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BOOK OF ABSTRACTS

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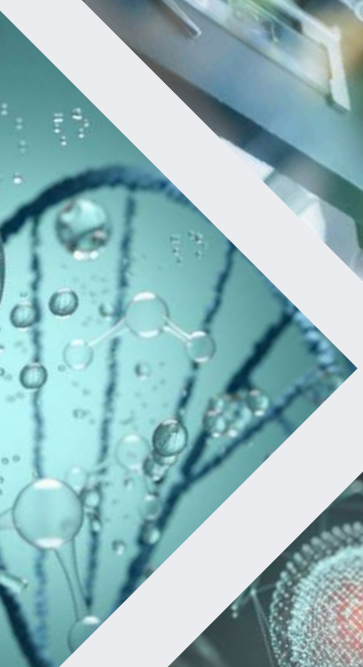

ABSTRACT 1 - Clinical investigation of Agilik, a new Class I exoskeleton for children

Topic: Paediatric Medical Devices

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Abstract: Cerebral palsy (CP) is one of the most prevalent disorders that affect children. Crouch gait is a common walking pattern in CP that increases energy costs of walking and contributes to ambulatory decline. In recent years, there is increasing research into exoskeletons to improve gait function in children with CP. Agilik is a motorized exoskeleton that consists of 2 customized Knee-Ankle-Foot Orthosis (KAFOs), one for each leg, with 2 electro-mechanical actuators at the knee level that allow to assist or resist motion independently in each gait phase (Class I medical device according to MDR since September 2022). Force sensitive resistors are integrated in the foot-bed of the KAFOs and connected to the actuators. The foot sensor and the knee angular velocity are used to detect the gait phase of the patient and communicate with the motor controller to provide a unique torque for each gait phase. Differently from the market common strategy, Agilik is one of the few available non-stationary exoskeletons developed for children. The goal of this investigation is to assess the assistive and rehabilitative efficacy of Agilik on patients with CP through a pre-post single group study. The first visit was for T0 assessments. After the exoskeleton preparation, the intervention consisted of 10 training sessions with Agilik during which patients practiced walking with the device and parameters were adjusted according to patient's gait. Finally, patients underwent T1 assessments. T0 and T1 assessments were: joint range of motion and muscle lengths, spasticity level using the Modified Ashworth scale, distance walked and walking speed during 6-minute (6MWT) and 10-meter (10mWT) walking tests, quantification of the static balance detecting the Centre of Pressure and Centre of Mass and 3D gait analysis on the GRAIL system. At T0, the assessments were performed only without the orthosis, while at T1 6MWT, 10mWT and gait analysis were collected both with and without Agilik to evaluate the assistive and rehabilitative effect. Finally, during the T1 assessments, children's satisfaction using Agilik was evaluated with a modified version of the QUEST 2.1. To date we enrolled five subjects (2M, 3F; age range [8-17 yo]). At this time, only Agi01 (M, 10 years, GMFCS II) and Agi02 (F, 8 years, GMFCS II) have completed the trial with the whole dataset. Both patients have shown motor improvements: Agi01 exhibited significant enhancements in kinematics, whereas Agi02 experienced improvements in velocity and endurance. Regarding the assistive capabilities, Agilik effectively facilitated the patients in achieving a more physiological gait pattern, even if both patients required walkers or assistance in nearly every session. Equilibrium tests showed an improvement in balance for both patients. Results also demonstrated an improvement in the spasticity levels, joint ranges and muscle lengths. At this stage, preliminary results regarding user satisfaction with Agilik indicate that the service provided during training received more positive evaluations compared to the device itself. Despite the promising results, there is potential for further enhancement. The duration of the training could be extended: 10 sessions may be enough to assess the assistive efficacy, but not the rehabilitative potential. Moreover, prolonging and intensifying the training period, patients could feel more comfortable and confident while walking with Agilik. Additionally, extending the investigation to younger children could offer a more comprehensive understanding of how early intervention with robot assisted gait training may influence motor development and functional outcomes in children with CP. In conclusion, initial findings have shown promising results of Agilik in addressing crouch gait in children with CP, with strengths such as customization, lightweight design, and versatility for clinical and home use.

ABSTRACT 2 - Legal and ethical issues of using AI in Pediatric Biobank in countries with an average income level

Topic: Paediatric Biomarkers and Biosamples

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Abstract: Middle-income countries stand at a unique juncture, striving to harness the potential of AI while con-fronting diverse socio-economic, cultural, and regulatory landscapes. In these nations, biobanking initiatives often intersect with issues of equity, sovereignty, and data governance, necessitating a nuanced approach to AI integration. This topic aims to elucidate the maltifaceted legal and ethical dimensions inherent in the fusion of AI and paediatric biobanking within Middle-income countries contexts. We managed a multidisciplinary retrospective investigation of the biobanking market to clarify paediatric Biobanks attitude to AI. To specify the data a survey was designed and sent to biobank managers and IT biobank specialists worldwide on the basis of online pools through cpy e-mail distributions.

Results: Privacy concerns, particularly in AI analyzing sensitive genetic and health data, necessitate the establishment of robust safeguards to protect donors' confidentiality. Intellectual property rights become a legal intricacy as AI-generated findings raise questions about ownership. Legal challenges may arise in cross-border collaborations, necessitating a global perspective to address ethical concerns on an international scale.

Conclusion. As a result of the project, we have identified comprehensive aspects of the legal and ethical related to integrating AI into biobanking in middle-income countries. By addressing these challenges, it seeks to contribute to the development of robust frameworks that balance scientific progress with ethical imperatives, fostering responsible AI use in the advancement of medical research.

ABSTRACT 3 - Usability and efficacy of an assistive awakening device for the Congenital Central Hypoventilation Syndrome

Topic: Paediatric Medical Devices

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Abstract: Congenital Central Hypoventilation Syndrome (CCHS) is a rare genetic disease characterised by impaired breathing control associated with Autonomic Nervous System dysfunction. Immediately after birth, patients with CCHS are unable to respond adequately to hypoxemia or hypercapnia during sleep. Since there is no definitive therapy, CCHS patients require assisted ventilation (AV) while asleep. In these cases, oxy-haemoglobin blood concentration (SpO2) is monitored and an alarm integrated in the ventilators and pulse-oximeters is triggered during desaturation (standard setting), posing risks of habituation (in patients and caregivers) and need of supervision. To overcome these issues, we developed and tested an assistive awakening device, which is coupled with a pulse-oximeter and which carries out various multisensory stimulation strategies, depending on the SpO2 blood concentration level and the duration of the desaturation. The device has an Android tablet that acquires the SpO2 values from the pulse-oximeter and activates different actuators such as: a piezoelectric buzzer (acoustic stimuli), a small air fan (tactile stimulation), a vibrating pillow (tactile/proprioceptive stimulation) and a fire alarm (strong acoustic stimulation). The aim of the clinical experimentation is to test if the device is efficient in the awakening of patients without interfering with sleep quality.

