# The Effects of Propofol on Efflux Activity in Alzheimer's Disease Human Stem Cell-Derived Blood-Brain Barrier Models

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Propofol is a common induction anesthetic that recently has been shown to diminish the integrity of the blood brain barrier (BBB) while maintaining efflux protein expression and activity. Furthermore, Alzheimer's disease (AD), a neurodegenerative condition, compromises the integrity of the BBB including suppressed efflux activity. Efflux transporters, notably MRP-1, BCRP, and P-gp, play a role in clearing cytotoxic metabolites. The role of propofol on the activity of efflux proteins in AD patients is unknown. The goal of this study was to utilize human induced pluripotent stem cell (iPSC)-derived brain microvascular endothelial cells (BMECs) differentiated from familial AD iPSCS (*APP*, *PSEN1*, and *PSEN2*) and healthy iPSCs to determine the effects of propofol on efflux activity and expression.

To measure the effect of propofol on efflux activity, treated cells were exposed to 50μM propofol for three hours and then specific efflux fluorescent substrates and inhibitors were utilized to determine efflux activity ( P-gp: Rhodamine 123/CsA; MRP-1: DCFDA/MK571; BCRP: Hoechst/KO143). Cells were lysed and the fluorescent substrate was quantified by a plate reader and normalized to the uninhibited group. The difference between the inhibited and uninhibited groups were used to determine the efflux activity. Efflux protein expression was also qualitatively assessed using immunostaining.

Our preliminary results demonstrated that propofol did not affect efflux activity similar to previous literature. Interestingly, *PSEN 1* and *PSEN2* had suppressed baseline efflux transporter activity and did not show any change following propofol exposure. *APP*-derived BMECs displayed suppressed P-GP activity and similarly to *PSEN 1/2*-derived BMECs were not altered by propofol. Our preliminary results implicate that AD-derived BMECs have suppressed baseline efflux activity; however propofol exposure did not further alter activity level. Additional studies are needed to determine the role of anesthesia-induced injury on efflux activity and expression.