VABILO

IV. razred SAZU vljudno vabi na predavanje, ki ga bo imel

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Predavanje bo v angleščini.

Hrbtenjačna poškodba in bolezen motoričnega nevrona: novi pogledi iz multimodalnih študij z matičnimi celicami. (Spinal Cord Injury and Motor Neuron Diseases: new insight gleaned from stem cell-based multimodal studies)

Tajnik IV. razreda: akad. Robert Zorec

Povzetek: Nobelova nagrada za fiziologijo ali medicino je bila v letu 2012 podeljena za odkritje, da "iz zrelih celic lahko induciramo stanje matičnih celic". Zaradi pluri- oz. multipotentnosti matičnih celic so sprva menili, da biologija živčnih matičnih celic (NSCs) predstavlja idealno in edinstveno možnost za rekonstrukcijo poškodovanega osrednjega živčnega sistema (CNS) z nadomestitvijo z matičnimi celicami. Rezultati raziskav pa kažejo, da matične celice lahko popravijo CNS prek več mehanizmov, ki potekajo sočasno. Pri tem sodelujejo ne le kot izvor tkivnih dejavnikov za celično rekonstitucijo, ampak tudi kot vektorji za dostavo molekul [1]. Na temelju lastnih raziskav, kjer smo uporabili biorazgradljive polimere skupaj s človeškimi živčnimi matičnimi celicami za raziskovalne in za terapevtske namene, bom najprej razpravljal, da vsadek iz polimerov in iz človeških matičnih celic lahko predstavlja možnost za reparacijo poškodovane odrasle sesalske hrbtenjače [2,3]. Predstavil bom rezultate, ki kažejo na molekulske in celične dogodke, ki prispevajo k adaptaciji distalnega dela hrbtenjače pri indukciji nevroplastičnosti in funkcionalnem izboljšanju po poškodbi hrbtenjače glodalcev ob uporabi na polimer nasajenih človeških matičnih celic in ob genetsko zmanjšani reaktivni gliozi [4]. Nadalje bom pokazal rezultate, kjer je uporabljena podobna strategija uporabe matičnih celic za raziskave modela družinske oblike nevrološkega obolenja (amiotrofična lateralna skleroza ALS), ki je kot Lou Gehrigova bolezen v ZDA, s ciljem, da bi spoznali kritične patogene in patofiziološke sprožilce in možne nove tarče za zdravljenje bolezni motoričnih nevronov [5]. Naša odkritja lahko prispevajo večmodalni pristop, integriran z biologijo matičnih celic, za študij mehanizmov, ki vplivajo na mikrookolje v gostitelju z donorskimi matičnimi celicami in s tem omogočijo oblikovanje terapevtske strategije za pospešitev izboljšanja kliničnega stanja po poškodbi hrbtenjače in pri nevrodegenerativnih boleznih.

The Nobel Prize in Physiology or Medicine 2012 was awarded for the discovery that "returns mature cells to the stem cell stage". Based on pluripotency or mutlipotency of developmental cells, it was initially hypothesized that the biology of neural stem cells (NSCs) makes them ideally and uniquely suited to reconstructing the damaged central nervous system (CNS) through cell replacement. Emerging evidence, however, increasingly suggests that NSCs may repair the CNS through multimechanistic strategies that are often concurrent. They may serve not only as tissue engineering mediators of cellular reconstitution, but also as vectors for the delivery of molecules [1]. Buoyed by tangible results derived from our recent studies in which biodegradable polymer seeded with human NSCs (hNSCs) was applied for both investigative and therapeutic purposes, I propose to first discuss that how a polymer based implant containing hNSCs may hold significant promise for providing a broad range of insight regarding essential neurological mechanisms required for repairing the adult mammalian spinal cord after injury [2,3]. I will present data elucidating molecular and cellular events underlying distal spinal cord adaptation in the process of invoking neuroplasticity and functional recovery post rodent spinal cord injury (SCI), resulting from polymer scaffolded hNSCs implantation plus genetic reduction of reactive gliosis [4]. Additionally, data obtained by adopting similar stem cell biology to investigate a murine model of familial amyotrophic lateral sclerosis (ALS), also referred to as Lou Gehrig's disease in the United States, will be analyzed for understanding critical pathogenic and pathophysiologic triggers as well as novel candidate therapeutic targets in motor neuron diseases [5]. Our findings may provide a multimodal approach integrated with stem cell biology for investigating mechanisms mediating the host microenvironment and donor stem cell interaction and help formulate therapeutic strategies to enhance clinically meaningful improvement for SCI and neurodegenerative conditions.

[1] Teng, Y.D. et al., Curr. Neuropharmacol. 9, 574 (2011); [2] Teng, Y.D. et al., Proc. Natl. Acad. Sci. USA. 99, 3024 (2002); [3] Yu D. et al., Stem Cells 27, 1212 (2009); [4] Teng Y.D. et al., Euroglia Meeting, Prague, Czech Republic (2011); [5] Teng Y.D. et al., Science (Transl. Med.) 4, 165 (2012)