

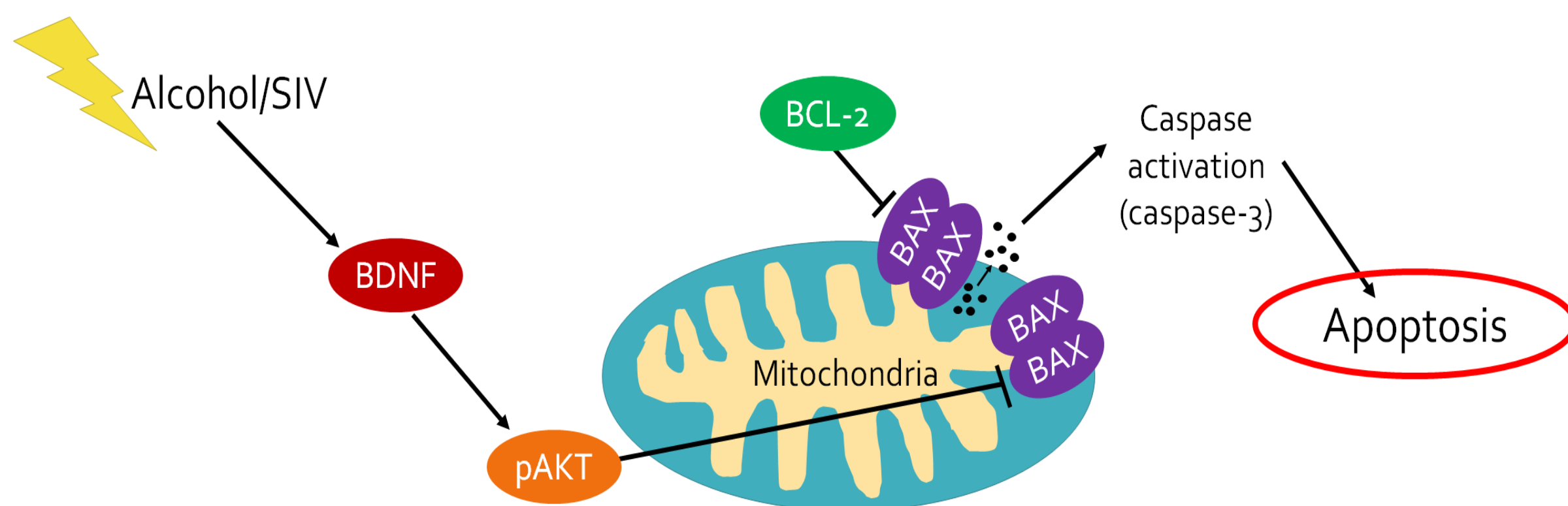
# Chronic Binge Alcohol Administration Enhances Pre-Frontal Cortex Apoptotic Signaling In SIV-Infected Rhesus Macaques

Jacob Elnaggar, John Maxi, and Patricia Molina, M.D., Ph.D.

