

A Helping HAND: Therapeutic Potential of MAGL Inhibition Against HIV-1-associated Neuroinflammation

Alexis F. League^{1,*}, Barkha J. Yadav-Samudrala¹, Ramya Kolagani¹, Calista A. Cline¹, Ian R. Jacobs¹, Jonathan Manke², Micah J. Niphakis³, Benjamin F. Cravatt³, Aron H. Lichtman⁴, Bogna M. Ignatowska-Jankowska⁵, and Sylvia Fitting^{1,*}

¹ Department of Psychology and Neuroscience, University of North Carolina at Chapel Hill, Chapel Hill, NC 27599, USA

² Department of Pharmaceutical Sciences, Skaggs School of Pharmacy and Pharmaceutical Sciences, University of Colorado Anschutz Medical Campus, Aurora, CO 80045, USA

³ Department of Chemistry, Scripps Research, La Jolla, CA 92037, USA

⁴ Department of Pharmacology and Toxicology, Virginia Commonwealth University, Richmond, VA 23284, USA

⁵ Neuronal Rhythms in Movement Unit, Okinawa Institute of Science and Technology, Okinawa, 904-0495, JP

* Correspondence: leagueaf@protonmail.com, sfitting@email.unc.edu

Keywords: HIV-1; inflammation; transactivator of transcription (Tat); endocannabinoids; HETE; monoacylglycerol lipase (MAGL)

Supplemental Material

Figure Caption

Figure S1. Quantification of hippocampal lipid mediators. Heatmap of all lipid mediators assessed (**top**). Summary data from significant findings (**A-D**). (**A**) A significant genotype x drug interaction was noted for 12-HETE with group comparisons revealing no significant differences. (**B, C**) MJN110 treatment significantly decreased 15-HETE and 5-HETE/14(15)-EET levels. (**D**) Tat expression significantly increased 11-HETE levels, which was specifically seen in the vehicle-exposed groups, also demonstrated by a significant genotype x drug interaction. All data are expressed as mean $\pm$ the standard error of the mean (SEM). Statistical significance was assessed by ANOVAs followed by Tukey's post hoc tests when appropriate; $^*p = 0.046$ main effect of genotype, $^{\#}p < 0.05$ main effect of drug, $^{\S}p \leq 0.05$ genotype x drug interaction, $^ap = 0.032$ vs. vehicle-treated Tat(+) mice. Individual subject data are represented by open circles.