The device has been validated on 15 patients (age 5-39 years) during 3 nights of testing. During the first night, polysomnographic (PSG) data were acquired while the participant used its standard setting; this night was used to perform a baseline evaluation of patient sleep. During the second and the third nights, the device was connected to the patient's pulse-oximeter; during one night the subject wears PSG sensors and a clinician induces at least one desaturation, while during the other one only spontaneous desaturations are monitored. To evaluate the whole system functionality, the percentage of awakenings with the device was computed for each actuator. Differences between percentage of awakenings in the two nights with the device with respect to the reference night was evaluated using nonparametric Wilcoxon signed-rank tests; $p < 0.05$ was considered significant. Moreover, PSG data were analysed in order to compute sleep efficiency (sleep/wake ratio scored using EEG data). Data were divided into young adults and children sub-groups and medians (interquartile ranges, IQR) were computed.

The percentage of awakenings in young adults (N=11, age=22 ±7) was 100 (57)% for the fire alarm, while the vibration and the air fan showed a comparable efficacy (37 (60)%). Worst results were obtained due to buzzer (24 (67)%). Therefore, the device is always efficient in case of dangerous situations, since the fire alarm was the alarm set in the situations with higher risk for the health of the patient. Percentage of awakenings on nights with the device was much higher than on the night with the standard setting, 25 (20)% and 6 (8)% of awakening respectively (p=0.018). Moreover, sleep efficiency in young adults was comparable in both nights with PSG (88.2 (9))% and thus not affected by the presence of the device. On the other hand, the device seems to have reduced effect on children (N=4, age=8±4) with 11 (7)% of awakenings with the device and 3(5)% in standard setting. The vibration was the most effective device (18(16)% of awakenings). In conclusion, our device is efficient on adolescents/youth affected by CCHS while it is less effective on children. However, it could be useful to wake up caregivers in response to child desaturation. The results suggested that the assistive device proposed is effective in improving domiciliary care and quality of life.

ABSTRACT 4 - Multi-omics data integration and machine learning (ML) explaining the molecular basis of the complex microbiota-gut-brain axis and predicting possible biomarkers of autism

Topic: Paediatric Biomarkers and Biosamples

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Abstract: Introduction: Complex traits, such as Autism Spectrum Disorders (ASD), are influenced by the interplay of multiple factors. The impairment of the Gut-Brain Axis (GBA) plays a key role in ASD and the challenging study of such complex process in the context of a complex trait necessitates a multi-omics approach performed on different tissues from numerous subjects and utilizing various analytical platforms. Here, a bioinformatics approach identifies statistically relevant, biologically meaningful, and reproducible molecular "players" involved in the GBA, reusing genetics, brain transcriptomics, gut microbiome and interactomics data. Methods The R package mND was used to perform Multi-layer network diffusion1. Input ASD data were sourced from the literature: 862 ASD related genes from SFARIgenedb, 2,925 genes expressend in the brain, and 2,472 microbial genes distinguishing ASD from neurotypical individuals2. A molecular interaction network was constructed by integrating a protein-protein interaction network from STRING3 with published host-gut microbiome gene-gene interactions4. Pathway and orthology data were obtained from KEGG5 while the dmfind tool6 to extract gene networks enriched in modules of "affected genes". ML models were developed using support vector machines, random forests, generalized linear models, and neural network algorithms via the Caret R package7 on brain transcriptomics and shotgun metagenomic datasets2. Gene count matrices were downloaded, filtered, and normalized using the edgeR package8. ML models were constructed for each omic dataset separately, both using individual cohorts and all cohorts combined. Data were split into training and test sets with a 7:3 ratio. Optimal model tuning was achieved through cross-validation, and training and testing performances were assessed using accuracy.

Results: We assembled a gene-centered interactome involving gene-gene host interactions and host-gut microbiota gene-gene interactions, resulting in a network of approximately 19,000 genes and 184,000 interactions. We mapped gene-level scores from each omic information source (referred to as "layers") reflecting the association of each gene with ASD (termed "affected genes") onto this scaffold. Using multi-layer network diffusion, we extracted gene networks connecting the affected genes. These networks (~500 genes each) include genes whose association with ASD arises from genetic susceptibility, ASD brain transcriptomics and significant presence in the gut microbiome of ASD subjects. The networks display a modular structure, indicating the involvement of different molecular mechanisms associated with ASD. Notably, pathways including microbial genes regulate the metabolism of amino acids involved in neurotransmission. We then evaluated the ability of the genes identified by network analysis to distinguish between ASD and control individuals in brain transcriptomics and gut metagenomics using ML models. We explored various feature selection and extraction methods, including recursive feature elimination and principal component analysis. We achieved accuracy values ranging from 0.6 to 0.9, with random forests and support vector machines performing slightly better than other algorithms. These variations highlight the inherent challenges in analyzing such datasets, characterized by heterogeneity (e.g., sample size, batch effects, technological platforms). In conclusion, network identified genes potentially mediating cross-talk between multiple biological contexts along the GBA. Furthermore, these genes represent promising biomarkers of ASD and ASD microbiota.

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ABSTRACT 5 - Exploring the impact of developmental clearance saturation on propylene glycol exposure in adults and neonates using physiologically based pharmacokinetic modelling

Topic: Paediatric Medicines Formulations

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Abstract: Propylene glycol (PG) is a pharmaceutical excipient which is considered mostly safe though clinical toxicity has been reported. Much of its toxicity has been attributed to its accumulation due to the potential for its alcohol dehydrogenase (ADH)-mediated clearance pathway to be saturated at high doses in adults and neonates. This study aims to explore the impact of the ADH-mediated saturability of PG metabolism on its developmental clearance in adults and neonates and assess the impact of a range of doses on clearance saturation and toxicity. Physiologically based pharmacokinetic (PBPK) models for PG in adults and neonates were developed using maximum velocity (Vmax) and Michaelis Menten's constant (Km) of ADH-mediated metabolism determined in vitro in human liver cytosol, published physicochemical, drug-related and ADH enzyme ontogeny parameters. The models were validated and used to determine the impact of dosing regimen on PG clearance saturation and toxicity in adults and neonates. The Vmax and Km of PG in human liver cytosol were determined to be 25.9 nmol/min/mg protein and 74.8 mM respectively. The PG PBPK model adequately described PG PK profiles in adults and neonates. The PG dosing regimens associated with saturation and toxicity were dependent on both dose and dosing frequency and the doses resulting in saturation were higher than those associated with clinically observed toxicity. This suggests that in formulations without excipients that may interact with PG clearance, adults and neonates without impaired clearance mechanisms may tolerate higher PG doses than the EMA and FDA daily recommendations for adults and children.