Department of Physiology, LSU Health Sciences Center

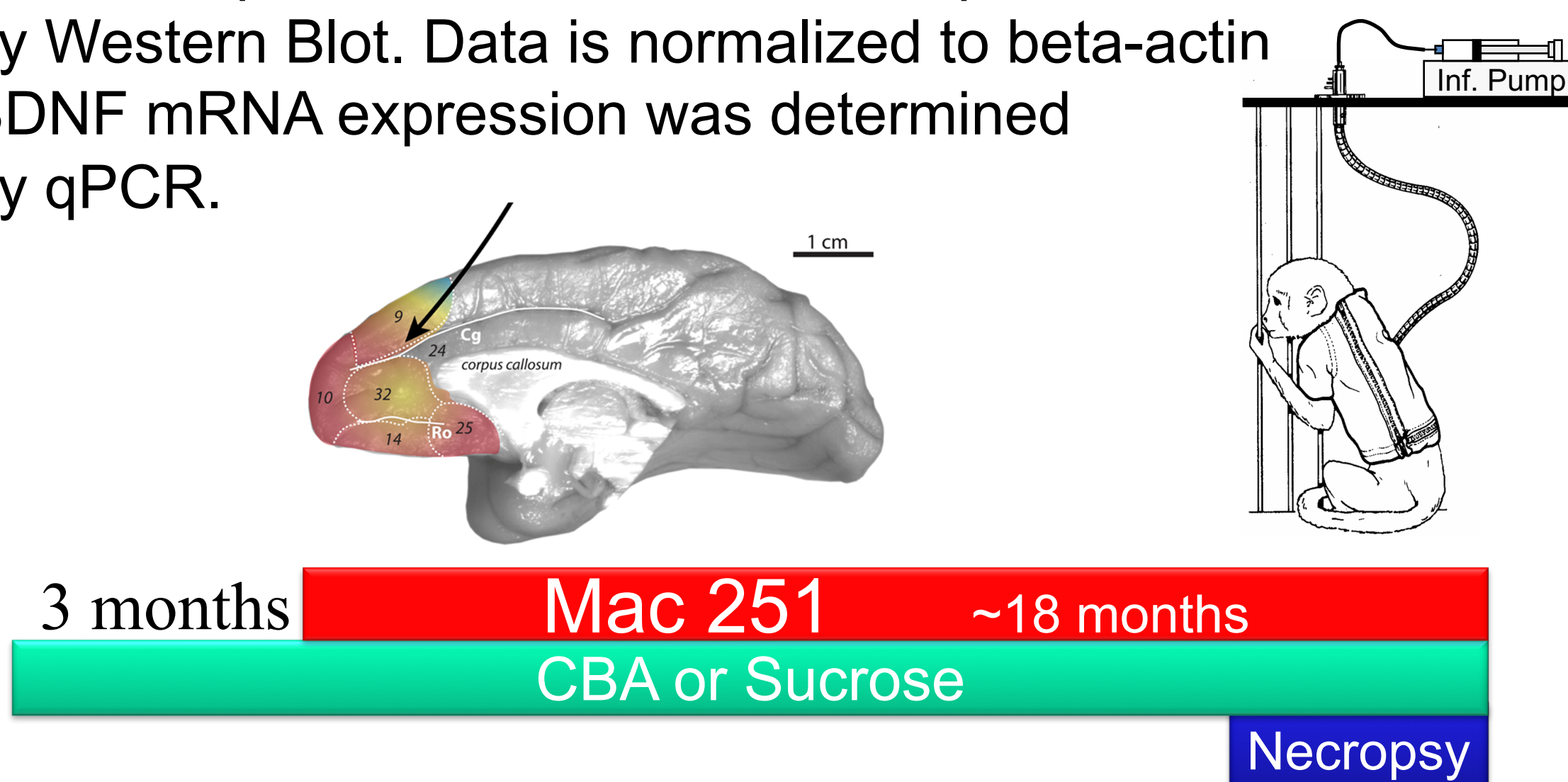
## Introduction

- The frequency of heavy alcohol use in individuals living with HIV/AIDS is double that of the general population. Alcohol abuse increases the rate of HIV-associated neurocognitive disorder (HAND) development.
- In our non-human primate model of HIV infection, chronic binge alcohol (CBA) administration unmasks neurocognitive deficits in Simian Immunodeficiency Virus (SIV)-infected macaques.
- Neuronal apoptosis may be an underlying mechanism for neurocognitive disorders in CBA-administered SIV-infected macaques.
- We hypothesized that there is an increase in pro-apoptotic signaling in the pre-frontal cortex of CBA/SIV infected macaques.**

