 6 and 8 of the canine DMD gene to CXMDJ, a dystrophin-deficient canine animal model, efficiently restored functional dystrophin proteins at the sarcolemma of these dogs and improved phenotypes of affected dogs without serious adverse effects. We, then, optimized AO sequences, which allow exon 53 skipping of the human DMD gene, together with Nippon Shinyaku Co. Ltd. After numbers of toxicology study of the AOs, NS-065/NCNP-01, we proposed an early phase clinical trial of exon 53 skipping of DMD patients, which was approved by Japanese Pharmaceutical and Medical Devices Agency (PMDA) and the trial, has been successfully carried as an investigator-initiated trial in NCNP hospital. Following the excellent results of the early phase trial, phase I/II trial in Japan and phase II trial in US are carrying by either Nippon Shinyaku Co. Ltd. or NS Pharma, Inc.

Biography

Shin'ichi Takeda is currently the Director General of National Institute of Neuroscience in the National Center of Neurology and Psychiatry (NCNP). He initially trained as a Clinical Neurologist and received a PhD degree in Muscle Biology from Shinshu University, Graduate School in 1981 and has a long time laboratory experience including Paris Pasteur Institute (1987-1992). He focused his research on development of molecular therapy of Duchenne muscular dystrophy (DMD), since he came back from France and has gotten the position in NCNP in 1992. He has showed a proof of concept study of exon skipping in the colony of dystrophic dogs that he established and he recently finished the early phase clinical trial of exon 53 skipping of the dystrophin gene among DMD patients in Japan as a PI. He is working as an Associate Editor for review of *J. Neuromuscular Diseases* since 2013 and an Associate Editor of *Am. J. Pathology since 2014.*

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Lisa Baumbach-Reardon, J Genet Syndr Gene Ther 2016, 7:5 (Suppl)
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Rare disease research: Opportunities and challenges

Lisa Baumbach-Reardon
Translational Genomics Research Institute, USA

Human rare diseases also referred to as an orphan disease, is any disease that affects a small percentage of the population. Most rare diseases are genetic and thus are present throughout the person's entire life, even if symptoms do not immediately appear. Many rare diseases appear early in life and about 30 percent of children with rare diseases will die before reaching their fifth birthday. No single cutoff number has been agreed upon for which a disease is considered rare. A disease may be considered rare in one part of the world or in a particular group of people, but still be common in another. There is no single, widely accepted definition for rare diseases, which places constant demands on disease advocates, parents, clinicians and researchers to bring their concerns to national agencies regarding recognition of the disorder and treatment options for relatively rare diseases. Out research group has had the unique opportunity to identify a rare genetic disorder, X-Linked Spinal Muscular Atrophy (XL-SMA) and to work with clinicians and families throughout the world to identify these rare families. We have collected blood samples from family members to perform DNA linkage analysis and finally, disease gene identification in a subset of these families. Surprising, as DNA identification technologies have developed, so has our sub-classification of even rarer "genetic" disorders evolved, demonstrating the additive strength of analyzing clinical phenotypes to causative genotypes which may well be overlapping in primary or secondary disease pathways.

Biography

Lisa Baumbach-Reardon has completed her PhD from University of Florida, Gainesville and then entrenched her further training in Human Molecular Genetics at two subsequent Post-doctorates at Baylor College of Medicine and University of Colorado; this lead to dual certification in Clinical Molecular Genetics and Biochemical Genetics by the ABMG. She has operated two CLIA molecular DX labs during her academic career and joined TGEN in 2011 to operate a state-of-the art-CLIA lab, as well as pursued her further studies in XL-SMA.

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Annemieke Aartsma-Rus, J Genet Syndr Gene Ther 2016, 7:5 (Suppl)
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COST action BM1207: Involving all stakeholders to overcome challenges of genetic therapy development for Duchenne muscular dystrophy

Annemieke Aartsma-Rus
Leiden University Medical Center, Netherlands

Duchenne muscular dystrophy (DMD) is a rare, progressive muscle-wasting disease leading to severe disability and premature death. Treatment is currently symptomatic but multiple experimental therapies are in development. Implemented care standards, validated outcome measures correlating with clinical benefit and comprehensive information about the natural history of the disease are essential for the regulatory approval of any therapy. However, for DMD and other rare diseases, these were not in place when potential therapies entered the clinical trial phase. This has resulted in suboptimal trials for DMD therapy. To address this, a cooperative effort of DMD stakeholders, including representatives from patient groups, academia, industry and regulatory agencies aimed at identifying strategies to overcome challenges, developing the tools required and collecting relevant data. This is ongoing work, but already a huge effort has been made to develop new outcome measures, collect natural history data and to develop potential biomarkers. The open and constructive dialogue among stakeholders has positively influenced therapy development for DMD and this should serve as a paradigm for rare disease therapies' development in general.

Biography

Annemieke Aartsma-Rus has obtained her PhD at Leiden University, Netherlands in 2005. She became a Group Leader in 2007 and she is currently a Professor of Translational Genetics at Leiden University Medical Center, Netherlands. She currently chairs the TREAT-NMD Alliance (an infrastructure network for clinical trial readiness for neuromuscular disorders) and a networking action (funded by Cooperation of Science and Technology (COST)). She has published more than 100 papers in peer reviewed journals, written multiple book chapters and generated and maintains pages to explain Duchenne therapies in lay terms to the patient community. In 2009 she received the Duchenne award from the Dutch Duchenne Parent Project for her dedication to the field.

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Prasanth Puthanveetil, J Genet Syndr Gene Ther 2016, 7:5 (Suppl)
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Overlap of metabolic and endocrine dysregulation during orphan disease-special focus on cardiovascular disease

Prasanth Puthanveetil
Roosevelt University College of Pharmacy, USA

Statement of the Problem: The prediction of rare diseases has always been a limiting factor associated with these complications. By the time the presence of disease is confirmed the onset of disease must have been prominent leading to devastating and uncontrollable aftermaths. Understanding the complexity of events occurring during these disease conditions would provide us with a better insight not only to treat these diseases but also to prevent the debilitating effects in the respective tissues and save the organ systems or prolong or hinder the damage. This study demands the need for understanding the metabolic and endocrine dysfunctions during a rare disease in detail and thus not only open up a new path for the scientists to explore the pathophysiological molecular mechanisms in detail but specifically help the clinicians/physicians to understand therapeutic strategies.