ABSTRACT 6 - PhiCube: bilateral upper limb device for neuromotor recovery

Topic: Paediatric Medical Devices

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Abstract: PhiCube is a modular robotic device designed to exploit gamification to promote bilateral neuromotor rehabilitation of the upper limbs in individuals with neuromotor disorders. Rehabilitation is crucial for patients with disabilities that impair normal motor function. Rehabilitation therapy typically involves high repetition, prolonged duration, and intensity, posing challenges for healthcare professionals. Consequently, upper limb rehabilitation robots have rapidly developed due to their precision, repeatability, and flexibility. These robots offer constant monitoring and active assistance of motor abilities through integrated sensors. Over the past two decades, there has been a significant increase in the development of rehabilitation systems, particularly robotic systems for upper limb rehabilitation. Despite this progress, many devices are unilateral, mobilizing only one limb. Bilateral training, however, is more effective than unilateral training for activating the primary motor cortex and promoting interhemispheric communication. Bilateral training, especially in neurological conditions where the motor disorder is predominantly on one side of the body, can improve the function of the more affected upper limb by engaging both the paretic and the healthy controlateral limb simultaneously. Moreover, play provides a valuable context for learning and adaptation, a fundamental principle in pediatric rehabilitation: incorporating gamification elements supports the developmental needs of children undergoing rehabilitation. Play facilitates learning, adaptability, and overall well-being in children during rehabilitation. The core of PhiCube features a central robotic body with two motorized rotating axes and a mechanical interface for quick connection of specially designed handles. This design enables various joint movements for the shoulder, elbow, and wrist of both arms simultaneously within a compact device. Thanks to these features, PhiCube overcomes some of the known limitations of the state of the art. Some of the available solutions lack in versatility since bilateral rehabilitation is not provided. PhiCube allows users to work both their limbs independently or in coordination, providing high levels of flexibility. Assistance can be provided with respect to the task to be completed or bilaterally, where the support action of each limb depends on the action of the contralateral limb. Therapists can adjust device parameters via an intuitive graphical interface for planning and modifying therapy sessions. Usage data is saved, analyzed for performance metrics, and accessible through a dedicated dashboard. PhiCube's compactness, portability, and ease-of-use make it ideal for home rehabilitation therapy, promoting continuity of care. Its highly flexible and modular design supports a wide range of movements, combining effective rehabilitation strategies with high levels of personalization to the user's motor and cognitive capabilities. PhiCube's portability sets it apart from other solutions which, despite providing antigravity support, are complex, expensive, and cumbersome. Thanks to the consolidation of PhiCube design and functionalities, the device is now undergoing clinical validation whithin the PNRR-Fit4MedRob project, which aims to revolutionize the current rehabilitation and assistance models. In particular, a multicentic study has been designed involving five IRCCS on the Italian territory: Fondazione Stella Maris, Eugenio Medea, Fondazione Don Carlo Gnocchi, Fondazione Mondino and Istituto Giannina Gaslini. The clinical trials will involve pediatric users with upper limb mobility and motility deficiencies due to conditions such as congenital or acquired brain injury, developmental coordination disorder (DCD), stroke, Parkinson's disease, multiple sclerosis, and orthopedic diseases.

Funding: This work has been partially supported by the Italian Ministry for Universities and Research (MUR) under the grant FIT4MEDROB (MUR: PNC0000007)

ABSTRACT 7 – Evaluation of silver nanoclusters as nanotechnology-based solutions for generating a therapeutical approach against epidermolysis bullosa

Topic: Other

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Abstract: Epidermolysis bullosa (EB) is a group of genetic conditions characterized by blistering and fragility of the skin. EB can produce painful wounds and erosions in the skin, eyes, and mucosal tissues, can be mild or severe, and can heal with severe scarring or no scarring. There is currently no cure, various treatments are being studied, including gene therapy. Patient care consists in careful monitoring the appearance of blisters and their prevention through meticulous protection of the skin, also the adoption of appropriate lifestyles is required for preserving the affected tissues from being seriously compromised as for example, by secondary infections. This scenario becomes even more complicated with patients affected by types of EB associated with a high risk of extracutaneous complications. In this frame, nanotechnology may pave the way to innovative treatments by employing nanocarriers for gene delivery with antimicrobial properties. For this reason, we have designed and produced sub-nanometer-sized silver nanoclusters (AgNCs) able to inhibit microbial growth. Briefly, AgNCs synthesis was performed by using bovine serum albumin (BSA) as protein model that acts both as reducer for silver salts and nanostructuring/capping agent. A morphological characterization of AgNCs was performed through TEM microscopy, while their photophysical properties were deeply assessed trough different spectroscopic techniques. After that, AgNCs were tested on different yeasts and bacteria strains, including pathogens and saprophytic ones. Results confirmed the ability of AgNCs to inhibit growth of microorganisms, in particular of the opportunistic bacterial pathogen Staphylococcus aureus and of the ubiquitary yeast pathogen species Cryptococcus neoformans, Candida parapsilosis and C. albicans, often associated to and colonizing skin lesions and infections. Our results demonstrate that AgNPs produced by protein-mediated reduction can be properly employed as building block to generate nanotechnology-based solutions for EB consisting of nanocarriers for gene delivery able to control secondary infections in the epidermolysis bullosa.

Acknowledgment: This study was supported by “Tecnopolo per la medicina di precisione” (TecnoMed Puglia) - Regione Puglia; EU funding within the PNC Italian Health Ministry PNRR-MR1-2022-12376725, “Preclinical Development of Gene Therapy for Dystrophic Epidermolysis Bullosa”; PRIN PNRR 2022- P2022EPK9B "Nanodelivery of Slpi Prevents Inflammatory-associated UC Development in the Spontaneous Model Winnie", funded by European Union – Next Generation EU. A financial support was received from “PON Ricerca e Innovazione 2014–2020”, Asse IV “Istruzione e ricerca per il recupero” Azione IV.4 “Dottorati e contratti di ricerca a carattere industriale su tematiche dell’innovazione”, A.Y. 2022-23, XXXVII Cycle, for the PhD project grant of Annamaria Tarantini.

