

# **N-TERMINAL DOMAINS OF NEUROCALCIN $\delta$ AND HIPPOCALCIN DETERMINE DIFFERENCE IN THEIR $\text{Ca}^{2+}$ -DEPENDENT SIGNALING**

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Hippocalcin (HPCA) and Neurocalcin  $\delta$  (NCALD) are the members of neuronal  $\text{Ca}^{2+}$ -sensor (NCS) protein family. In spite of minor distinctions in AA sequence between HPCA and NCALD, these proteins demonstrate a substantial difference in their  $\text{Ca}^{2+}$ -sensitivity and kinetic of translocation to the plasma membrane. Both proteins contain myristoylated N-terminal region responsible for interaction with cellular membrane and 3 EF-hand domains responsible for binding of  $\text{Ca}^{2+}$ . Here we compared translocation of wild type NCALD with NCALD-HPCA chimera protein, NCHC, consisting of the first N-terminal region of NCALD and three other domains from HPCA (three  $\text{Ca}^{2+}$ -binding EF-hands). We suggested that NCHC translocation to the plasma membrane would tend to be HPCA-like if cytosolic  $\text{Ca}^{2+}$  affinity is important for protein signaling, and NCALD-like if stabilization of  $\text{Ca}^{2+}$ -bound form on the membrane plays a crucial role. NCALD and NCHC tagged by different fluorescent proteins were co-expressed in cultured rat hippocampal neurons. Protein translocation to the plasma membrane was induced by membrane depolarization resulting in fast  $[\text{Ca}^{2+}]_i$  transients and was assayed by fluorescent measurements in dendrites of hippocampal neurons. We have demonstrated that NCALD and NCHC had very similar translocation kinetics and  $\text{Ca}^{2+}$ -sensitivity, whereas NCALD and HPCA had substantial difference in these biophysical parameters. We conclude that the difference in signaling between NCALD and HPCA may be attributed to the distinctions of their N-terminal domains.