Hypothesis and Methodology: Wolff Parkinson White Syndrome is one of rare disease connected to the cardiovascular system. Multiple factors have been shown to play an important role in the etiology of this disease. A major share goes to PRKAG2 gene mutation leading to glycogen accumulation in the cardiac tissue and resulted in atrial fibrillation in patients. Studies from preclinical data suggest that over activation of AMPK protein, the major energy sensor or metabolic switch could be playing an important metabolic role in bringing about this complication. Some of my previous studies using glucocorticoid excess revealed that they were able to increase AMPK. Thus using *in vitro* and *in vivo* model systems, I was able to see an increase in cardiac AMPK and glycogen accumulation. This raises the concern that the pathogenesis of Wolff Parkinson White Syndrome can result from any other route rather than just PRKAG2 conclusion.

Conclusion & Significance: Glucocorticoids in excess in heart resulted in uncontrollable AMPK activation with resulting glycogen accumulation in cardiac tissue. Physiological situations like fasting and stress and pathological conditions like Cushing's syndrome could result an increase in glucocorticoid excess release into the systemic circulation. Now whether these metabolic changes associated with endocrine abnormalities could result in Wolff Parkinson White like syndrome or no is not fully studied and is one of the area I would like to shed more light upon and tried to minimize the detrimental effects.

Biography

Dr. Prasanth Puthanveetil has done his PhD in Pharmacology especially in the area of cardiovascular diseases from the University of British Columbia. Following his post-doctoral training at NIEHS/NIH, University of Western Ontario and University of Michigan, he was selected for a full time tenure track faculty position at Roosevelt University School of Pharmacy. Till date, he has published more than 20 peer-review manuscripts, including 10 first-author publications. He is an active member of many professional associations, including American Heart Association and Canadian Diabetes Association. He has and continues to serve as invited reviewer and editorial board member of several peer-reviewed journals. At RUCOP, Dr. Prasanth Puthanveetil is setting up his research lab focusing on metabolic signaling in cardiovascular tissue especially during metabolic stress. Also he has special interests in endocrine disorders like diabetes and Cushing's syndrome and its impact on cardiovascular health.

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Notes:

Nasir Ali Afsar, J Genet Syndr Gene Ther 2016, 7:5 (Suppl)
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Tapping untapped: Exploring role of ALDH in pharmacogenetic and toxicogenetic studies

Nasir Ali Afsar
Alfaisal University, KSA

The response to a xenobiotic may be influenced by polymorphic genes of metabolizing enzymes and transporters. We had previously reported, selected genotype profiles for the breast cancer patients on fluorouracil, doxorubicin and cyclophosphamide (FAC) in a Pakistani set of population and compared them with allele frequencies in North America, Europe, Africa, China and other regions as represented in HapMap database. Our current study explores the previously reported as well as additional genotypes in healthy adults from different population subgroups at Karachi which remains unreported so far.We included 155 healthy adults after informed consent and institutional approval. The DNA was extracted from saliva collected and stored in Oragene-DNA® kits. Relevant SNPs of genes involved in drug metabolism and transport were genotyped either through restriction fragment length polymorphism or pyrosequencing after PCR amplification. We genotyped selected drug metabolizing enzymes involved in Phase-I metabolism (CYP1A1*2A/*3, CYP1A1*2C, CYP2B6*4, CYP2B6*6, CYP2C9*2, CYP2C19*2, CYP2C19*17, CYP2D6*4, CYP2D6*10, CYP3A4*22 and CYP3A5*3), Phase-II metabolism (ALDH3A1, GSTA1-69, GSTM1) and efflux transporters (ABCB1 1236, ABCB1 2677, ABCB1 3435, ABCC2-24, ABCC2 3972, ABCC2 1249) along with such frequencies in other population sets represented in HapMap. Interestingly, we found that although there were certain differences in allele frequencies, most notably, ALDH2 variant allele frequency is much higher in our population, thus drawing possible implications regarding environmental toxicity, atherosclerosis and other situations marked by oxidative stress. The presentation would emphasize upon the fact that molecular research outcome from one field could be used in other disciplines because of biological overlap.

Biography

Nasir Ali Afsar is a Pharmacologist and is a Member of British Pharmacological Society, Canadian Society of Pharmacology and Therapeutics, Association of Medical Education in Europe as well as Certified Researcher in Medical Education by American Association of Medical Colleges. He is affiliated to Academia since 1999 in different capacities. His research interest includes pharmacogenetics, clinical pharmacology, clinical simulation and medical education. He has several publications, invited lectures as well as conference presentations to his credit and serves as a peer Reviewer and Editorial Board Member of repute.

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Notes:

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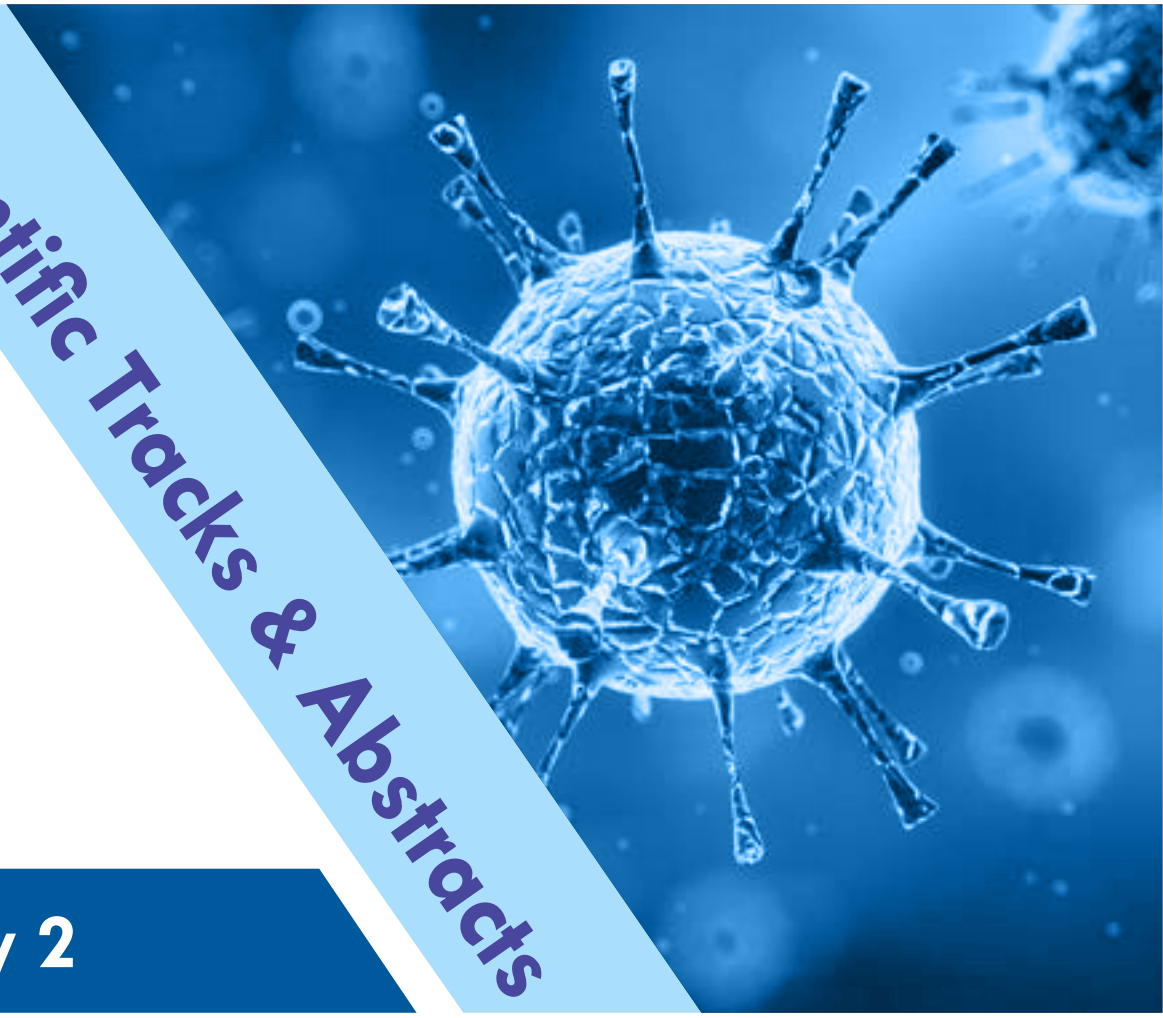
Scientific Tracks & Abstracts



Day 2

Rare Diseases 2016

Daniel Cohen, J Genet Syndr Gene Ther 2016, 7:5 (Suppl)
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Network pharmacology based repurposed drugs combination for orphan diseases treatment

Daniel Cohen
Pharnext, France

Charcot-Marie-Tooth type 1a is an orphan genetic progressive de/dysmyelinating peripheral neuropathy affecting 125 000 persons across US and Europe. Disease, although clinically heterogeneous, impairs and quite often badly disables life of patients who could be wheelchair bound. It is primarily due to Schwann cells PMP22 protein over-expression from gene duplication. PXT 3003 , allow dose combination of 3 drugs including Baclofen, naltrexone and sorbitol, each already approved for other indications, was designed from network pharmacology based screening. Preclinical experiments showed ability to lower of PMP 22 expression, to re-myelinate axons and to improve histological, electrophysiological and clinical endpoints in the CMT1A PMP22 transgenic rat model over-expressing PMP22 protein. An exploratory double blind placebo controlled multicenter phase 2 was conducted on 80 mild to moderate adult patients over one year testing 3 different doses of the combination at a given ratio against Placebo. Anticipated safety was confirmed. Eleven endpoints were analyzed, 2 widely used clinical composite Scores such as ONLS (disability) and CMTNS (impairment) and 9 clinical and electrical quantitative measures. The most significant response was obtained with the clinical scores and some relevant electrical measures with a clear global dose effect. Milder patients responded better. Under the highest dose, which was still a 1/10 of usual dose of these drugs, disease state was stabilized in half of the patients when, beyond stabilization, it was improved in the other half of patients. These encouraging results led us to design a pivotal phase 3 to start end of 2015 on 300 mild to moderate adult patients across US and Europe, with ONLS as a primary clinical efficacy endpoint. Highly encouraging preliminary data obtained at the Max Planck Institute in post-natal CMT1A young RAT has also paved the way towards a pediatric trial hoping to prevent symptoms when treating young children early enough. Network pharmacology based strategy can be systematically applied to any rare or common disorders.

Biography

Daniel Cohen is a former Professor of Medical Genetics in Paris University has authored more than 150 peer reviewed papers in HireWire Journal, including the first integrated map of the Human Genome back in the 90's. While he has discovered or co discovered numerous genes for rare and common diseases, he has also pioneered several key technologies like Large Scale Biology at Genethon. He was the Co-Founder of Millennium Pharmaceuticals in Boston, MA. He is currently the Chairman, CEO and Co-Founder of the France Based company, Pharnext, focusing on treatment of unmet neurodegenerative disorders by using Network Pharmacology.