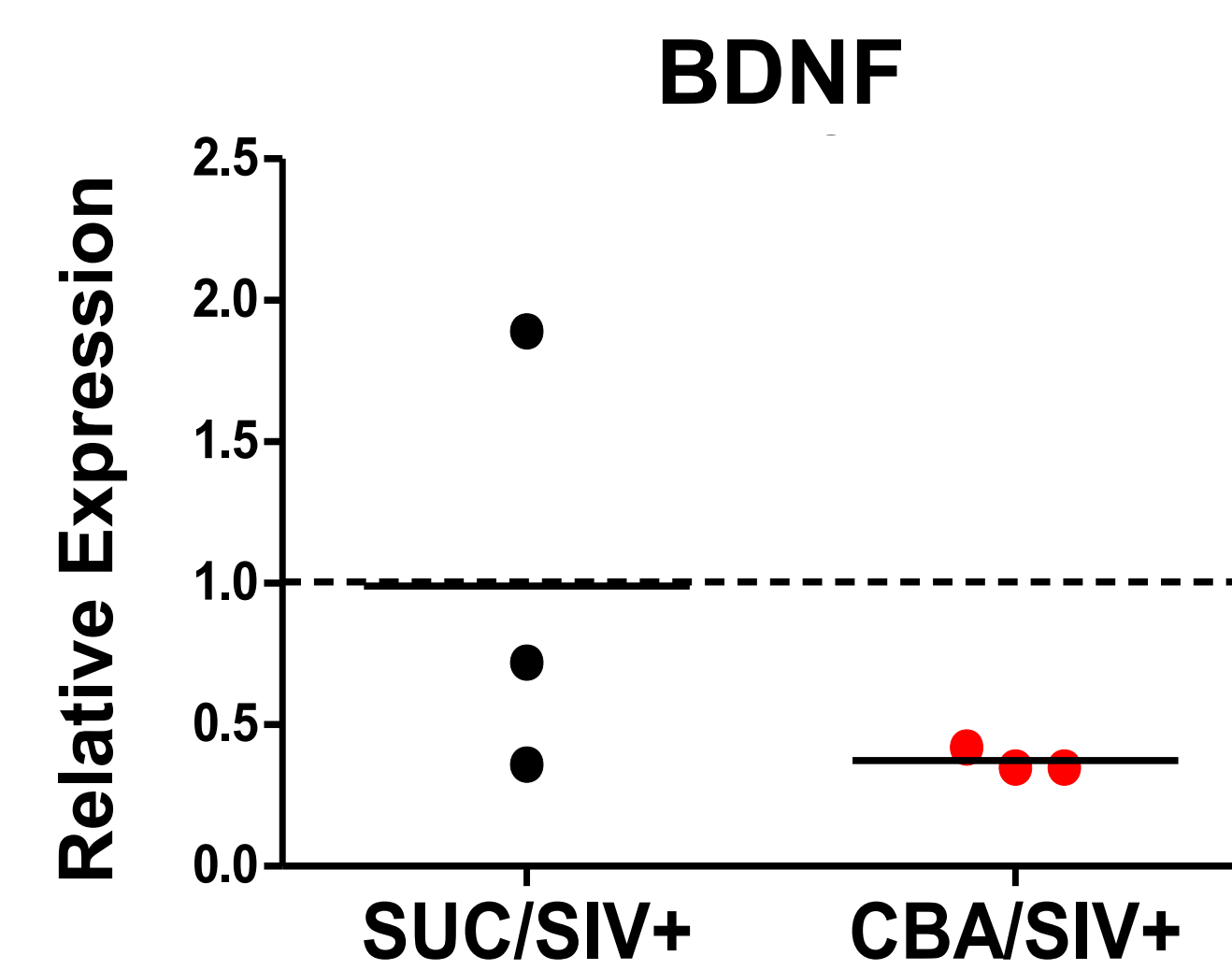


## Methods

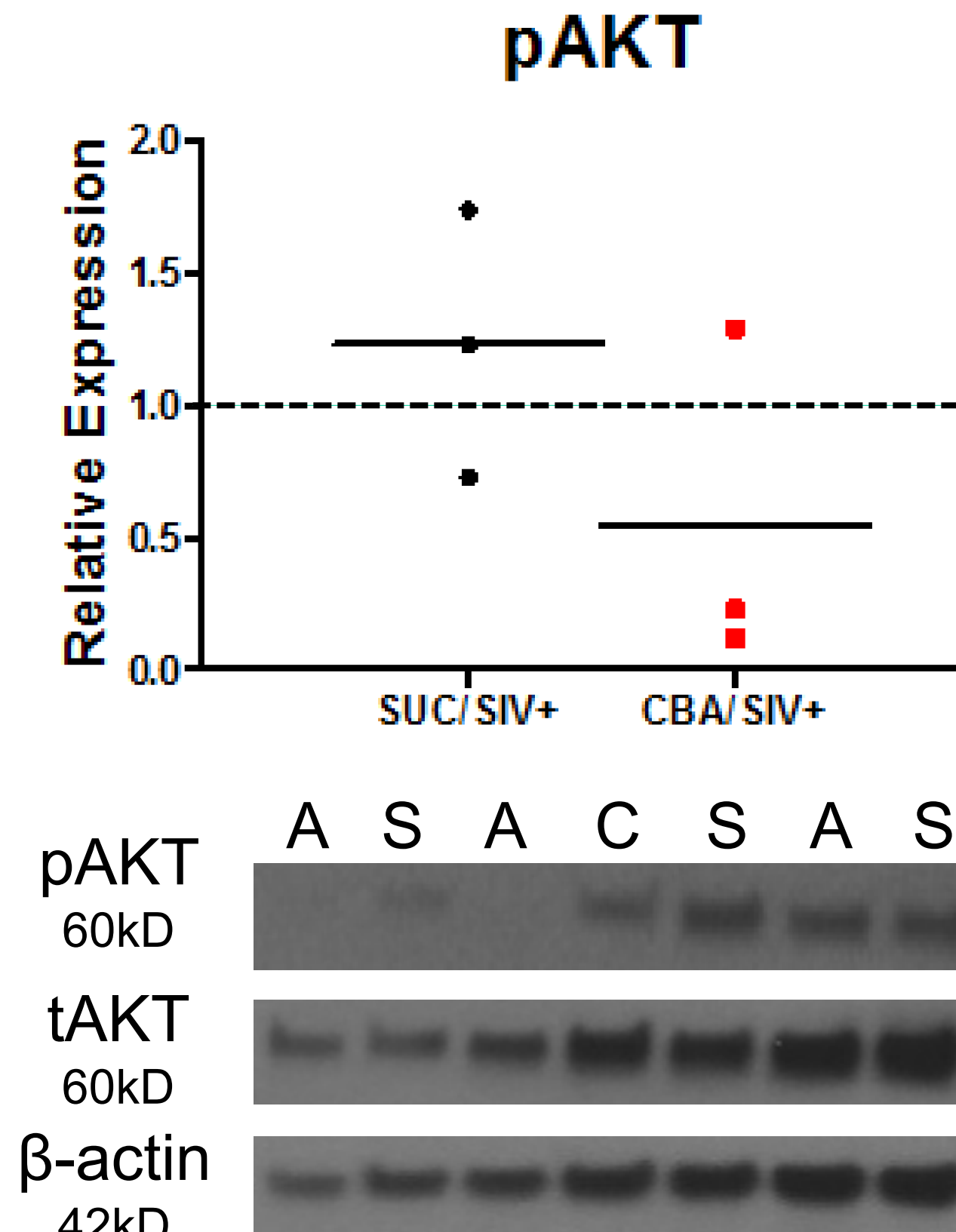
- Male rhesus macaques were surgically fitted with a gastric catheter for the infusion of alcohol (13–14 g of ethanol/kg body weight per week; 30% w/v water) or sucrose starting 3 months prior to inoculation with SIVmac251.
- Three experimental groups: CBA/SIV (n=3), sucrose/SIV (n=3), and Naïve, SIV- (n=1)
- Animals were sacrificed at ~18 months after SIV
- Brains were excised and pre-frontal cortex isolated
- Protein expression of Bax, Bcl-2, and pAKT was determined by Western Blot. Data is normalized to beta-actin
- BDNF mRNA expression was determined by qPCR.