ABSTRACT 8 – Nanoparticles for Target Therapy in Pediatric Brain Cancers

Topic: Paediatric Medicines Formulations

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Abstract: CNS tumors represent the primary cause of cancer-related death in children. The gold standard for treating brain cancer in children is tumor excision followed by radiotherapy/chemotherapy (PMID 35054340, 21788981). The last two treatments are often associated to neurotoxicity with resulting disabilities. The challenge is to deliver diagnostic/ therapeutic agents to CNS overcoming the BBB (PMID 30018882). Nanoparticles (NPs) have been investigated since they show great promises as diagnostic tools such as contrast agents and vectors for gene/drug therapy for pediatric brain cancer. Thanks to the reduced dimensions they can increase biocompatibility, bioavailability, and stability of different compounds (PMID 38391759). New generation of NPs are made of a core structure that ensure the encapsulation of active payloads or diagnostic compounds and a functionalization which increase targeting abilities thanks to interaction with the proteins and molecules on the cancer cell surface (PMID 35491189). These enhanced targeting abilities will specifically target tissues or cells, thus minimizing systemic toxicity and maximizing drug concentration at the specific site, thereby improving treatment outcomes (PMID 34267523). In this frame, we designed a biomimetic nanosystem that uses a biocompatible, nanostructured polymeric core and a bio-coating constituted of glioblastoma cancer cell membrane. This approach aims to enhance the delivery of active payloads to tumors since the outer membrane of cancer cells carries specific proteins to evade the immune system allowing a longer circulation time in the bloodstream, and at the same time exhibiting enhanced targeting capabilities. The specific proteins and receptors on the cancer cell membrane can facilitate the active targeting of these NPs to cancer cells, due to the homotypic targeting thus improving their accumulation at the tumor site. First, a polymer with a defined length is produced in order to achieve small NPs below 100 nm to be employed as NPs core. In particular, polycaprolactone a biocompatible FDA-approved polymer was synthetised starting from Ɛ-caprolactone by employing an organo-mediated ring opening polymerization, and NPs core have been synthetized by solvent evaporation method. In the second part, we optimized a protocol for extracting glioblastoma cell membrane assessing the presence of cell membrane proteins and specific surface biomarkers through western blotting analysis. The correct coating of PCL NPs with cancer cell membranes was confirmed by DLS analyses thanks to changes in both size and surface charge, morphologically by TEM images for the presence of a layer surrounding NPs core and by FRET studies employing two different fluorophores to stain PCL core and glioblastoma cell membrane coating. Then, the uptake and biomimetic effect of these nanoparticles was investigated in 2D and 3D cell culture models of glioblastoma and medulloblastoma by CLSMand flow cytometry. In particular, it was shown that cell coated biomimetic NPs mimicked the source cells' surface features, thus gaining the capacity to target homotypically compared to other cells. Since children have a different maturation of immune system compared to adults, biomimetic-NPs could be used as a non-invasive approach in precise cancer immunotherapy to treat pediatric brain tumors for the possibility to employ patient-derived cell membranes.

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ABSTRACT 9 – Model informed precision dosing in paediatric intensive care units: a randomized clinical trial

Topic: Developmental Pharmacology

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Abstract: Background: Model-informed precision dosing (MIPD) also called Target Concentration Intervention (TCI) is a hybrid machine learning/pharmacokinetic approach to optimizing targeted dose using maximum a posteriori (MAP) Bayesian estimation and population-specific parameters such as pharmacokinetic/pharmacodynamic, age, sex, weight. Aim: This prospective study aimed to compare to MIPD-based dose adjustments versus standard dosing in terms of the duration of treatment, adverse events and mortality.

Method: This pilot study was conducted between January and June 2024 in a Pediatric Intensive Care Unit (PICU). The patients were randomly assigned to MIPD (intervention) and standard (control) dosing. This study used the MIPD tool named InsightRx® program to compare the difference between predicted and observed plasma levels, including patients treated with amikacin, vancomycin, or fluconazole and had at least one therapeutic drug monitoring (TDM) level evaluated. InsightRx uses population-based modeling to predict patients' TDM scores and categorizes them as “poor”, “intermediate” or “good” to assess the patient's fit to the model.

Results: Total of 66 patients were admitted to the PICU with relevant treatment, but only 27(40.9%) met inclusion criteria [55.6% males, median age 100 months (range:7-548 months)]. The majority of patients were receiving vancomycin (44.4%), while those receiving amikacin (18.5%) and combination therapy (37.2%) were noted separately. Modeling program predicted that 82.1% of 39 TDM levels would be classified as "good." Total of 7(17.9%) TDMs were subjected to a second assessment, with program correctly identifying 100% of these as within the acceptable level. Based on 39 TDM, only 12(30.8%) recommendations were accepted, with 27 TDM continuing with the existing dose. Of the 12 accepted recommendations, 9 were for dose increase and 3 were for dose reduction. Among the accepted dose recommendations, 7 of them showed the TDM level for the second time and 2 of them were modified and classified as "good"(the first TDM’s were poor and intermediate). There were no significant differences between groups in terms of duration of treatment adverse events and mortality.

Conclusion: To the best of our knowledge, this is the first randomized clinical trial to compare MIPD versus standard dosing in children. As the sample size and frequency of TDM increase, the feedforward and predictive power of the models will also increase. Therefore, there is a need to evaluate different populations in different countries, hospitals and PICUs in terms of covariates such as genetics, age groups and dosage guidelines.

ABSTRACT 10 – AI-assisted drug repurposing studies for the identification of new promising vasopressin V2 receptor ligands for pharmacotherapy in pediatric nephrology

Topic: Paediatric Medicines Discovery

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Abstract: Background: Autosomal recessive polycystic kidney disease (ARPKD) is a rare genetic disorder highly relevant in pediatric nephrology. ARPKD is characterized by hepatorenal fibrocystic syndrome and cysts at renal collecting ducts. Clinical manifestations may occur in utero or at birth. Autosomal dominant polycystic kidney disease (ADPKD) and ARPKD share many similarities such as increased cyclic adenosine monophosphate (cAMP). The vasopressin V2 receptor (V2R) antagonist, tolvaptan, has been recently approved for the treatment of progressive disease in adult ADPKD patients. Conversely, there is no current cure for ARPKD. Besides water reabsorption, the activation of V2R is involved in abnormal cell proliferation, cancer, and cyst enlargement in polycystic kidney disease. In this perspective, we performed an inverse screening of a large collection of known drugs to identify novel V2R ligands that might modulate different receptor-mediated effects. Methods: The inverse screening campaign was run by using PLATO, our homemade target fishing platform. Structure-based studies were also carried out. Renal collecting duct MCD4 cells, stably expressing human V2R and aquaporin-2 (AQP2), were used as an experimental model to test the effects of drugs. Fluorescence Resonance Energy Transfer (FRET), and calcein fluorescence quenching (CFQ) were applied to evaluate changes in intracellular cAMP and DDAVP-induced water flux. Results: Our in-silico prospective repurposing studies prioritized five drugs, each of them belonging to a diverse group according to the ACT (Anatomical Therapeutic Chemical) classification system, as potential V2R ligands. FRET studies were carried out to test whether these compounds affect the DDAVP-induced cAMP responses. Interestingly, one of them (coded as F2544) at 1nM concentration significantly reduced the DDAVP-dependent cAMP production. Functional CFQ studies revealed that this drug reduced the DDAVP-induced water reabsorption, with effects comparable to tolvaptan, that is a well-established V2R antagonist used as positive control. In this respect, an in-depth computational investigation showed a nice overlap of the molecular interaction fields generated from the binding sites of V2R and F2544. Finally, molecular docking simulations returned a promising posing and scoring of F2544 in the V2R binding site. Conclusions: Our studies identified for the first time new V2R ligands by applying an AI-based approach. Combining in-depth computational investigations and functional studies, F2544 was prioritized for being repurposed for treating diseases associated with abnormal V2R signaling, such as ARPKD in pediatric nephrology.

