Pathogenic Yeast Candida parapsilosis and Its Carbonic Anhydrase

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The yeast Candida parapsilosis is a so-called opportunistic pathogen. It is harmless for healthy people, however, it is a serious threat to immunocompromised individuals, e.g organ transplant recipients, or HIV/AIDS patients. Pathogenic Candida species can be disseminated into the entire body of these patients, causing infections with high mortality rates. C. parapsilosis is successful pathogen due to its ability to adapt to different conditions, such as changes in pH, temperature, or atmosphere. Candida can thrive on human skin, as well as in bloodstream. These environments differ, among other, in CO2 concentration. While in the air there is less than 0.04 % CO2, in the bloodstream the CO2 concentration reaches approximately 5%. To cope with these dramatic changes, living organisms use enzymes called carbonic anhydrases (CAs). They catalyse reversible hydration of CO2 to HCO3-. Although this reaction proceeds spontaneously in nature, CAs accelerate it by 10000-fold. Analysis of C. parapsilosis genome has revealed only one gene potentially encoding CA. It has been denominated NCE103 on the basis of homology with a gene in Saccharomyces cerevisiae, encoding an enzyme with a CA activity. However, over 90% of C. parapsilosis genes have not been characterised, and it has been unclear, whether the gene product of NCE103 is really a CA. Therefore I expressed NCE103 in Escherichia coli, optimised chromatographic procedures in order to obtain purified protein from bacterial lysates, and finally, I proved that Nce103p, the protein encoded by NCE103, displays a carbonic anhydrase activity. I also measured inhibition constants for several potential inhibitors. At present, I am trying to obtain Nce103p crystals for structural analysis, as well as to search more Nce103p inhibitors

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