The intrinsically disordered C-terminal F domain of the ecdysteroid receptor from *Aedes aegypti* exhibits metal ion-binding ability.

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Rok wydania

2019

Czasopismo

Journal of Steroid Biochemistry and Molecular Biology

Numer woluminu

186

Strony

42-55

DOI

10.1016/j.jsbmb.2018.09.008

Kolekcja

Naukowa

Język

Angielski

Streszczenie

The dominant vector of dengue and Zika diseases is a female *Aedes aegypti* mosquito. Its reproduction is controlled by the formation of an active heterodimer complex of the 20-hydroxyecdysone receptor (EcR) and Ultraspiracle protein (Usp). Although EcR exhibits a structural and functional organization typical of nuclear receptors (NRs), the EcR C-terminus has an additional F domain (AaFEcR) that is rarely present in the NRs superfamily. The presence of F domains is evolutionarily not well conserved in the NRs. The structure-function relationship of EcR F domains in arthropods is unclear and enigmatic. To date, there have been no data concerning the structure and function of AaFEcR.

Our results showed that AaFEcR belongs to a family of intrinsically disordered proteins (IDPs) and possesses putative pre-molten globule (PMG) characteristics. Unexpectedly, additional amino acid composition *in silico* analyses revealed the presence of short unique repeated Pro-His clusters forming an HGPHPHPHG motif, which is similar to those responsible for Zn^{2+} and Cu^{2+} binding in histidine-proline-rich glycoproteins (HPRGs). Using SEC, SV-AUC and ESI-TOF MS, we showed that the intrinsically disordered AaFEcR is able to bind metal ions and form complexes with these ions. Our studies provide new insight into the structural organization and activities of the F domains of NRs. This unique for the F domains of NRs ion-binding propensity demonstrated by the AaFEcR domain may be a part of the ecdysteroid receptor's mechanism for regulating the expression of genes encoding oxidative stress-protecting proteins.

Słowa kluczowe

Aedes aegypti, Ecdysteroid receptor, Zika and dengue vector, nuclear receptors, Intrinsically disordered proteins

Adres publiczny

http://dx.doi.org/10.1016/j.jsbmb.2018.09.008

Strona internetowa wydawcy

http://www.elsevier.com