



Title	Chondroitinase ABC-I and -II linked chitosan microbeads increase neurite length in CSPG-enriched astrocyte culture
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Citation	The 2014 Hong Kong Inter-University Biochemistry Postgraduate Symposium, Hong Kong, 14 June 2014. In Program Booklet, 2014, p. 49, poster no. 67
Issued Date	2014
URL	http://hdl.handle.net/10722/203875
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Semaphorin3A, Associated with Perineuronal Nets, Regulates the Development of the Maturation of the Central Vestibular Circuitry

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During the formative period of neural circuits, perineuronal nets (PN) are established to restrict plasticity of the circuit. The role of PN in vestibular plasticity can be tested by studying the emergence of negative geotaxis with postnatal maturation of the vestibular circuitry for gravity detection.

Using rats as model, we observed that negative geotaxis was mature by postnatal day (P) 9, in correlation with consolidation of PN around GABAergic neurons in the vestibular nucleus (VN). Treatment of the VN at P6 with chondroitinase ABC (ChABC) cleaved chondroitin sulfate (CS) moieties of PN and delayed emergence of negative geotaxis to P13. Delay to P13 was also observed following treatment of the VN with a GABAA receptor antagonist, reinforcing GABAergic transmission as regulated by perineuronal CS is a crucial step for the maturation of negative geotaxis.

Throughout postnatal development of the VN, CS moieties of PN colocalized with semaphorin 3A (Sema3A), a secreted glycoprotein that regulates neuronal polarization. The expression of Sema3A in VN was confirmed by in-situ hybridization. In addition, Sema3A regulated the dendrite growth pattern of GABAergic neurons in VN. We infer that the morphological changes of the dendritic arbor can contribute to the vestibular plasticity.

Our results suggest that, as the VN circuitry undergoes maturation, perineuronal CS moieties retain Sema3A and limit the participation of Sema3A in the modulation of morphological and functional properties of GABAergic interneurons in the VN, thereby contributing to the hardwiring of the central pathway for vestibular behavior. [Grant Supported by HKRGC 774608M & 777911M]

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Chondroitinase ABC-I AND -II linked chitosan microbeads increase neurite length in CSPG-enriched astrocyte culture.

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After spinal cord injury, axonal regrowth is often restricted due to upregulation of chondroitin sulfate proteoglycans (CSPGs) at the lesion site. Chondroitinase ABC I and II (recombinant ChABC-I & -II) cleave CS moieties of the PGs enhancing prospects of axonal regrowth through the lesion. We attempted to use glutaraldehyde to immobilize ChABC-I or-II separately on chitosan beads. Immobilized ChABC-I demonstrated CS-cleaving activity both in biochemical assay and in CSPGs-enriched astrocyte cultures that had been activated by transforming growth factor beta (TGF- β). Neurite length was increased in co-cultures of TGF- β activated astrocytes and cortical neurons mixed with immobilized ChABC-I, immobilized ChABC-II or both. Given CSPG enrichment at astrocyte-Schwann cell (A/S) encounters, A/S confrontation co-culture was used in a further bioassay of immobilized enzyme activity. Preliminary data showed that neurite length was increased in ChABC-I treated A/S co-culture. In future, the effect of immobilized ChABC-I and -II on neurite length will be tested in A/S co-culture.