論文の内容の要旨

論文題目：Cerebellin precursor protein (Cbln) subtypes induce synapse formation of cortical neurons by binding to neurexins containing splice segment 4

（Cerebellin precursor protein (Cbln)群 はスプライスセグメント 4 を含む neurexin に結合して大脳皮質神経細胞のシナプス形成を誘導する）

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The *trans*-synaptic interaction of postsynaptic glutamate receptor δ2 and presynaptic neurexins (NRXNs) through cerebellin precursor protein 1 (Cbln1) mediates synapse formation in the cerebellum (Uemura, T., Lee, S. J., Yasumura, M., Takeuchi, T., Yoshida, T., Ra, M., Taguchi, R., Sakimura, K., and Mishina, M. (2010) *Cell* 141, 1068–1079). This finding raises a question whether other members of the Cbln family interact with NRXNs to regulate synapse formation in the forebrain. Here, I showed that Cbln1 and Cbln2 induced presynaptic differentiation of cultured cortical neurons, while Cbln4 exhibited little activity. When compared with neuroligin 1, Cbln1 and Cbln2 induced preferentially inhibitory presynaptic differentiation rather than excitatory one in cortical cultures. The synaptogenic activities of Cbln1 and Cbln2 were suppressed by the addition of the extracellular domain of NRXN1β to the cortical neuron cultures. Consistently, Cbln1 and Cbln2 showed robust binding activities to NRXN1α and three β-NRXNs, while only weak interactions were observed between Cbln4 and NRXNs. The interactions of Cbln1, Cbln2 and Cbln4 were selective for NRXN variants containing splice segment 4. Affinities for NRXNs estimated by surface plasmon resonance analysis were variable among Cbln subtypes. Cbln1 showed higher affinities to

NRXNs than Cbln2. The binding ability of Cbln4 was much lower than those of Cbln1 and Cbln2. The affinities of Cbln1 and Cbln2 were comparable between NRXN1α and NRXN1β, but those for NRXN2β and NRXN3β were lower. These results suggest that Cbln1 and Cbln2 play a role in synapse formation of cortical neurons by interacting with NRXNs containing S4.