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Yong Moon Choi, J Genet Syndr Gene Ther 2016, 7:5 (Suppl)
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JBPOS0101: A new generation mGluR and BBB targeted broad spectrum antiepileptic drug for the treatment of super-refractory status epilepticus

Yong Moon Choi
Bio-Pharm Solutions Co. Ltd., South Korea

JBPOS0101 is an antiepileptic drug candidate which possesses highly potent and broad spectrum antiepileptic activity as demonstrated in testing done by Bio-Pharm Solutions and NIH NINDS Anticonvulsant Screening Program. NINDS has provided a Red Book for JBPOS0101 due to its promising anticonvulsant profile. JBPOS0101 shows efficacy in a broad range of animal models including electrically and chemically induced seizures. JBPOS0101 shows efficacy in pharmaco-resistant epilepsy models and also in the 6 Hz psychomotor seizure test with similar ED50 values at both 32 mA and 44 mA stimulation. In particular, JBPOS0101 shows strong efficacy in several benzodiazepine-resistant status epilepticus models in which lithium-pilocarpine is administered 30 minutes after the first observed seizure: Behavioral seizures with 90 minute observation, electrographic seizures, in terms of gamma wave power (20-70 Hz) on EEG with 10 hour observation, protection against hippocampal cell loss after 14 days of observation and spontaneous recurrent seizures with 14 day observation. JBPOS0101 is an antagonist of metabotropic glutamate receptors 1 and 7. Additionally, JBPOS0101 may have a strong functional role in blood brain barrier related neuroprotection against lithium-pilocarpine induced status epilepticus, collagenase induced hemorrhage and tPA induced cell death. JBPOS0101 has completed phase-1 clinical trials in Toronto, Canada. No serious or severe treatment emergent adverse events occurred. All adverse events were characterized as mild. No subject in any treatment group experienced a treatment emergent adverse event related to vital sign measurements. Regarding the pharmacokinetic profile observed in phase-1, plasma concentrations of JBPOS0101 were observed to increase proportionally with increasing dose levels of JBPOS0101. We are currently planning a phase 1/2 trial for the treatment of patients with super-refractory status epilepticus. The preclinical data, especially the refractory status epilepticus models and phase-1 results suggest that JBPOS0101 is a promising drug candidate for the treatment super-refractory status epilepticus with anti-epileptogenic and neuroprotective properties.

Biography

Yong Moon Choi has completed his PhD from the State University of New York and Postdoctoral studies from Purdue University under 1979 Nobel Laureate Herbert C. Brown. He is currently the President and CEO of Bio-Pharm Solutions based in South Korea. He has founded SK Biopharmaceuticals (New Jersey, Seoul/DIT, Shanghai) in 1993. While at SK Biopharmaceuticals, he has established a global R&D network with NIH National Institute of Neurological Disorders and Stroke, university institutes and Johnson & Johnson. He has filed 104 patents and published 29 papers in renowned journals.

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Stephen P Arneric, J Genet Syndr Gene Ther 2016, 7:5 (Suppl)
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Digital measurements of health-regulatory science challenges opportunities in rare diseases

Stephen P Arneric
Critical Path Institute, USA

Interest in identifying, evaluating and qualifying innovative technologies for use in drug development is growing. While FDA guidance documents exist for pursuing novel Drug Development Tools (DDTs) and Medical Devices Development Tools (MDDTs) for qualification, the use of Digital Measurements of Health (DMH) (i.e., measured biological events or patient function captured through a device or sensor technology) for use in clinical development remains ill-defined. FDA issued in 4Q2015 a Federal Register request for comments that could accelerate the assessment of innovative drug treatments. The Coalition Against Major Diseases (CAMD), a consortium within the Critical Path Institute, aims to accelerate the development of tools that increase the efficiency of delivering innovative treatments for Alzheimer's Disease and related neurodegenerative/Rare Diseases that impair cognition and function. This presentation highlights CAMD's perspective on use of DMHs as drug development tools, the challenges faced and the need for; Data standards: Consensus on standardized ways to record, structure and report data generated by digital biosensors, employing CDISC standards to provide the consistent data model/structure to enable data sharing across technology platforms; DMHs as drug development tools: Development of standards for validating the analytic performance of devices; and Context of Use (COU) statements: Implementation of COU statements based on the current state-of-evidence for their application in drug development. CAMD's perspective supports the use of DMHs in clinical trials for; Function: Electronic monitoring of activities in/outside of home (patterns of sleep, drug adherence, walking, social interactions via phone and computer, cognitive task assessments) and fine motor skills (e.g., typing or key stroking on computer/smartphone); and Physiological measures: ECG, EEG, movement (accelerometer), speech/voice analysis, etc. Having open/frequent dialogue with regulators is critical to shape the development, validation and clinical relevance of this research.

Biography

Stephen P Arneric has joined the Critical Path Institute as Executive Director of the Coalition Against Major Diseases (CAMD), a consortium focused on developing Drug Development Tools for advancing innovative treatments of Alzheimer's disease and related dementias in 2015. Previously he was VP Research/Preclinical Development (Neuromed Pharmaceuticals), CSO of the Pain/Migraine Drug Hunting Team (Lilly) and held senior management positions at Pfizer, Pharmacia, DuPont Pharmaceuticals and Abbott. He has extensive leadership and scientific expertise in the areas of neurology, pain, psychiatry and urology and over the last 25 years his teams have delivered more than 30+ drug candidates into clinical development. He has earned BS degree in Physical Sciences from Michigan State University and PhD in Pharmacology from University of Iowa, USA. He is an accomplished author with 145 peer-reviewed articles, 190 abstracts, 17 chapters, 1 book & numerous IND submissions and is Co-Inventor of 15 patents. He is also the President of Horizons Pharma Consulting, LLC.

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Notes:

Alan B Moy, J Genet Syndr Gene Ther 2016, 7:5 (Suppl)
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Novel viral-free and oncogene-free induced pluripotent stem cell for orphan disease cell therapies

Alan B Moy[1, 2]
[1]The John Paul II Medical Research Institute, USA
[2]Cellular Engineering Technologies, USA

Pluripotent stem cells represent a potential regenerative medicine for several orphan diseases because the cells exhibit broad plasticity. Induced pluripotent stem cells (IPSC) have the potential to serve as an autologous as well as an allogeneic cell therapy. However, IPSC therapy has not yet been fully realized because the IPSC reprogramming methods have historically required viral gene delivery and oncogenes in order to create a final IPSC product. Non-integrating IPSC reprogramming approaches like self-replicating ribonucleic acid and Sendai virus have been developed to reduce the tumorgenicity risk. However, these reprogramming methods still pose significant costs and oncogenic risk because they utilized the oncogenes, c-Myc and Lin28. Episomal reprogramming is a safe reprogramming approach to produce clinical-grade IPSC therapies. However, the reprogramming efficiency of episomal vectors has been inefficient and has required c-Myc and Lin28 to compensate for the low efficiency. We have developed a combinatorial reprogramming approach of small molecules and a novel episomal construct that is free of c-Myc and Lin28. The combinatorial approach significantly increased the reprogramming efficiency. Further, the reprogramming method also utilized a well-defined tissue cultured media that is feeder-free, xeno-free and matrigel-free. This combinatorial reprogramming approach is now poised to transition into GMP operations, which would satisfy regulatory requirements. The opportunity now exists to develop clinical-grade and safe IPSC for a variety of orphan diseases.