ABSTRACT 11 – Bridging Pediatric Disease Research and Developmental Toxicology with Artificial Intelligence-based Public Web Platforms

Topic: Paediatric Medicines Discovery

Authors: Nicola Gambacorta[3]; Fulvio Ciriaco[1]; Nicola Amoroso[2]; Daniela Trisciuzzi[2]; Maria Vittoria Togo[2]; Fabrizio Mastrolorito[2]; Antonella Liantonio[2]; Paola Imbrici[2]; Giuseppe d'Orsi[3]; Massimo Carella[3]; Orazio Nicolotti[2]; Cosimo D. Altomare[2]

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Abstract: In the search of new cutting-edge tools to tackle drug discovery and repurposing in pediatrics and predicting toxicological endpoint, we designed three public web platforms that are PLATO1, TISBE2 and CIRCE3. PLATO (Polypharmacology pLATform for predictiOn) is a ligand-based polypharmacology predictive platform designed for target fishing and bioactivity prediction. PLATO has a two-fold objective: to shortlist a few putative protein drug targets and to computationally assess biological affinity values. Utilizing a multi-fingerprint similarity search algorithm, PLATO is particularly effective for running reverse screening in prospective drug repurposing, aiming to find potential candidates for pediatric disease treatment. TISBE (TIRESIA Improved on Structure-Based Explainability) is a powerful tool for predicting developmental toxicity, a crucial health endpoint for safeguarding maternal and child well-being. TISBE implements four fundamental advancements for in-silico analyses: a large and manually curated dataset, a transparent XAI (explainable artificial intelligence) framework employing a fragment-based fingerprint coding, a novel consensus classifier based on five independent machine learning models, and a new applicability domain method based on a double top-down approach for better estimation. These features make TISBE particularly suited for assessing the safety of chemicals in pediatric populations. CIRCE (Cannabinoid Iterative Revaluation for Classification and Explainability) includes a multi-layer machine learning framework designed to predict selective and unselective CB1/CB2 binders. Shapley values4 were computed to identify features determining correct predictions and explain machine learning models. Given the impact of Cannabinoid System in the pediatric illness such as refractory epilepsy and inflammatory bowel disease, CIRCE can assist the design of CB1/CB2 binders and effectively address the repurposing of known drugs for pediatric diseases. Together, these platforms represent a significant advancement in the field of pediatric disorder research and drug repurposing, providing robust tools for discovering and validating new therapeutic options while ensuring safety and efficacy through explainable AI methodologies.

The above platforms are available at the following links:

PLATO is free available at https://prometheus.farmacia.uniba.it/plato/

TISBE is free available at https://prometheus.farmacia.uniba.it/tisbe/

CIRCE is free available at https://prometheus.farmacia.uniba.it/circe/

ABSTRACT 12 – Innovative Drug delivery Systems

Topic: Paediatric Medicines Formulations

Authors: Konstantina Chachlioutaki[1]; Paraskevi-Kyriaki Monou[1]; Christina Karavasili[1]; Dimitrios G. Fatouros[1]

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Abstract: Technical description of the service: The research group has an Additive Manufacturing suite equipped with 3D printers namely; fused deposition modelling (FDM), Bioprinter, Digital Light Process (DLP) printer, stereoloithography (SLA) 3D printing, Food printer, Selective Laser Sintering (SLS) and a uni- coaxial electrospinning system and a large formulation and drug delivery laboratory.

The available techniques include: Polarized Microscopes, FTIR (ATR & RAIRS facilities), Fluorescence spectrophotometer, liquid chromatography (HPLC), mass spectrometry (LCMS), thermal analysis (DSC, TGA), UV-VIS and NIR spectrometry, Freeze-dryer, Spray-dryer, BET Instrument, Porosimeter (Hg), equipment for measuring zeta potential and particle size (photon correlation spectrometry), rheology equipment, He-pycnometers, tensile strength instruments, pH-titrator and Franz cells. Specific cellular models (Caco-2, Calu-3, TR146) are used for uptake/interaction studies, transport across cellular models of barriers, biocompatibility/toxicity testing.

Output: Type of output Development of personalized paediatric-friendly dosage forms using 2D/3D printing and electrospinning for peroral and intraoral drug delivery (ODFs, buccal patches, semi-solids) for low and high molecular weight molecules. Fabrication of 3D printed microneedles (solid, coated, hollow) for use in paeditaric populations. Permeability studies on excised animal tissues using the Franz cell assembly for skin, buccal, nasal, ocular and intestinal routes of drug administration. Physicochemical characterisation of solid, semisolid and liquid dosage forms. Mucoadhesion studies. In vitro lipid digestion studies (lipolysis model).

Significance of bringing this output: Point-of-care manufacturing of bespoke dosage forms for paediatric populations. Use of microneedles for non-invasive skin delivery for paediatric patients. Permeability and cellular uptake studies for different routes of administration.

ABSTRACT 13 – NIHR HealthTech research centre - A national network transforming paediatric healthcare

Topic: Paediatric Medical Devices

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Abstract: The NIHR HealthTech Research Centre (HRC) in Paediatrics and Child Health (UK), hosted by Sheffield Children's NHS Foundation Trust, is a national network that is transforming paediatric healthcare through collaboration with industry experts, healthcare professionals, academics, children and young people (CYP), and their families. The HRC focuses on facilitating the development and implementation of innovative technologies for paediatrics and child health that have real-world impact. The HRC builds on the success of the national TITCH Network and NIHR CYP MedTech Co-operative, which achieved the following milestones: Secured £22 million to build the National Centre for Child HealthTechnology Founded and hosted three international Child Health Technology conferences Leveraged over £50 million in funding Worked on 180 projects Hosted 13 PhD students and early career researchers Collaborated with 139 SMEs and 44 global companies. The HRC has five key themes, focussing on birth-25 years: Early Life, Long-Term Conditions, Transition, Mind-Body Integration, and the Child Health Artificial Intelligence Network. These themes will be advanced through three core strategies: Industry/Commercial Engagement: The HRC collaborates with industry and investors to develop and commercialise innovative paediatric health technologies, providing expert advice, project management, and regulatory guidance from ideation to adoption. Education/Training: The HRC is committed to advancing education and research, with a particular focus on supporting early career researchers (ECRs). The HRC is creating and launching the Elevate2Innovate programme, a bespoke training programme that aims to equip innovators and researchers to develop effective paediatric health technologies. The programme will include placements, online training modules, mentorship, and development workshops. The HRC is also developing a bespoke, online educational hub, providing comprehensive training and education featuring modules on identifying unmet needs, PPIE, intellectual property (IP), NHS regulations, commercialisation, and adoption. Public and Patient Involvement (PPIE): Central to the HRC's mission is the involvement of children, young people, and their families throughout the innovation pathway. The HRC integrates PPIE into all stages of product development, from identifying unmet needs to testing and validation. Our aim is to co-create a methodological framework around meaningful PPIE with CYP that translates across organisations.

