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Proliferative effect of tri-deoxyribonucleotides on mouse neural stem cells

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We have recently demonstrated that nucleic acid fraction (NAF) of hydrolyzed salmon milt extract promotes proliferation of neural stem cells (NSCs) in primary culture and enhances memory function in mice. However, the mechanisms underlying remain unclear. The purpose of this study was to clarify which component in the NAF is responsible for promotion of the proliferation of NSCs. Since the NAF highly contains tri-deoxyribonucleotides compared with other nucleotides, NSCs in primary culture were incubated with each tri-deoxyribonucleotide, followed by evaluation of proliferative activity. Interestingly, only tri-deoxycytidine (CCC) among all 64 tri-deoxyribonucleotides significantly promoted the proliferation. Concentration of CCC and its putative metabolites in culture medium were then simultaneously quantified by LC-MS/MS. CCC in the medium was decreased in time-dependent manner, whereas deoxycytidine, deoxycytidine monophosphate, and cytidine were gradually increased. However, exposure to these metabolites did not affect proliferation of NSCs, suggesting that CCC itself may promote the proliferation. Further proteomics analysis showed that CCC altered expression of several unidentified proteins in addition to proliferation-related proteins such as RPS27A which would be possibly involved in CCC-induced proliferation of NSCs.