Biography

Alan B Moy has established a successful career in academia, non-profits and industry. He has received his MD from Creighton University, completed his Internal Medicine Residency at St. Louis University and Pulmonary Fellowship at the University of Iowa. He has served on Faculty at the University of Iowa College of Medicine and College of Engineering with a research expertise in cellular and tissue engineering. He is the Founder and Scientific Director of the John Paul II Medical Research Institute, a 501 (C)(3) and is the CEO and Co-Founder of Cellular Engineering Technologies, a leading stem cell manufacturing company. He is listed in the Leading Physicians of the World by the International Association of Healthcare Professionals. His area of expertise includes pulmonary medicine, cytoskeletal biology, vascular biology, tissue engineering and industrial stem cell manufacturing.

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Irmak Duygu Koyuncu, J Genet Syndr Gene Ther 2016, 7:5 (Suppl)
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Orphan drugs: Getting arms around rare diseases

Irmak Duygu Koyuncu
INC Research, Turkey

Finding ways to bring drugs for rare diseases to patients is an important public health challenge. The complexity of the rare diseases, incomplete understanding of disease pathophysiology, limited population and heterogeneity of the patients suffering from rare conditions, difficulties in diagnosis, 'rare physicians' availability, high-cost of the R&D of orphan drugs, regulatory risks in the road of clinical trials conduct, marketing authorization and reimbursement are all factors having an impact on this challenge. Undoubtedly, the most challenging part of this is the clinical trials conduct on the orphan drug molecules. The limited number of patients together with the diversity of the rare conditions makes the protocol design a sensitive topic to consider; access to the rare patients, getting interest and the engagement of the physicians are also amongst the challenges in this process. There are a number of stakeholders playing key roles in the Orphan drug R&D including regulatory authorities, policymakers, patient advocacy groups, scientists and clinical investigators, research institutes, academic or non-academic associations. In the speech, we will focus on the ways to overcome all difficulties, discussing how to find the most cost-effective and having the least or no regulatory risks during the clinical trials conduct and evaluate the value of local and global expertise and the cooperation of the stakeholders.

Biography

Irmak Duygu Kuyuncu has joined the clinical research industry in 2003 and worked as CRA. She has worked as a Clinical Operations Manager for more than 5 years in CROs and Pharma having responsibilities in clinical resources management, ensuring successful and compliant clinical operations, management of the process improvement in Turkey and in Middle East Countries. She was an Advisory Board Member and Consultant of the Scientific and Technological Research Council of Turkey in 2013. She has been a Board Member of the Clinical Research Association in Turkey and one of the Board Members in the Neuromuscular Diseases Research Association in Turkey. She has been involved in publication projects with close co-authoring with key opinion leaders from regulatory, academy and industry. She is currently leading the INC Research Turkey as Clinical Operations Associate Director.

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Notes:

Karen S Ho, J Genet Syndr Gene Ther 2016, 7:5 (Suppl)
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The role of clinical genomic testing in treatment discovery for rare neurodevelopmental diseases

Karen S Ho
Lineagen Inc., USA

Genomic testing by high resolution chromosomal microarray (CMA) is the guideline-recommended first tier test for neurodevelopmental disorders. Widely used in the clinical setting, accurate and informative interpretation of CMA results can enhance not only the diagnostic understanding of, but also the medical management of, these often rare genetic conditions. We will present the results of our efforts to bring the power of ultra-high resolution microarray analysis, combined with newly developed tools and relational databases, to bear on the complex challenges of interpretation of genomic data. Using our custom microarray optimized for the detection of known critical genomic changes associated with neurodevelopmental disorders, we have performed over 10,000 consecutive CMAs on a US-based, neurodevelopmentally-affected pediatric population. We detected relevant copy number variants (CNV) in approximately 30% of this population, a rate which depends on patient age and indication for testing. A significant proportion (~20%) of these finding were classified as variants of unknown significance (VOUS). We have developed novel technologies and approaches in partnership with patient support groups and members of the medical and academic research communities to bring additional interpretative power to bear on these VOUS. As an example of the clinical utility of ultra-high resolution CMA to map critical genes, we recently reported the identification of a seizure susceptibility candidate region/gene for Wolf-Hirschhorn Syndrome (WHS). Subsequent work using novel analysis techniques has led to identification of additional genes potentially related to congenital heart defects and other conditions associated with WHS. Using these strategies, we have correlated fine-resolution genetic mapping with other rare conditions and predicted potential molecular mechanisms connecting various rare diseases to one another. This in turn impacts the potential for common pharmacotherapeutic development strategies for previously unrelated orphan disorders.

Biography

Karen S Ho is a Principal Scientist of Translational Research Initiatives at Lineagen, Inc., where she is working since five years. She holds MSc degree in Genetics from Cambridge University where she was a Marshall Scholar after graduating summa cum laude from Washington University with a BSc in Biochemistry. She holds a PhD in Developmental Biology from Stanford University and completed her Postdoctoral training as a Howard Hughes Medical Institute Fellow and National Sleep Foundation Fellow in the Department of Neuroscience at the University of Pennsylvania. She is also an Assistant Adjunct Professor in the School of Medicine, Department of Pediatrics at the University of Utah and serves on the Board of two non-profit foundations, NGLY1.org and Rare and Undiagnosed Network, both of which are dedicated to rare disease.