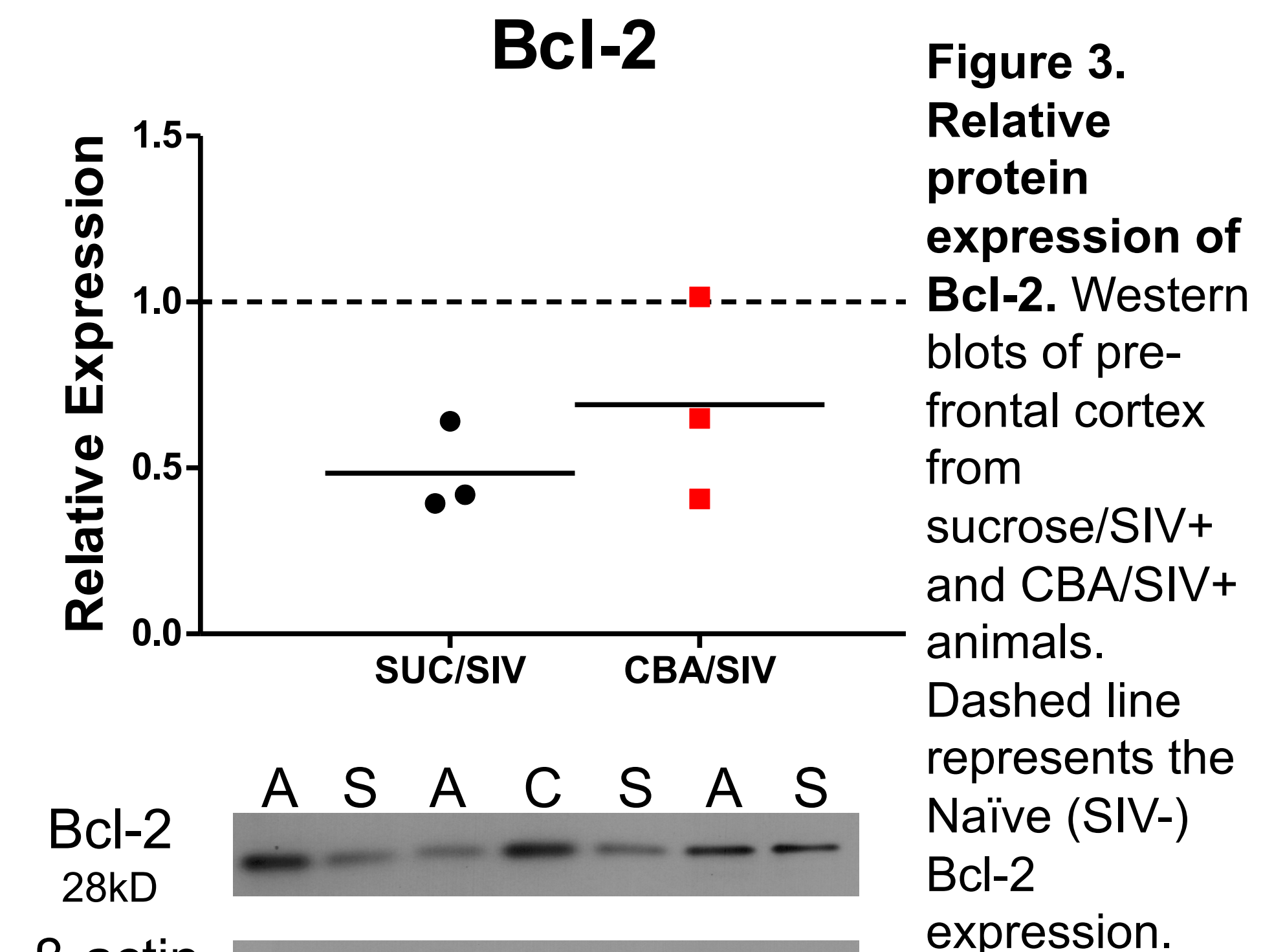
## Anti-apoptosis



**Figure 1. Relative mRNA expression of *Bdnf*.** qPCR of pre-frontal cortex from sucrose/SIV+ and CBA/SIV+ animals. Dashed line represents the Naïve (SIV-) BDNF expression.

