suggesting differences in promoter activity of transduced hepatocytes' subsets. Overall, our results indicate that LV-based liver gene therapy is more efficient in young mice, and that age of treatment impacts on LV transduction efficiency, spatial distribution of transduced hepatocytes and transgene output. These studies will inform further development of liver-directed LV gene therapy towards application to pediatric patients.

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Clinical effect of intradiscal application of allogeneic mesenchymal stem cells derived from umbilical cord Wharton's jelly (WJ-MSC) in adults with degenerative disc disease (DDD) treated at BioXcellerator, Medellín, Colombia

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Mesenchymal stem cell therapy could improve DDD symptoms by promoting intervertebral disc matrix natural repair processes. The aim was to analyze clinical effects of intradiscal WJ-MSC cell therapy. A retrospective cohort was followed. Clinical outcomes measures included: Short Form-12 questionnaire, Pain Visual Analog Scale (VAS), Oswestry disability Index (ODI), Neck Disability Index (NDI). Follow-ups were at pretherapy time and 3, 6, 12 months after intradiscal application of a single dose of $5x10^6$/mL cells per disc as a treatment protocol. WJ-MSCs were expanded in culture medium supplemented with 10% human platelet lysate (hPL) up to passage 7. Cell marker expression, in vitro differentiation to mesodermal lineage, and microbiological tests were performed. 53 patients were included (August/2019-June/2022), 62% men. Median age = 48 (IQR = 28-64). 53.8% had cervical, 21.02% thoracic, 41.7% lumbar disc injuries. 91.4% had multiple disc injuries. MODIC changes = 29.3%. The most frequent Pfirrmann grade was II (26.3%). The SF-12 scores were increased (0-month = 47, 3-month = 67, 6-month = 84, 12-month = 78, Wilcoxon p-value = 0.04). VAS, ODI and NDI scores were reduced (0 = 8,60,72, 3 = 7,48,65, 6 = 5,40,60, 12 = 4,28,45, Wilcoxon p-values = 0.10, 0.03 and 0.09 respectively). The fit predictors at Multivariate GEE model mainly associated with the final result of the SF-12 at twelve months were: age (b = -0.278,p = 0.03), Pfirrmann grade (b = -0.019,p = 0.04) and WJ-MSC treatment (b = 0.157, p = 0.02). In relation to ODI at one year: sex (male) (b = -0.098,p = 0.02), MODIC changes (present) (b = 0.61,p = 0.01) and WJ-MSC-treatment (b = -0.099,p = 0.04). Approval was obtained by an ethics committee. No serious adverse events were reported. We conclude that intradiscal application with WJ-MSC is safe and has shown relevant clinical effects on DDD.

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Preclinical optimisation of lentiviral gene therapy delivery for surfactant deficiencies in piglets

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Surfactant protein deficiencies account for 10% of childhood interstitial lung disease and the prognosis depends on the protein that is deficient. Infants with surfactant protein B (SP-B) deficiency or double null mutations in ABCA3, present shortly after birth with respiratory distress and failure. Despite ventilation and treatment with surfactant replacements, they rarely live beyond the first few months of life. We have delivered vector expressing EGFP by bronchoscopic instillation via an endotracheal tube to the lungs of ventilated neonatal piglets to model delivery of vector to the lungs of ventilated children. We compared multisite instillation with small volumes of concentrated vector at two doses with lavage-like delivery of the same highest dose of vector in a larger volume. Multisite instillation with small volumes resulted in dose-dependent expression of GFP with significant heterogeneity (47% and 39% captured images with no GFP at low and high dose) and efficiency ranging from 0% to 98% in individual images. Delivery of the high dose in larger volumes resulted in only 17% images with no GFP signal and a range from 0% to 17%. The overall average efficiency in the latter study was 4%. Further studies in piglets will help to optimise dose and delivery protocols and will aid calculations of the required dose projected to reach the therapeutic level of expression in the target cells in clinical trials.

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Advanced humanized immune system mouse models: An efficient pre-clinical mouse model to evaluate immune targeted therapies in cancer research

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Engraftment of CD34+ haematopoietic stem cells in NCG mouse allows the reconstitution of a complete human immune system, with mature T, NK cells and macrophages. The human immune system could be further enhanced by the expression of human cytokines that will improve the immune system development. This mouse model provides a relevant in vivo context, to assess the therapeutic efficacies of immune targets in the oncology field such as checkpoint inhibitors, bi-specific antibodies, oncolytic viruses or cell-engineered based therapies. At TransCure bioServices, we have developed a comprehensive database of CDX engrafted in advanced humanized immune system mouse models. The tumor infiltrating leukocytes were analysed by flow cytometry, revealing high differences of infiltration between the different CDX models and the importance of the tumor microenvironment to drive the immune infiltration. Thanks to this preclinical mouse model, we were able to demonstrate efficacy of drugs targeting macrophages polarization or T cell activation.

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Production of ATMPs: What are the specificities for quality aspects?

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