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Notes:

Gail Adinamis, J Genet Syndr Gene Ther 2016, 7:5 (Suppl)
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Rare disease studies facilitated by taking study visits to the patients

Gail Adinamis
GlobalCare Clinical Trials LLC, USA

Patient recruitment and retention are key factors in establishing the objectives and ultimate success of clinical trials. These can be particularly challenging in rare disease studies where patients reside distant to investigator sites and may suffer from debilitating diseases making travel difficult. Patient advocacy groups have been playing a more influential role in drug development and commercialization especially in rare diseases. Advocacy groups represent the voice of the patient contributing to better clinical trial design by helping to remove barriers that made participation difficult or impossible. But many challenges remain. A patient-centric service model has evolved over the past years allowing study visits to be conducted at the patient's home where it is more convenient and comfortable than at the investigator site. By conducting selected protocol visits at home, workplace or other alternate location, ambulant healthcare providers offer a way for patients to participate in trials regardless of study duration, frequency of visits, disease state, distance to site and family, school, work or community obligations. By making trials more convenience and comfortable for patients, more patients are willing and able to participate and remain in the study. This innovative service model is available on a global basis and has been shown to triple enrollment rates and reduce patient dropout rates to 3 percent. Services include study drug administration, blood draws, clinical assessments, patient training and education and study compliance checks in all age groups, a variety of therapeutic areas and in all phases of development. This ambulant care service model provides a win-win benefit for all stake holders by providing patient's a convenient and comfortable way to participate in studies, offering investigators the ability to recruit patients from broader geographic areas, reducing development times for sponsors developing new therapeutics and ultimately getting life enhancing products to consumers sooner.

Biography

Gail Adinamis is the Founder and CEO of GlobalCare Clinical Trials LLC, USA and has over 35 years of comprehensive global clinical trials experience including over 12 years of global trials management at Abbott Laboratories and Astellas. She has founded the in-home business model for study visits in 1992 and established and headed clinical trials divisions for three national home infusion companies and was the Founder, President and CEO of the first independent ambulant care service company for clinical trials. She is a Member of the Women Presidents' Organization, National Association of Professional Women and DIA and has been an invited speaker at several industry conferences and recipient of numerous awards/recognitions including twice being among INC 5000's fastest growing private companies and Game Changer and CEO of the Year.

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Notes:

Alan B Moy, J Genet Syndr Gene Ther 2016, 7:5 (Suppl)
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A robust reprogramming approach to create viral-free and oncogene-free, orphan-disease specific induced pluripotent stem cells from peripheral blood mononuclear cells

Alan B Moy[1, 2]
[1]The John Paul II Medical Research Institute, USA
[2]Cellular Engineering Technologies, USA

Innovations are needed to reduce the time, cost and failure rate of drug discovery. 58% of new molecular entities approved by the FDA in the past ten years have utilized phenotypic screening; a drug screening process that uses patient-specific cultured cells that reflect the patient's diseased characteristics. Induced pluripotent stem cells (IPSC) are excellent patient-specific stem cells for phenotypic drug screening platforms for orphan disease. Disease-specific IPSC has the advantage over prior conventional approaches to better predict drug efficacy and safety and for patient stratification in clinical trials. Yet, one major hurdle in creating disease-specific IPSC for infants and children has been developing reliable methods to reprogram target cells derived from peripheral blood, which is the ideal minimally invasive approach to transform target cells. However, efficient reprogramming of peripheral blood mononuclear cells has not been achieved without viral and the oncogenes, c-Myc and Lin28. These oncogenic transcriptional factors and viral elements may alter the native phenotype of a patient's cell and skew drug screening outcomes. We have solved this problem by developing a combinatorial approach of small molecules and a novel episomal construct to reprogram adherent cells and peripheral blood mononuclear cells. While the combinatorial approach is efficient for reprogramming adherent cells, the approach requires an additional intermediate conversion of peripheral mononuclear cells (PMNC) into CD34+ hematopoietic stem cells. PMNC were exposed to a defined tissue cultured media that converted PMNC into a sufficient number of hematopoietic stem cells. Upon conversion to hematopoietic stem cells, IPSC reprogramming became feasible. Without an intermediate hematopoietic stem cell conversion, we observed no IPSC colony formation. The opportunity now exists to develop a repository of IPSC for infants and children suffering from orphan diseases from a simple venipuncture, which should accelerate hit to lead identification, drug optimization and drug formulation.

Biography

Alan B Moy has established a successful career in academia, non-profits and industry. He has received his MD from Creighton University, completed his Internal Medicine Residency at St. Louis University and Pulmonary Fellowship at the University of Iowa. He has served on Faculty at the University of Iowa College of Medicine and College of Engineering with a research expertise in cellular and tissue engineering. He is the Founder and Scientific Director of the John Paul II Medical Research Institute, a 501 (C)(3) and is the CEO and Co-Founder of Cellular Engineering Technologies, a leading stem cell manufacturing company. He is listed in the Leading Physicians of the World by the International Association of Healthcare Professionals. His area of expertise includes pulmonary medicine, cytoskeletal biology, vascular biology, tissue engineering and industrial stem cell manufacturing.

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Moji C Adeyeye, J Genet Syndr Gene Ther 2016, 7:5 (Suppl)
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Challenges and opportunities in development of orphan drugs

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Development of orphan drugs for rare diseases is fraught with opportunities and challenges globally, in legislative policies, research and development, clinical trials, time to reach the market and disparity in affordability and accessibility. The opportunities include incentivizing of researchers and manufacturers in fee reduction or no fees for protocol assistance, preauthorization inspections, marketing authorization, grant funding, priority review voucher for rare pediatric disease and granting of market exclusivity. These were stimulated by the US 1983 Orphan Drug Act and heightened awareness of the public health impact and ramifications in many countries. The number of orphan drug designations has increased in recent years and so is the number of marketing approvals. However, there challenges that could limit the development include understanding the disease and sometimes the co-morbidities, establishing the clinical relevance and cost effectiveness, difficulties in setting up clinical trials for the small populations and high cost of bringing a new product to market especially an orphan drug with limited target population and market opportunities. The purpose of the presentation is to underscore the opportunities, successes in orphan drug development and challenges using relevant case studies. Review of orphan drugs categories and designations for rare diseases in several countries, opportunities that include legislative and regulatory incentives, challenges in development and recent successes were done. Using USA as a reference country, examples of opportunities and challenges in the development of pediatric orphan drugs for rare diseases such as pediatric HIV/AIDS and sickle cell disease were given. Perspectives on academic-industry-government collaboration relating to the opportunities and challenges were also presented. The significance in the successes in orphan drug approvals, ongoing and increasing awareness of impact of development of orphan drugs on the life of the patients and the low market opportunities and difficulty in bringing the products to market were emphasized.

