Fusobacterium nucleatum's Copper-FomA Proteins: Driving Cancer Forward

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Streszczenie

FomA is a major outer membrane protein of *Fusobacterium nucleatum* (Fn) overexpressed in colorectal cancer (CRC) tissues, where increased levels of Cu ions together with reactive oxygen species (ROS) were noted. In this comparative study, the connection between *Fn* surrounded by copper ions and the ROS overgeneration leading to the development of CRC is examined. Our study focused on a model peptide Ac-KGHGNGEEGTPTVHNEYH-NH_2 (**6L**) derived from the FomA reflecting a fragment of the protein loop no. 4, exposed to the external environment, which facilitates the binding of Cu ions. The coordination studies (potentiometric titration, UV–Vis, CD, EPR) showed that the **6L** bound Cu(II) and formed mono-, di-, and trinuclear complexes depending on the solution pH. The ability to generate ROS by promoting the Cu(III)/Cu(II)/Cu(I) redox cycle was proven by CV and EPR techniques. We also confirmed that upon adding Asc, the **6L** was fragmented and after copper coordination, the ROS production increased (e.g., $^{\bullet}OH$, $^{1}O_2$, $O_2^{\bullet-}$), leading to DNA damage. Stimulation of model mouse colon carcinoma cells by Cu(II) complex with **6L** demonstrated an abundant cellular ROS production, resulting in pronounced lipid peroxidation. Hypothetically, this action mode leads to the damage of colon cells and triggers carcinogenesis processes.

Słowa kluczowe

Free radicals, Hydroxyls, Ions, Ligands, Peptides and proteins