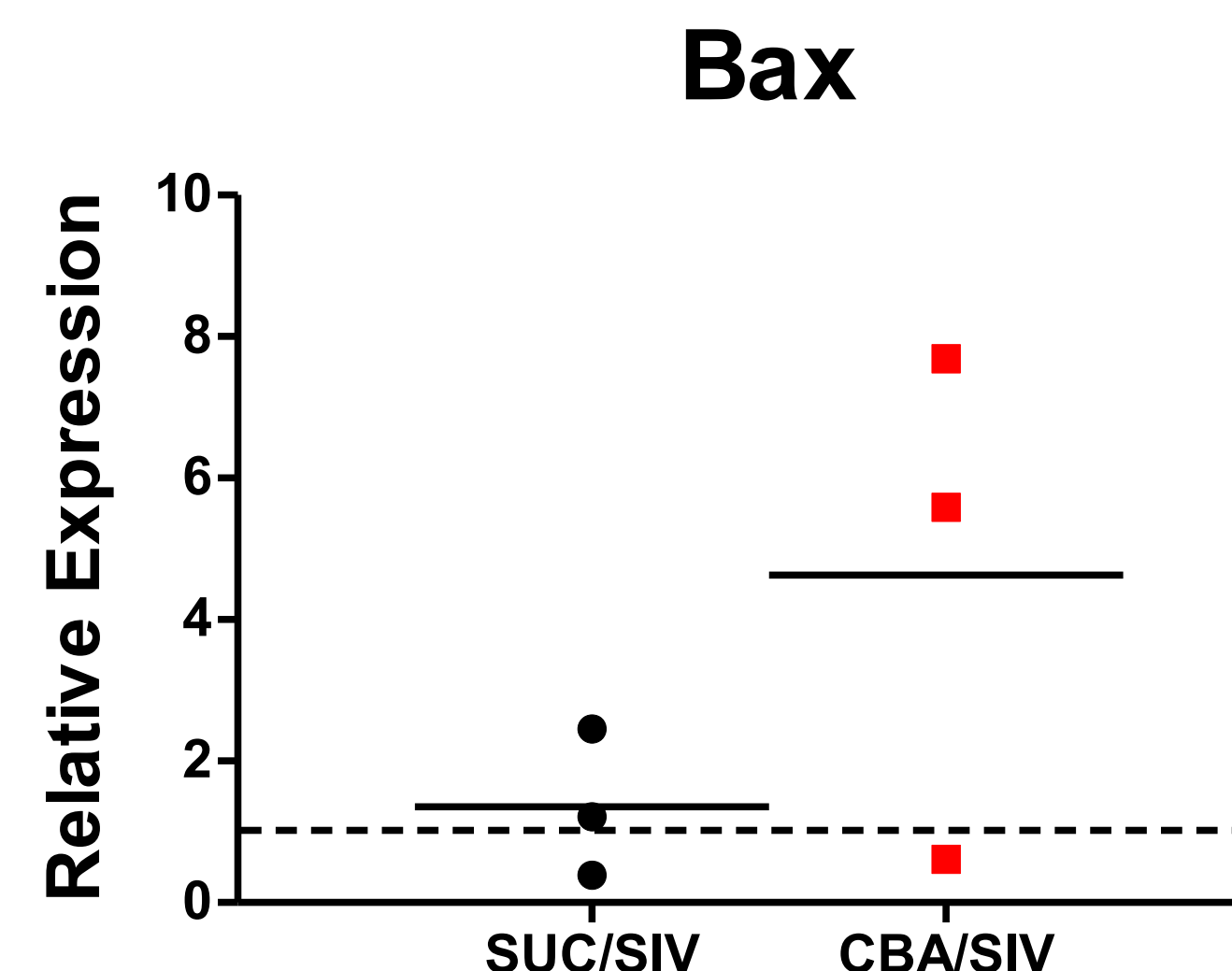


**Figure 2. Relative protein expression of pAKT.** Western blots of pre-frontal cortex from sucrose/SIV+ and CBA/SIV+ animals. Dashed line represents the Naïve (SIV-) pAKT expression.