Biography

Moji C Adeyeye is the Founding Chair of Biopharmaceutical Sciences Department and Professor of Pharmaceutics and Drug Product Evaluation at the College of Pharmacy, Roosevelt University (RU) in Schaumburg, Illinois. Her research interest include pre-formulation, pediatric and adult drug product (solids, liquids and semisolids) development and evaluation investigational new drug application-driven bench-to-bedside translational research, preclinical and clinical trials, analytical/bioanalytical assay development, bioavailability and bioequivalence quantitation, fixed dose combination dosage forms for various drug classes including antiretrovirals, anti-malarials and anti-sickling agents. She is a Senior William J. Fulbright Scholar and Specialist, 2016 Nigeria National Academy of Science Fellow and 2008 American Association of Pharmaceutical Scientists (AAPS) Fellow. She has earned her BS and MS/PhD from the University of Nigeria, Nsukka, Nigeria and University of Georgia, Athens, GA, respectively. She has 5 patents, 57 peer-reviewed manuscripts, book chapters and books, more than 150 scientific presentations and has successfully mentored many MS and PhD candidates.

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Jacques P Tremblay, J Genet Syndr Gene Ther 2016, 7:5 (Suppl)
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Annual Congress on
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October 26-27, 2016 Chicago, USA

Potential treatments for rare diseases: Cell therapy, gene therapy and genome editing

Jacques P Tremblay
Laval University, Canada

All hereditary diseases are due to modification in the patient genome insertion, deletion or modification of one or several nucleotides among the 6 billion nucleotides of the human genome. Several potential therapeutic approaches to treat these hereditary diseases have been developed over the years. For some recessive diseases the transplantation of allogenic cells obtained from a healthy donor can permit to deliver the normal gene to compensate for the mutated gene. This approach is under clinical trial for Duchenne Muscular Dystrophy. A compensatory normal gene to treat a recessive hereditary disease may also be introduced in the patient own cells in culture or directly *in vivo* by using viral vectors. The Adeno Associated Viruses (AAV), are currently the vectors of choice for such a therapeutic approaches. Various specific nucleases (meganucleases, Zinc Finger Nucleases, TALENs and the CRISPR/Cas9 system) have been investigated during the lasts 10 years and now permit to precisely correct a gene responsible for a hereditary disease. This type of approaches is the only one that can be used for dominant diseases. This approach may also be used to correct large genes, which are too big to be delivered by AAV. My team and several others have already used this approach to correct the dystrophin gene, as a treatment for Duchenne Muscular Dystrophy. Indeed by using these specific nucleases, it is possible to induce double strands breaks in the dystrophin gene to restore the normal reading frame by micro-insertions, micro-deletions or by deleting complete exons or parts of exons. My team is also attempting to restore a completely normal dystrophin protein by inserting the exons, which are missing in the patient genome. My team has also been able to remove with the CRISPR/Cas9 system the long trinucleotide repeat in intron 1 of the frataxin gene responsible for Friedreich ataxia and thus increase the expression of frataxin in patient cells. The TALE proteins and a defective Cas9 nuclease (dCas9) may also be fused with a transcription activation domain, such as VP64, to target a gene promoter to increase specifically the expression of that gene. My team has successfully used that approach in cells of Friedreich patients. The CRISPR/Cas9 technology may also be used to correct a gene by a process called homology directed repair. This technique permits to modify one or several nucleotides in the whole human genome. Thus the progress in cell therapy, gene therapy and genome editing permits to dream of developing therapies for all hereditary diseases over the coming years. The main limiting factor is the financial support for this type of research.

Biography

Jacques P Tremblay has completed his PhD in Neurosciences in 1974 at University of California at San Diego. He has published 261 articles in peer-reviewed journals and has been serving as Deputy Editor of Molecular Therapy and Cell Transplantation. His laboratory is currently working on cell and gene therapies for Duchenne muscular dystrophy, Friedreich ataxia and Alzheimer disease.