Services Offered:

Expert Advice and Project Management: Guidance from leading NHS clinicians

Knowledge Centre: An online resource for training and education.
Testing and Clinical Trials: Assistance with rapid research and real-world clinical evaluation within the NHS.
Regulatory, IP, and Human Factors Guidance: Support with regulatory compliance and IP. Funding Application Support: Support to secure funding through collaborative applications.
Co-design and co-development expertise: PPIE support.
Commercialisation support: market analysis facilitating a route to market.
Access to NHS and NIHR Infrastructure: Facilitating connections with relevant NHS and NIHR organisations.
Stakeholder collaborations: We have extensive networks across healthcare, industry and academia.

Strategic Partners: The HRC is aligned to multiple strategic partners to enhance its capabilities and extend its reach. In particular, the HRC is closely aligned with the National Centre for Child Health Technology, a world-leading centre with state-of-the-art facilities, focused on addressing the biggest health challenges of our time. Other partners include NIHR-funded organisations, NHS Foundation Trusts, leading universities, national and international companies, and SMEs.

Together, the NIHR HRC in Paediatrics and Child Health and its strategic partners are positioned to drive significant advances in paediatric healthcare, leading to better outcomes for patients, families and clinical teams.

ABSTRACT 14 – Pediatric Medicines in Kosovo: A State-of-the-Art Analysis and Strategic Vision for Future Research

Topic: Other

Authors: Aida Loshaj Shala[1]; Dafina Fondaj[2]

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Abstract: Following its independence in 2008, Kosovo has embarked on significant efforts to transform its healthcare infrastructure. Despite these efforts, the healthcare system still grapples with persistent challenges such as funding deficiencies, limited services, and uneven access across regions. Demographic studies highlight a predominantly young population, with a substantial portion under the age of 18, underscoring the necessity for robust pediatric healthcare services. However, in Kosovo, as in many other countries, most available drug formulations are designed for adults. These formulations often require modifications for pediatric use, which compromises both accessibility and appropriateness. The Kosovo Agency for Medicines and Medical Devices (KMA) is crucial in regulating pharmaceuticals, yet the current legislative framework only partially aligns with EU standards. Additionally, the list of essential medicines covered by the government has not been recently updated. This situation calls for a comprehensive analysis of pediatric medication availability and regulatory frameworks to ensure children in Kosovo have access to safe, effective, and age-appropriate medications. This study aims to analyze the current landscape of pediatric medication authorization in Kosovo, evaluating the approved medications for pediatric use, their suitability for different age groups, and the associated regulatory frameworks. Specifically, it seeks to identify gaps and challenges in the availability and appropriateness of pediatric medications and conduct a comprehensive analysis at both national and EU levels. The project employs a mixed-methods approach. To assess the availability and age-appropriateness of pediatric medicines and active chemical entities in Kosovo, a comprehensive review will be undertaken using data from the Kosovo Medicines Agency database and the Summary of Product Characteristics (SPC). This review will involve categorizing medicines based on their route of administration, type of oral dosage form, and therapeutic category. Each medicine's age-appropriateness will be assessed by considering factors such as dose flexibility, the suitability of the dosage form for pediatric use, and the presence of potentially harmful excipients. By comparing these findings with the 2023 WHO List of Essential Medicines for Children, this methodology aims to classify and analyze all approved pediatric medications in Kosovo while providing a detailed examination of their suitability for children. A gap analysis will be conducted to identify challenges in the availability and age-appropriateness of pediatric medications. This will be achieved through a multi-step approach, including a comprehensive inventory assessment of pediatric medications available in Kosovo, gathering quantitative data on medication types and quantities, and engaging stakeholders through interviews and surveys to obtain qualitative insights into the challenges and opportunities surrounding pediatric medication access and utilization. The collected data will be analyzed both quantitatively to identify availability gaps and qualitatively to detect underlying barriers. By integrating these findings, actionable recommendations will be developed to enhance pediatric healthcare in Kosovo. Additionally, a comparative analysis will be conducted to examine the regulatory frameworks and availability of pediatric medicines in Kosovo, Northern Macedonia, Albania, and Italy. This will involve extensive desk research and regulatory analysis methods to assess the marketing authorization status and labeling of medicines listed in the 2023 WHO Model List of Essential Medicines for Children. The findings across the countries will be compared to identify similarities and differences in the marketing authorization and labeling of essential pediatric medicines. This research will provide the first comprehensive analysis of the pediatric medication landscape in Kosovo. It will highlight critical gaps and proposes strategies to enhance the regulatory framework, aiming to improve the availability and appropriateness of pediatric medicines. Future initiatives: will focus on the use of off-label pediatric medicines and explore the potential of advanced printing technologies, such as 3D printing, to create age-appropriate formulations in clinical settings in Kosovo.

ABSTRACT 15 – Low use of hydroxyurea among children living with Sickle Cell Disease in a tertiary hospital in Northern Nigeria

Topic: Other

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Abstract: Background: Use of Hydroxyurea (HU) can improve the health condition of about 300,000 individuals born each year with sickle cell disease (SCD) in sub-Saharan Africa, particularly in Nigeria which has the largest population of people living with SCD. This study was conducted during an African Research and Innovative initiative for Sickle cell Education (ARISE, EC GA No 824021) staff exchange programme.

Aims: To determine the use of HU among paediatric SCD patients reported at clinic visits at Ahmadu Bello University Teaching Hospital, Zaria, Nigeria from 2014 to 2022. Methods: We reviewed records of paediatric SCD patients in our paediatric registry and extracted the records of HU usage among paediatric SCD patients reported at clinic visits using structural query searching.

Results: Data of 1961 SCD paediatric patients was retrieved from the registry.1041 (53.1%) were male children, 906 (46.2%) female and 14 (0.7%) gender not recorded. 280 (14.3%) children were using HU and 1248 (63.6 %) not using it. There was no record about using it or not among 433 (22.1%) of the children.

