Developing topics

Tyramine and amyloid beta 42: A toxic synergy

Sudip Dhakal | Ian George Macreadie

RMIT University, Melbourne, Australia

Correspondence
Sudip Dhakal, RMIT University, Melbourne, VIC, Australia.
Email: dhakal.sudip001@gmail.com

Abstract

Background: In synaptic cleft, trace amines play a crucial role as neurotransmitter signaling through the trace amine associated receptors. Tyramine, an important trace amine formed by decarboxylation of tyrosine, has been reported to be implicated in various diseases including schizophrenia, Parkinson’s disease, migraine and Huntington’s disease. However, there are no investigations to find its connection with Alzheimer’s disease (AD).

Method: Genetically modified Saccharomyces cerevisiae BY4743 producing different forms of amyloid beta 42 (Aβ42) peptide including native Aβ42 and green fluorescent protein (GFP) fused to Aβ42 were treated with various concentrations of tyramine. Reactive oxygen species (ROS) produced in these strains were measured using 2′,7′-dichlorodihydrofluorescein diacetate (H2DCF-DA) staining in a flow cytometric analysis. Growth inhibition of the yeast strains producing GFP and GFP-Aβ42 were analysed in presence of tyramine. Petites generated due to tyramine were estimated in both these strains and petite frequency calculated.

Result: Tyramine was found to induce ROS formation in S. cerevisiae BY4743 as well as its genetically modified variants. ROS formation in yeast strains producing native Aβ42 treated with tyramine was significantly synergistically higher as compared to experimental controls. Similarly, yeast strains producing GFP-Aβ42 was found to be inhibited more in media containing ethanol as sole carbon source compared to GFP producing controls in presence of 3 mM tyramine. Additionally, petite frequency in yeast strains producing GFP-Aβ42 were found to increase significantly from around 20% to nearly 80% when grown in presence of tyramine.

Conclusion: These findings suggest that tyramine in presence of Aβ42 is synergistically toxic to yeast cells by inducing ROS formation and causing petite mutation, implying possible cause of mitochondrial damage evident in AD patients. The study also demonstrates yeast as model to study compounds that have potential to exacerbate AD.