

Molecular and Structural Characterization of *Entamoeba histolytica* tRNA-guanine transglycosylase. An integrated study using structural biology and physiology.

Initiative: zukunft.niedersachsen (nur ausgewählte Ausschreibungen)

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Amebiasis is an intestinal disease transmitted by the protist parasite *Entamoeba histolytica*, following the ingestion of contaminated food and water. Poor sanitary conditions and unsafe hygiene practices existing in many parts of the world make of amebiasis a global medical problem: the World Health Organization estimates that 50 million people in India, Southeast Asia, Africa, and Latin America suffer from amebic dysentery and amebiasis causes the death of at least 100,000 individuals each year. The parasite resides in the colon and most infected individuals are asymptomatic. For unknown reasons, the parasite can become virulent and invasive, cause amebic dysentery, and migrate to the liver, where it causes hepatocellular damage. No vaccine against amebiasis currently exists; the only available treatment is based on metronidazole, which however may have severe side effects. Additionally, emergence of metronidazole-resistant strains have been reported in hospitalized patients. In this work the scientists want to investigate a pathway of stress-survival of *E. histolytica* based on tRNA chemical modifications. The goal is establishing the key players along this pathway as drug-targets. RNA modifications are emerging as an essential means to maintain the cell life cycle in numerous contexts, ranging from infection to neuropathologies and cancer. More than 100 RNA chemical modifications are known to date, addressing all RNA species. Nevertheless, RNA modifying enzymes have not yet been exploited as drug targets. In this project, an Israeli laboratory, with expertise in molecular biology of *E. histolytica*, joins forces with a German laboratory, with experience in structural biology and enzyme mechanisms, to establish a specific tRNA modification pathway as a novel drug target to treat amebiasis.

Projektbeteiligte

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