Conclusion: there is low use of HU among paediatric SCD patients in our institution despite its importance in improving the health condition of SCD patients. We do not know whether the low use of it is due to lack of availability, affordability, accessibility and adherence, hence the need for more studies to determine the cause.

Key words: Use of Hydroxyurea, sickle cell disease.

This study has been conducted within the African Research and Innovative initiative for Sickle cell Education (ARISE) that has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 824021.

References: Okocha EC, Gyamfi J, Ryan N, Babalola O, Etuk E-A, Chianumba R, Nwegbu M, Isa H, Madu AJ, Adegoke S, Nnebe-Agumandu U, Brown B, Peprah E and Nnodu OE (2022) Barriers to Therapeutic Use of Hydroxyurea for Sickle Cell Disease in Nigeria:A Cross-Sectional Survey.Front.Genet.12:765958.doi:10.3389/fgene.2021.765958. Adewoyin AS, Oghuvwu OS, Awodu OA. Hydroxyurea therapy in adult Nigerian sickle cell disease: a monocentric survey on pattern of use, clinical effects and patient's compliance. Afri Health Sci. 2017;17(1): 255-261. https://dx.doi.org/10.4314/ahs.v17i1.31.

ABSTRACT 16 – Impact of polyphenols on Hyperoxia-Induced Airway Inflammation in Neonatal Rats

Topic: Other

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Abstract: Prolonged exposure to high levels of oxygen (hyperoxia) is detrimental to neonatal lung health, contributing to conditions such as bronchopulmonary dysplasia, which is characterised by airway hyperreactivity and inflammation. Despite the importance of oxygen therapy in preterm and low-birth-weight neonates, effective treatments for hyperoxia-induced lung injury are still elusive. The purpose of this study was to look into how polyphenols could protect neonatal rats from hyperoxia-induced airway hyperreactivity, impaired relaxation, oxidative stress, and lung inflammation. Newborn rats were exposed to high oxygen levels or normal air for a week. Some groups received treatments with polyphenols. Tracheal samples were examined for muscle contraction responses, and the effects of polyphenol were tested. Relaxation responses were also assessed using electrical stimulation. Additionally, levels of inflammatory markers in the lungs and activities of antioxidant enzymes were measured. Neonatal rats exposed to hyperoxia had higher airway hyperreactivity and inflammation than those exposed to ambient air. Polyphenols significantly reduced airway hyperreactivity and improved relaxation in hyperoxia-exposed tracheal smooth muscle. Furthermore, polyphenol treatment preserved antioxidant enzyme activity while decreasing pro-inflammatory cytokine expression in hyperoxic animals. Polyphenols exhibit protective effects against hyperoxia-induced airway hyperreactivity, impaired relaxation, oxidative stress, and lung inflammation in neonatal rats. These findings suggest that polyphenols may serve as potential therapeutic agents to attenuate the adverse effects of neonatal hyperoxia exposure and prevent the development of conditions such as BPD.

ABSTRACT 17 – Comparison of clinical events, haematological and biochemical profile of children with sickle cell anaemia with and without hydroxyurea treatment at a tertiary health facility in Northern Nigeria

Topic: Other

Authors: Abubakar Elishaq[1]; Niyi Mustapha Adebiyi[1]; Jibril Elbashir[2]; Jamilu Abdullahi Faruk[1]; Muhammad Aminu Idris[3]; Hafsat Rufai Ahmad[1]

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Abstract: Background: Sickle cell anaemia (SCA) is the most common form of sickle cell disease found in Nigeria, and is associated with high morbidity and mortality. Hydroxyurea treatment is gradually becoming an accepted therapeutic intervention in spite of perceived fear for its' haematological side effects and biochemical toxicity to the liver.

Aims: This study was aimed at comparing the clinical, haematological and some biochemical parameters of SCA patients on hydroxyurea with those not on hydroxyurea treatment.

Methodology: It was a cross-sectional study carried out at a paediatric outpatient clinic of a tertiary hospital in North West Nigeria. Ten milliliters of blood sample were collected for full blood count analysis using the Sysmex Xt 2000i automated hematology analyser. Biochemical analysis (ALT, LDH and bilirubin) were analyzed using Erba xl 200.

Results: Results of hundred and eight (60 HU; 48 non-HU) subjects is presented. The male: female ratio was 1.1:1. The overall mean age of the subjects was 8.91 ± 4.72, the age range was 1.2 to 18 years, while the most frequent age group was 6-12 years comprising 55 (50.9%). The mean number of painful crisis, hospital admissions, blood transfusions, stroke episodes and acute chest crisis episodes were 1.32 ±1.47, 0.84 ± 1.34, 0.44 ± 0.73, 0.054 ±0.22, 0.28 ± 0.88 in the HU group against 2.21 ± 1.99, 0.63 ± 0.78, 0.31 ± 0.62, 0.034 ± 0.237, 0.10 ± 0.367 in the Non-HU group. The mean total LDH was 1285.49 ± 398.46, Serum alanine transferase (ALT) was 34.29 ± 11.96, total bilirubin 30.93 ± 24.24 umol/l and 12.98 ± --umol/l conjugated bilirubin. Lactate dehydrogenase (LDH) (t-3.1855; p 0.0017) and conjugated bilirubin (t-3.8601; p 0.0002) were significantly higher in the non-HU group. The mean total RBC for all subjects was 3.08 ± 2.97, mean MCV was 79.51 ± 11.19 fl, mean HCT 26.29 ± 37.58 x 10 9 /l, mean HB 7.56 ±6.68 mg/dl, mean platelet concentration 305.35 ± 169.93 x 10 9 /l and WBC 15.7 ± 6.20 x 10 9 /l. Among all the haematological parameters, only MCV was statistically significantly higher in the HU group.

Conclusion: The HU group had lower clinical events, LDH, conjugated bilirubin and MCV than the Non-HU.