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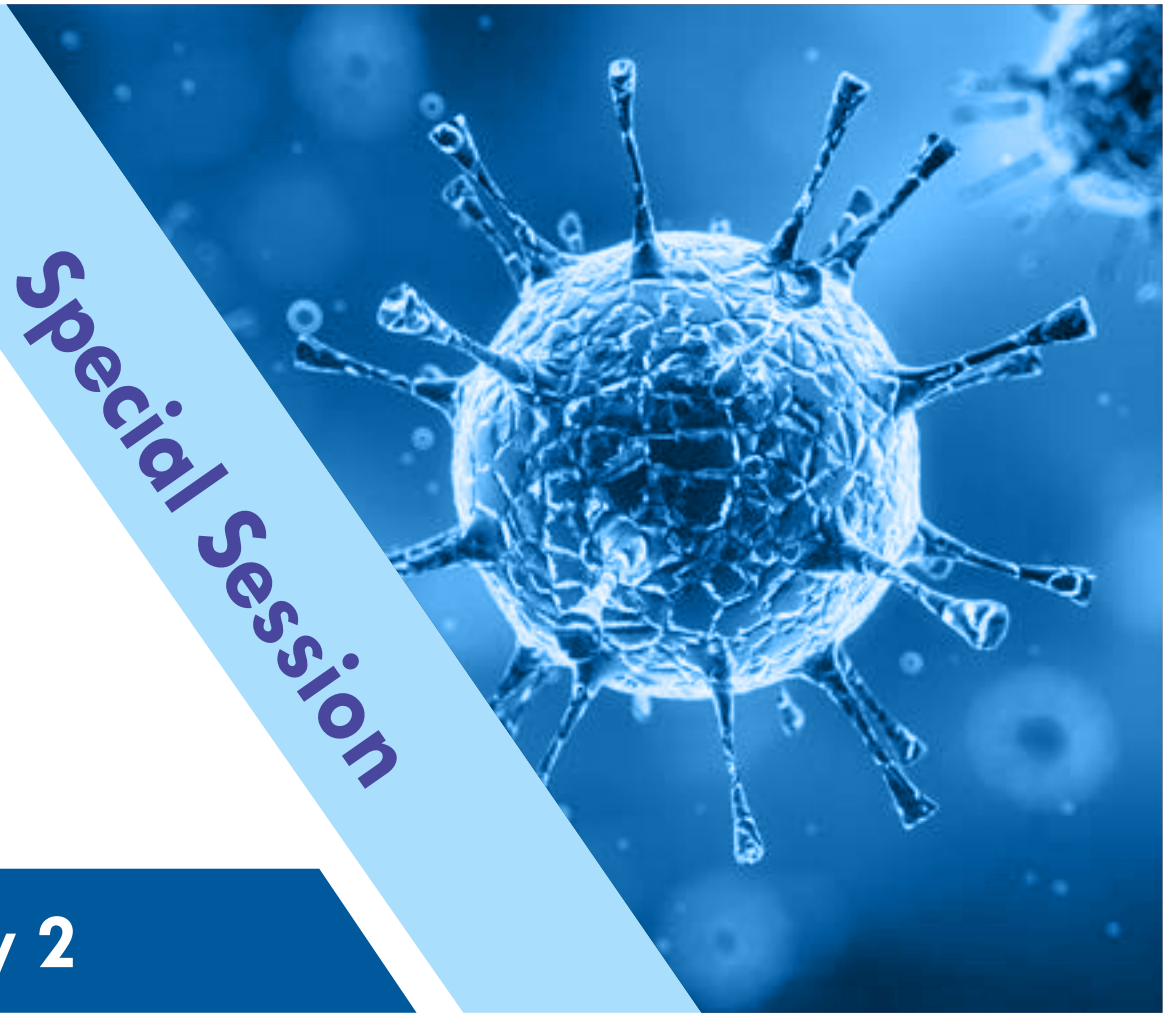
Annual Congress on

RARE DISEASES & ORPHAN DRUGS

October 26-27, 2016 Chicago, USA



Special Session

Day 2




Rare Diseases 2016

Stephen Shrewsbury, J Genet Syndr Gene Ther 2016, 7:5 (Suppl)
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Cellular therapies for rare diseases

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Clinical programs directed at rare diseases present many unique challenges for clinical research. Most druggable targets have been identified and exploited and the sciences of drug (be they small molecules including oligonucleotides or biologics) or device development has dramatically advanced in recent decades. With that advance, the opportunity to develop products for large populations of common diseases has largely disappeared. At the same time the phenotypes for many common diseases have been split into multiple smaller populations and even genotypes focusing more and more programs on smaller populations. Planning to complete increasingly complex studies in smaller but more homogeneous patient groups has become increasingly competitive and costly. Against this clinical research landscape, cellular therapies as the third major branch of clinical research have arrived. Initially working with fetal, embryonic, bone marrow, adipose or cord blood derived stem cells, the field has been less regulated than drugs and devices, leading to a proliferation of clinics and claims that have not all been through a rigorous and appropriate review. Attention is now evolving from the ethically and immunologically challenging programs involving allogeneic stem cells to autologous, organ specific stem cells. This can be best achieved by generating directly reprogrammed precursor cells for that organ. These promise greater safety and easier production, for a very complex product and will allow this third branch of medical research to start to tackle many rare diseases where cellular regeneration may be required for clinical benefit. To capitalize on this timely opportunity, time and cost efficient direct reprogramming to lineage-specific precursor cells is vital. With this advance, cellular therapies will take their rightful place in the physicians'armamentarium against injury, disease and degeneration, just as healthcare costs in advanced countries look set to spiral completely out of control.

Biography

Stephen Shrewsbury is currently an Executive Vice President of Development and Chief Medical Officer at Fortuna Fix, leading their novel cellular technology into multiple clinical programs focused on regenerative medicine, several of which are rare diseases. He moved to lead inhaled antibiotic programs at Chiron Corporation (in Cystic Fibrosis and other rare diseases) before becoming CMO sequentially to MAP Pharmaceuticals, Adamas Pharmaceuticals, AVI BioPharma (now Sarepta Therapeutics; where he opened their first IND for Eteplirsen in Duchenne muscular dystrophy and planned their oligomer programs against Ebola and Marburg Hemorrhagic Fevers) and Aquinox Pharmaceuticals. He is the author of Defy Your DNA and over 70 scientific papers, holds several patents and contributed to many awarded grants, mostly for work on rare diseases.

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Notes:

Anne Marie Finley, J Genet Syndr Gene Ther 2016, 7:5 (Suppl)
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Pricing, public health, & politics: Policy considerations for orphan products

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Drug prices in the United States are higher than anywhere else in the world. Orphan products have long been perceived as pricier than many other drugs by payers, manufacturers and consumers. The Affordable Care Act's expansion of insurance coverage and pharmaceutical benefits, along with a growing resistance to higher priced therapies, have added to the pharmaceutical pricing stress on the healthcare system and ultimately rare disease patients. Innovative responses to the current pharmaceutical pricing crisis have been developed by some drug companies, patient organizations, payers, regulators and legislators. The new Congress and new Administration have a number of options and opportunities by which to address pricing concerns in 2017.

Biography

Anne Marie Finley is the FDA Regulatory and Health Care Policy Strategist. She is the President of Biotech Policy Group, a consulting firm she founded in 2001 that focuses on development of products for rare diseases and unmet medical needs. She has more than 25 years' experience in senior management positions at the Food and Drug Administration, US Department of Health and Human Services, the US Congress. She was named a top 50 Thought Leader in Orphan Drugs and Rare Diseases in 2014.

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