Ni(II) interaction with a peptide model of the human TLR4 ectodomain.

Autorzy

Massimiliano Peana

Karolina Zdyb

Serenella Medici

Alessio Pelucelli

Giancarlo Simula

Elżbieta Gumienna-Kontecka

Maria Antonietta Zoroddu

Rok wydania

2017

Czasopismo

Journal of Trace Elements in Medicine and Biology

Numer woluminu

44

Strony

151-160

DOI

10.1016/j.jtemb.2017.07.006

Kolekcja

Naukowa

Język

Angielski

Typ publikacji

Artykuł

Streszczenie

Ni(II) stimulates innate immunity *via* the direct binding to human Toll Like Receptor 4 (hTLR4), the bacterial lypopolysaccharide receptor. The binding is specific for humans and causes nickel contact allergy. The protein sequence analysis of hTLR4 revealed that the ectodomain, the region supposed to coordinate the metal ions, contains a histidine-rich motif that is not conserved among all organisms. To elucidate the role of each histidine residue on the protein–nickel binding, we examined the formation of Ni(II) complexes with the model peptide NH_2-FQHSNRKQMSERSVFRSRRNRIYRDISHTHTR-COO^-, which encompasses the sequence 429–460 of hTLR4. The amino acid sequence of the peptide has been modified by the substitution of some selected lipophilic residues (Leu and Phe) with hydrophilic residues (Arg), aiming at increasing the peptide hydro solubility of the protein fragment. Potentiometric, ultraviolet-visible (UV–vis), nuclear magnetic resonance (NMR) and circular dichroism (CD) measurements demonstrate that the non-conserved histidines in the ectodomain cooperate in metal coordination and consequently enable the activation of the molecular mechanism of nickel hypersensitivity reaction.

Słowa kluczowe

nickel allergy, Human TLR4, Human toll-like receptor, Contact allergy, nickel hypersensitivity, nickel peptide interaction, metal complexes, ATCUN motif

Adres publiczny

https://doi.org/10.1016/j.jtemb.2017.07.006

Strona internetowa wydawcy

http://www.elsevier.com