KEY WORDS: Sickle cell anaemia, Hydroxyurea, liver function, haematological profile, LDH, ALT, BILIRUBIN

References: 1. Chide, OE, Gyamfi J, Ryan N, Oluwatoyin B, Eno-Abasi E, Chianumba R, et al.. Barriers to therapeutic use of hydroxyurea for sickle cell disease in Nigera: A cross sectional survey. Research Square: June 2020. https://doi.org/10.21203/rs.3.rs-33381/v1

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ABSTRACT 18 – Disruption and Recovery Mechanisms in Growth Plate Injuries: Insights from Ex Vivo Organotypic Bone Slice Models

Topic: Other

Authors: Annelie-Martina Weinberg[1]; Ute Schäfer[1]; Birgit Lohberger[1]; Muammer Ücal[1]

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Abstract: Postnatal bone growth critically depends on chondrocyte proliferation and osteogenic differentiation within the growth plate (GP) via endochondral ossification. Despite its essential role, the GP is susceptible to injuries, affecting 15-30% of bone fractures and leading to growth discrepancies that impact bone length and shape, thereby diminishing patient quality of life. Currently, no biological therapies exist to prevent bone bridge formation post-GP injuries (GPI), largely due to the unknown pathological repair mechanisms and their contributions to growth abnormalities. This underscores the urgent need for innovative GPI models to facilitate real-time investigation of the pathological regeneration process. This study aimed to elucidate the molecular and cellular physiological and pathophysiological responses following sustained GPI in an ex vivo rat femur organotypic culture (OTC) model, with a focus on postnatal endochondral ossification. Ex vivo bone cultures, 300 µm thick with a 2 mm horizontal GPI, were analyzed over 15 days of in vitro cultivation using electron microscopy, gene expression analysis, live/dead staining, histological examinations, and immunohistochemistry to assess key markers of endochondral ossification. In our ex vivo rat femur OTCs, regeneration commenced at 3 days in vitro (DIV), with stem cells, fibroblasts, and chondrocytes infiltrating the injury site by 7 DIV. Live/dead staining revealed the migration of elongated live cells from the zone of Ranvier toward the injury site at 7 DIV, forming a network spanning the entire epiphysis by 15 DIV. Notably, the endochondral ossification process was disrupted, indicated by altered expression patterns of collagen type 2 (Col2α1), aggrecan (Acan), and collagen type X (ColX). Gene expression analysis showed a significant increase in Sox9 expression at day 15 post-GPI. The Ihh-PTHrP feedback loop was disrupted, promoting chondrocyte proliferation and maturation, with Ihh levels significantly elevated on days 7 and 15, while PTHrP was downregulated on day 7. Our findings indicate that trauma induces alterations in structural architecture and organization, alongside notable impairment of chondrocyte maturation in the ex vivo organotypic GPI model, paralleling observations in animal models. This innovative GPI model holds significant promise as a valuable tool for advancing our understanding of both physiological and pathophysiological GP repair mechanisms. Additionally, it offers potential applications in tissue engineering and disease studies, providing insights into therapeutic interventions for growth-related complications resulting from GP injuries.

European Paediatric Translational Research Infrastructure

MEETING AGENDA

EPTRI General Assembly & Scientific Meeting 2024

18th - 19th July 2024

18 July 9:00 – 13:00 - EPTRI General Assembly 2024

EPTRI General Assembly and Scientific Meeting 2024		
09:00-09:15	Welcome Message and introduction	Karel Allegaert
09:15-09:30	The Birth of EPTRI AISBL	Donato Bonifazi
09:30-09:45	What will be EPTRI's impact in the future?	Marek Migdal
09:45-10:00	Review of the Paediatric regulation	Lucia Ruggieri
10:00-11:00	General Assembly discussion and decisions	All the Members
11:00-11:30	Break	
11:30-11:45	Unmet Needs and Paediatric Drug Development	Leanne West
11:45-12:00	Psychopharmacology in children and adolescents: unmet needs and opportunities	Samuele Cortese
12:00-12:15	Big data analytics in paediatric research	Ian Wong
12:15-12:30	Innovative studies design for small populations	Giorgio Reggiardo
12:30-12:45	Importance of the placenta for foetal development and programming	Frantisek Staud
12:45-13:00	A multi-omic platform to empower collaborative translational research	Nathan Ali

18 July 14:00 – 17:30 - EPTRI Scientific Meeting 2024

EPTRI Scientific Meeting 2024		
14:00- 14:15	**EPTRI Central Management Office (CMO) and the Centralised services**	Franco Bartoloni
14:15-14:30	Modelling and simulation as a tool for translation, prediction and extrapolation of pharmacokinetics, pharmacodynamics, safety and efficacy in children	Oscar Della Pasqua
14:30-14:45	The Ethics and Regulatory service	Viviana Giannuzzi
14:45-15:00	HTA in paediatric research	Fedele Bonifazi
15:00-15:15	ATMP development infrastructure for paediatrics	Giovanni Migliaccio
15:15-15:30	**EPTRI Paediatric Biomarkers and Biosamples TRP**	Marios Phylactides
15:30-15:45	Multi-omics data integration and machine learning (ML) explaining the molecular basis of the complex microbiota-gut-brain axis and predicting possible biomarkers of autism	Alessandra Mezzelani
15:45-16:00	Legal and ethical issues of using AI in Pediatric Biobank in countries with an average income level	Svetlana Gramatiuk
16:00-16:30	Break	
16:30-16:45	**EPTRI Developmental Pharmacology TRP**	Karel Allegaert
16:45-17:00	Placenta: an ephemeral organ with a lifelong impact on health	Frantisek Staud
17:00-17:15	PBPK modelling on lactation related drug exposure	Julia Macente
17:15-17:30	Model informed precision dosing in paediatric intensive care units: a randomized clinical trial	Nadir Yalcin

19 July 9:00 – 13:00 - EPTRI Scientific Meeting 2024

EPTRI Scientific Meeting 2024		
09:00-09:15	**EPTRI Paediatric Medicines Discovery TRP**	Cosimo Altomare
09:15-09:30	Bridging Pediatric Disease Research and Developmental Toxicology with Artificial Intelligence-based Public Web Platforms	Nicola Gambacorta
09:30-09:45	AI-assisted drug repurposing studies for the identification of new promising vasopressin V2 receptor ligands for pharmacotherapy in paediatric nephrology	Grazia Tamma
09:45-10:00	Gottingen minipig model to study drug milk excretion and breastfed infant drug exposure	Domenico Ventrella
10:00-10:15	What animal tests can tell us about safety of drugs for developing brain?	Hana Kubova
10:15-10:30	KIDS experience in the paediatric medicine discovery lab	YPAGs members
10:30-11:00	Break	
11:00-11:15	**EPTRI Paediatric Medicines Formulations TRP**	Nunzio Denora
11:15-11:30	Are the regulatory aspects of pediatric medicinal products really optimized?	Paola Minghetti
11:30-11:45	Innovative Drug delivery Systems	Dimitrios G. Fatouros
11:45-12:00	KIDS experience in the paediatric drug formulation lab	YPAGs members
12:00-12:15	**EPTRI Medical Devices TRP**	Emilia Biffi
12:15-12:30	Innovative technology-based interventions, including virtual reality for paediatric rehabilitation.	Tamar Weiss
12:30-12:45	Nanoparticles for Target Therapy in Pediatric Brain Cancers	Clara Baldari
12:45-13:00	PhiCube: bilateral upper limb device for neuromotor recovery	Giovanni Tauro

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