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### Efavirenz as a potential anti-Alzheimer's disease medication

Efavirenz is the anti-HIV medication given daily at a 600 mg dose to keep the viral load low. We found that in mice, a very low dose of efavirenz (100-times lower than that given to HIV patients) enhances the activity of the brain enzyme cytochrome P450 46A1 (CYP46A1), which converts cholesterol to 24-hydroxycholesterol. Cholesterol 24-hydroxylation is the major pathway of cholesterol elimination from the brain; CYP46A1 controls this pathway and thereby cholesterol turnover in the brain. 5XFAD mice, a model of rapid amyloidogenesis, were treated daily with a 0.1 mg/kg of body weight efavirenz dose, which was delivered in drinking water. The treatment started at one month of age and continued for eight months. Efavirenz administration stably activated CYP46A1 and enhanced cholesterol turnover in the 5XFAD brain. 5XFAD mice also had a significant reduction in amyloid- $\beta$  burden and microglia activation in the brain cortex and hippocampus. Mouse performance was improved in Morris water maze test, and the treated animals had a significant reduction in mortality rates. The data obtained suggest that efavirenz should be considered as an anti-Alzheimer's disease medication, and the pathway of the brain cholesterol removal as a therapeutic target for this disease. A clinical trial is in progress to evaluate efavirenz effects on people with mild cognitive impairment due to Alzheimer's disease.

### Biography

Irina A Pikuleva has completed her PhD in Biochemistry from the Belorussian Academy of Sciences and completed her Post-doctoral studies at Vanderbilt University. Currently, she is the Vice Chair for Research of the Department of Ophthalmology and Visual Sciences and Director of the Visual Sciences Research Center at Case Western Reserve University. She has published more than 100 peer-reviewed papers and has served as a Reviewer on the study sections of the National Institutes of Health as well as private foundations.

[iap8@case.edu](mailto:iap8@case.edu)



**Irina A Pikuleva**

Case Western Reserve University, USA

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