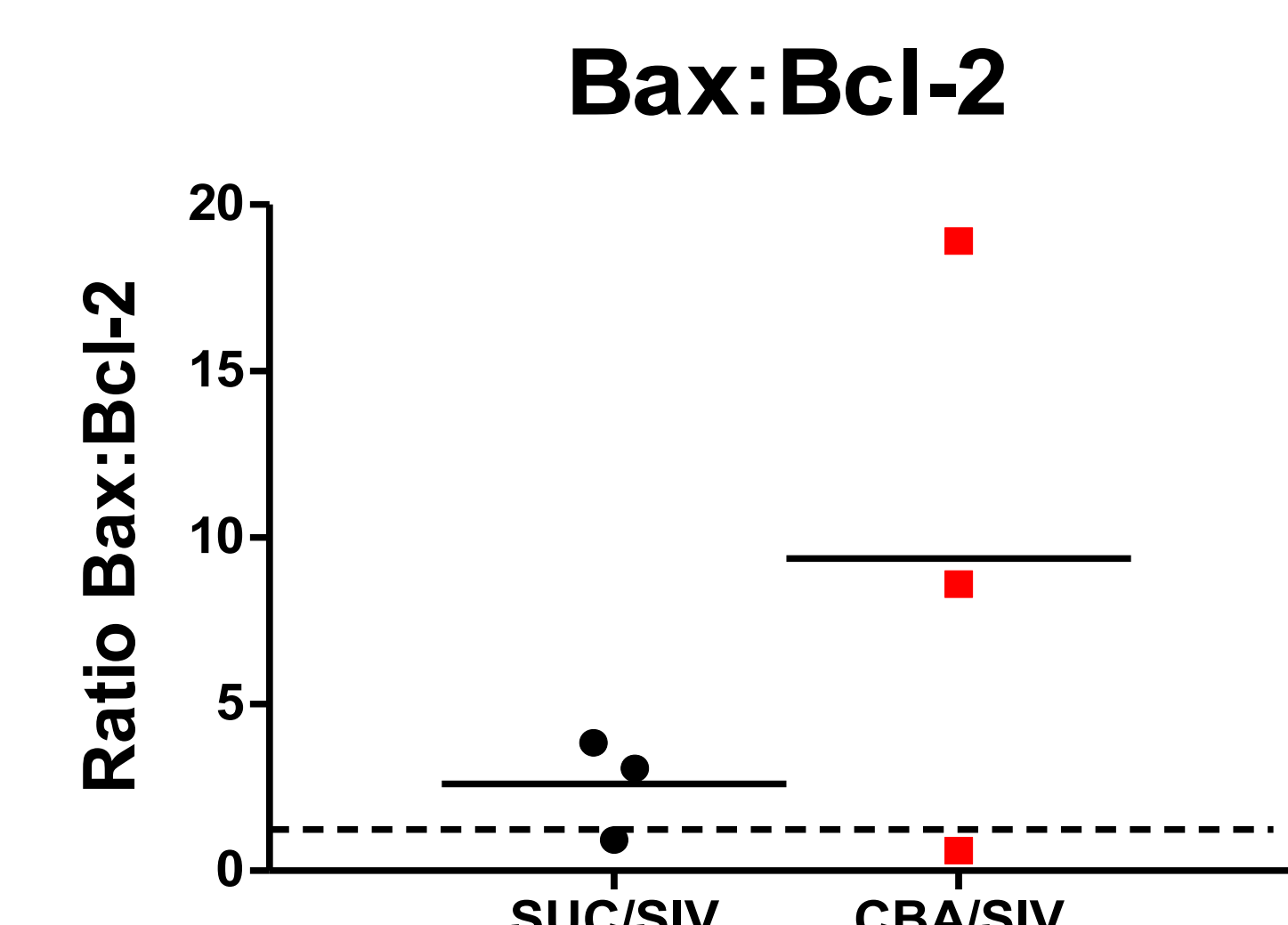


**Figure 3. Relative protein expression of Bcl-2.** Western blots of pre-frontal cortex from sucrose/SIV+ and CBA/SIV+ animals. Dashed line represents the Naïve (SIV-) Bcl-2 expression.

## Pro-apoptosis



**Figure 4. Relative protein expression of Bax.** Western blots of pre-frontal cortex from sucrose/SIV+ and CBA/SIV+ animals. Dashed line represents the Naïve (SIV-) Bax expression.



**Figure 5. Ratio of Bax to Bcl-2.** Ratio of the expression of Bax to Bcl-2. These proteins work in opposition of each other. Increased Bax/Bcl-2 ratio up-regulates caspase-3 and increases the apoptotic occurrence in the of pre-frontal cortex of the animal. Dashed line represents the ratio of the Naïve (SIV-) animal.

## Summary

- Our results showed enhanced Bax expression and suppressed Bcl-2 expression in two of the three CBA/SIV+ macaques, when compared to the sucrose/SIV+ macaques.
- The ratio between Bax and Bcl-2 suggests enhanced apoptotic signaling in CBA/SIV infected macaques.
- Decrease in pAKT and BDNF indicate less anti-apoptotic signaling in CBA/SIV infected macaques.
- These findings demonstrate the need for further investigation of the combination of alcohol and SIV infection on neuronal apoptosis in animals as a potential mechanism underlying cognitive deficits.