Binding of Homer1a Shifts *cis/trans* Equilibrium of Phosphorylated mGluR5

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Introduction

Post-synaptic density scaffolding proteins belonging to the Homer family have been implicated in regulating a variety of neural signaling pathways. All members of the Homer family with the exception of Homer1a are expressed constitutively and are able to form multimeric structures. Homer1a is a product of an immediate early gene and is expressed transiently in response to certain stimuli. It lacks the multimerization domain and is believed to play a crucial role in the potentiation of group II metabotropic Glutamate receptors (mGluRs) induced current. The goal of our research is to understand molecular basis for the regulation of mGluR5 by Homer proteins.

Experimental

The NHMFL 600 MHz solution magnet was used to collect triple-resonance experiments for assignments of the phosphorylated Homer binding site peptide from mGlur5 in complex with Homer1a EVH1 domain.

Results and Discussion

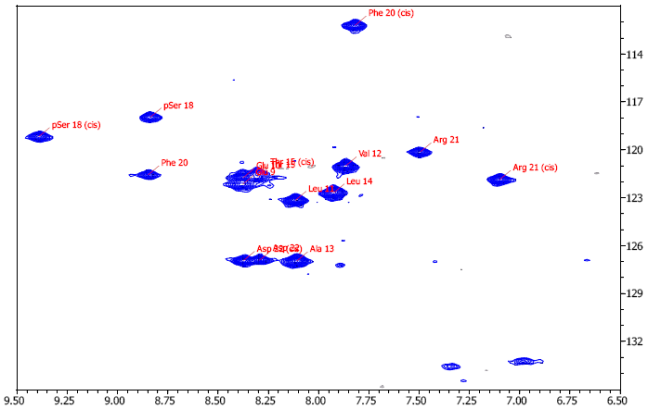

Fig 1 Resonance assignments of PHmR5-EVH1 complex.

Complete resonance assignments of the PHmR5-EVH1 complex were obtained and *cis/trans* populations were calculated based on ^{15}N-HSQC peak intensities. Upon binding of Homer1a the conformational equilibrium of phosphorylated mGluR is shifted significantly toward *cis* conformation. This conformational shift is not observed in the absence of phosphorylation.

Conclusions

The *cis/trans* equilibrium shift of mGluR upon phosphorylation and subsequent binding of Homer1a may be a key event in the regulation of mGluR activity.

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References

[1] Brakeman, P.R. *et al*., Nature, **386**, 284-288 (1997).