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A novel structure of calmodulin complexed with a binding domain peptide from HIV-1 genome products

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Introduction

Calmodulin (CaM) binds a large number of target proteins that are functionally and structurally diverse. It has been reported that CaM binds both envelope glycoprotein and MA of Gag protein. In order to reveal the solution structure and the role of CaM-binding, the SAXS studies have been performed [1, 2].

The HIV-1 genome is composed of nine genes, which encode various genome products, such as Env, Gag, Pol, and others. Fig. 1 shows organization of the HIV-1 mature viral particle. In order to understand the role of CaM-binding in these products, relevant proteins were scanned for the presence of potential CaM-binding domains (CaMBDs) using the Calmodulin Target Database [2]. Known or putative CaMBDs are also indicated in Fig. 2.

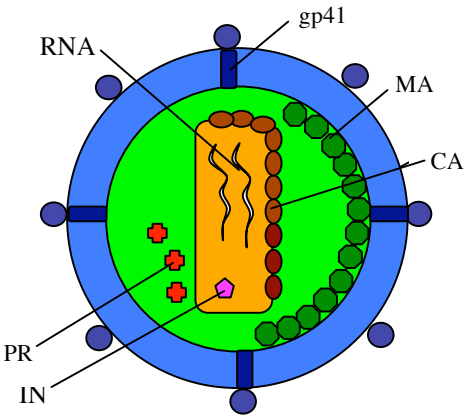

Fig. 1. Organization of the HIV-1 mature viral particle

Materials and Methods

The recombinant CaM and the peptides were prepared as described previously [3]. The SAXS measurements and the data analyses were made as described previously [3].

Results and Discussion

CaM binds each CaMBD of gp41, MA, CA, PR, and IN. The solution structure of each complex depends obviously on the tertiary structure of each CAMBD. Fig. 3 shows a tertiary structural model predicted for the complex of Ca^{2+}/CaM/MA(11-47) [2]. In this model, the two domains of CaM remain essentially unchanged upon complexation. The hinge motions, however, occur in a highly flexible linker of CaM. The complex is principally stabilized by electrostatic interactions. The hydrophobic patches of Ca^{2+}/CaM are not responsible to the binding with the hydrophobic residues in the peptide, suggesting that CaM plays a role to sequester the myristic acid moiety of p17. Further SAXS study has been applied to other complexes to reveal the role of CaM-binding.

Fig.2: Known or putative CaM-binding domain in HIV-1 genome products

Env: (Details are shown in ref. 1)
gp41 769-790 HRLRDLLLIVTRIVELLGRRGW
827-846 DRVIEVVQGACRAIRHIPRR

Gag:
MA 11-47 (Details are shown in ref. 2)
GELDRWEKIRLRPGGKKKYKLKHIVWASRELERFAVN
CA 259-278 GEIYKRWIILGLNKIVRMYS

Pol:
PR 531-549 KPKMIGGIGGFIKVRQYDQ
IN 1318-1335 HLKTAVQMAVFIHNFKRK

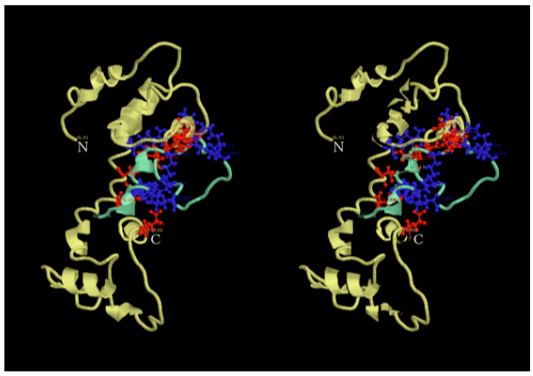

Fig. 3. Stereo view of a tertiary structural model predicted for the complex of Ca^{2+}/CaM/MA(11-47).

References

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