



and fluorescent labelled MSC containing sub-networks (D,E) was performed using ImageJ network analysis plugin. MSCs isolated from aortic ring co-cultures and analysed for endothelial (CD31,CD34) and pericyte(CD146) markers. **Results:** FTM-PVCs induced greater EPC sprouting, integrated more efficiently into the developing aortic ring tubular network with elongated morphology, induced more network formation and upregulated the endothelial markers CD31 and CD34 more than term-PVCs and BMSCs. **Conclusion:** FTM-PVCs are a promising candidate to support and induce angiogenesis for tissue regeneration therapy.

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IDENTIFICATION AND COMPUTER-AIDED DISCOVERY OF A POLY-CHEMICAL MOTIF-LIKE PHARMACO-PEPTIDOMIMETIC 4D-STRUCTURE TARGETED ON THE STEM CELL DEVELOPMENTAL STAGE-SPECIFIC MANNER CARDIAC DIFFERENTIATION AND PROLIFERATION MOLECULAR PATHWAY

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Life-threatening heart diseases, such as myocardial infarction and heart failure, are major causes of death in developed countries. The low levels of proliferation and regeneration ability of cardiomyocytes must be overcome to effectively treat these diseases. Due to the almost non-existent cardiomyocyte turnover in the human heart after birth, recovery of cardiac function after heart disease is insufficient. We hypothesized that a chemical biological approach would be a suitable answer to this problem. Thus, identifying novel chemicals have been an efficient approach to elucidate novel mechanisms regulating cardiomyocyte proliferation and finally employ cardiac regeneration as a therapeutic strategy. Nevertheless, no efficient chemical screening platform for cardiomyocyte proliferation has been explored to date. Here, for the first time we combined our cardiac stem cell network simulation technology and chemical-biology informatic automated cluster of our Bayesian Machine-based set of cardio-algorithms with HCS to identify and in silico designed of in silico conserved peptide targeted Poly-Chemical comprising superagonistic properties on cardiomyocyte proliferation molecular mechanisms. We also successfully identified several chemicals with distinct molecular targets and confirmed their binding pocket docking effects on cardiac differentiation molecular pathways.

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EX VIVO DERIVATION AND EXPANSION OF HUMAN NEUROPOIETIC CELL PROGENITORS USING HIGHLY CONSERVED POLY-PEPTIDOMIMIC LINKED-PHARMACOPHORES TARGETED TO NEURAL PATHWAYS FOR NEURODEGENERATIVE DISEASE MODELING. AN ADVANCED FRAGMENT-BASED MULTI-DIMENSIONAL CHEMICO-INFORMATIC APPROACH

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A representative ligand-fragment based 4D dimensional approach is the similarity zinc-ensemble approach which predicts new binding pocket domains using structure similarity technical fields of selected neuro-ligands whereas drug discovery requires billions of neuronics for high-throughput screening (HTS) campaigns. Neurodegenerative Devastating diseases are particularly challenging because neural tissue and human neurons are post-mitotic and cannot be expanded and clinically released for implementation in cell therapy regenerative clinical applications. Here, we demonstrate HTS for the identification of neuro-protective compounds requiring a specific cell type that is highly expandable and able to differentiate into all of the neuronal-tissue subtypes involved in neurogenetic disease pathogenesis. Here, we discover and report for the first time the derivation and the in silico

designation of a multi-compartment poly-pharmacophore using only an advanced cluster of cost-effective chemo-algorithms for the efficient linkage of small nano-molecules to a number ligand-based neurogenic peptides for the discovery of a number of novel chemo-compounds in identifying drugs with novel scaffolds that differ from those of reference compounds. We present here also for a first time that an in-silico poly-pharmacophore designed chemo-structure may target Neuro-poietic-like Stem Cell Neural Pathways with a potential to ex-vivo clonally and efficiently differentiate into mature and functional neural lineages, including motor neurons (MNs) and midbrain dopaminergic neurons (mDANs) as well as neural crest lineages, including peripheral neurons and mesenchymal cells.

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CORD BLOOD DERIVED CELL THERAPY PRODUCT, DUOC-01, ACCELERATES REMYELINATION IN A MURINE MODEL OF CUPRIZONE INDUCED DEMYELINATION

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We have developed a cell product, DUOC-01, derived from banked human umbilical cord blood [UCB] for use in the treatment of CNS demyelination. To assess the ability of these cells to help remyelinate neurons we have adapted the cuprizone [CPZ] model of reversible brain demyelination using immune-incompetent NOD/SCID-IL2Rg^{null}[NSG] mice. Mice were fed CPZ for 5 weeks and then were stereotactically injected in the corpus callosum [CC] region with 10⁵ DUOC-01 cells or with excipient. Brains were harvested one week following injections and CC myelination was evaluated by Luxol-fast blue-staining [LFB] and immunohistochemistry [IH]. In 4 experiments, the CC midline regions of NSG mice were severely demyelinated with glial infiltration following CPZ feeding. LFB and IH with anti-MBP antibody one week after cell treatment showed that mice injected with DUOC-01 had significantly increased myelination and decreased gliosis and cellular infiltration in the CC region compared to control mice injected with excipient. The number of proliferating mouse oligodendrocyte lineage cells co-labeled by Ki67 and olig2 antibodies was higher in DUOC-01 treated than excipient injected mice. Morphometric analysis of electron micrographs showed: (a) a significantly higher percentage of correctly myelinated axons per field, (b) higher g-ratio (the ratio of axon diameter and axon diameter wrapped with myelin) and (c) higher number of myelin sheath turns around an axon in the CC of DUOC-01 treated group, as compared to excipient injected controls. These data demonstrate that DUOC-01 is capable of accelerating the remyelination of neurons by reducing gliosis and promoting oligodendrocyte proliferation and suggest that could be beneficial in treating demyelinating conditions. A phase I clinical trial testing the safety of intrathecal administration of DUOC-01 cells as adjunct therapy to a standard myeloablative unrelated donor UCB transplant in children with leukodystrophies is underway.

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SYSTEMATIC REVIEW AND META-ANALYSIS OF EFFICACY AND SAFETY OF STEM CELL THERAPY IN AMYOTROPHIC LATERAL SCLEROSIS

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Stem cell therapy may be promising options for the treatment of ALS. However, the effects of these treatments are not yet fully understood and there is a lack of firm evidence on the efficacy of stem cell therapy for those patients due to the absence of sufficiently powered randomized controlled trials. Therefore, we performed a meta-analysis of available single-arm studies using stem cell-based therapy in patients with ALS.

A systematic search and critical review of the literature published from its inception through February 2013 was performed. The articles included in the search were restricted to the English language, studies with at least 5patients, 3 or more month follow-up, and efficacy evaluation using ALSFRS. Article selection and data extraction were conducted by two authors independently with standard methods. Data analyses were performed using Comprehensive