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14. ABSTRACT
The effect of fumaric acid esters (DMF/MMF) on the CAA outcomes after TBI is postulated to be positive, though several discrepancies remain. Nrf2 is one of the master regulators of redox and inflammation. DMF and its metabolite MMF hold antioxidative and anti-inflammatory by activating Nrf2. Thus, we expect that understanding the unique and respective roles of DMF and MMF on Nrf2 on CAA neuroprotection is essential, and its validation in TBI would strengthen their potential use for veterans and active military people. However, whether DMF has superior beneficial effects over MMF or vice versa is unclear. Furthermore, whether the therapeutic window would defer from acute TBI over a repetitive concussion-like brain insult leading to CAA needs to be tested. Considering these knowledge gaps, we aim to start answering these questions using preclinical models. We maintain/renewed the animal protocols approved by the Institutional IACUC from 07/18/2022 to 07/18/2025. During the institutional COVID-19 Lab shutdown, we had to sac mice and stop the breeding; we restarted the knockouts and the generation and characterization of the new cre-flox inducible conditional knockouts.

15. SUBJECT TERMS
NONE LISTED

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1. Introduction

Subject: Please be advised that the PI on this project, Dr Sylvain Dore, has recently resigned. This report was prepared by Cibele Castro who worked on the project as a post-doctoral associate. The effect of fumaric acid esters (DMF/MMF) on the CAA outcomes after TBI is postulated to be positive, though several discrepancies remain. Optimizing their respective effectiveness in both acute severe and mild repetitive head trauma is essential for the design of optimal TBI trials. Nrf2 is one of the master regulators of redox and inflammation. DMF and its metabolite MMF hold antioxidative and anti-inflammatory by activating Nrf2 and have been approved for multiple sclerosis and psoriasis. Thus, we expect that understanding the unique and respective roles of DMF and MMF on Nrf2 on CAA neuroprotection is essential. Its validation in two complementary TBI models would strengthen their potential use for veterans and active military people. Hypothesis and Purpose: Preclinical studies raised questions, and it is unclear whether DMF has superior beneficial effects over MMF or vice versa. Furthermore, whether the therapeutic window would defer from acute TBI over a repetitive concussion-like brain insult leading to CAA needs to be tested. Considering these knowledge gaps, it is essential to determine the optimal DMF and MMF therapeutic regimens and validate their respective effectiveness in two complementary TBI models. Goals: Aim 1 is to determine whether DMF/MMF treatment attenuates AD and/or CAA neurobehavioral and pathophysiological outcomes following TBI. Aim 2 is to test whether the DMF/MMF-associated CAA neuroprotective mechanism after TBI is mediated through the Nrf2 upregulation using global $Nrf2^{-/-}$. Thus far, we got the animal's protocols approved by the Institutional IACUC, and then by the ACURO, we got the CCI protocol standardized; we started the breeding to generate enough of the global knockout and also started the generation and characterization of the new cre-flox inducible conditional knockouts for the Aim 3. Though during the institutional COVID-19 Lab shutdown, we had to sac all mice and stop the breeding, we have only recently restarted the generation of knockouts and characterization of the new cre-flox inducible conditional knockouts.

2. Keywords

Alzheimer, Cerebral amyloid angiopathy, Fumaric acid esters, Transcription factor

3. Accomplishments

- What were the major goals of the project?

AIM 1

Subtask 2: Treat animals with DMF/MMF after TBI, do behavioral, harvest brains, and brain slicing

AIM 2

Major Task 2: Repeat the optimal conditions in the $Nrf2^{-/-}$ mice

AIM 3

Major Task 3: Based on the result from Aim 2, select the first cre mice to breed with the $Nrf2^{fl}$ mice (and compare results with matched controls)

- What was accomplished under these goals?

AIM 1

Following the behavioral tests, mice were sacrificed with the brain harvested. Each brain was sliced to a thickness of 2mm using a matrix and stained using mouse IgG, Ab3 Ab5, GFAP, H&E, and Iba1 antibodies, as well as Perls Prussian Blue and Cresyl Violet.

We have completed the inventory on -20C freezers and stained the remaining tissue from AIM 1. Our undergraduates and techs are actively working on the quantification process so we can complete the data analyses for Aim 1.

AIM 2

Major Task 2: Repeat the optimal conditions in the $Nrf2^{-/-}$ mice

We have made strides in our breeding scheme, moving forward with the F2 $Nrf2^{+/+}$ and $^{-/-}$ pups. The next step involves breeding these pups with the F1 CRND8 $Nrf2^{+/-}$ male. This particular choice primarily mitigates the risk of spontaneous death in mothers, a phenomenon observed when CRND8 females are involved in breeding. As a result of this process, we anticipate the generation of extra females; while it might seem like a surplus, these additional mice present an invaluable opportunity to improve the robustness of our research outcomes. Specifically, they will be instrumental in calculating the standard deviation to accurately estimate the standard

deviation in the effects of the surgery. This will be done until our experimental mice are born, which should be ~June 28th, 2023 – when we will begin LFAO at P0.

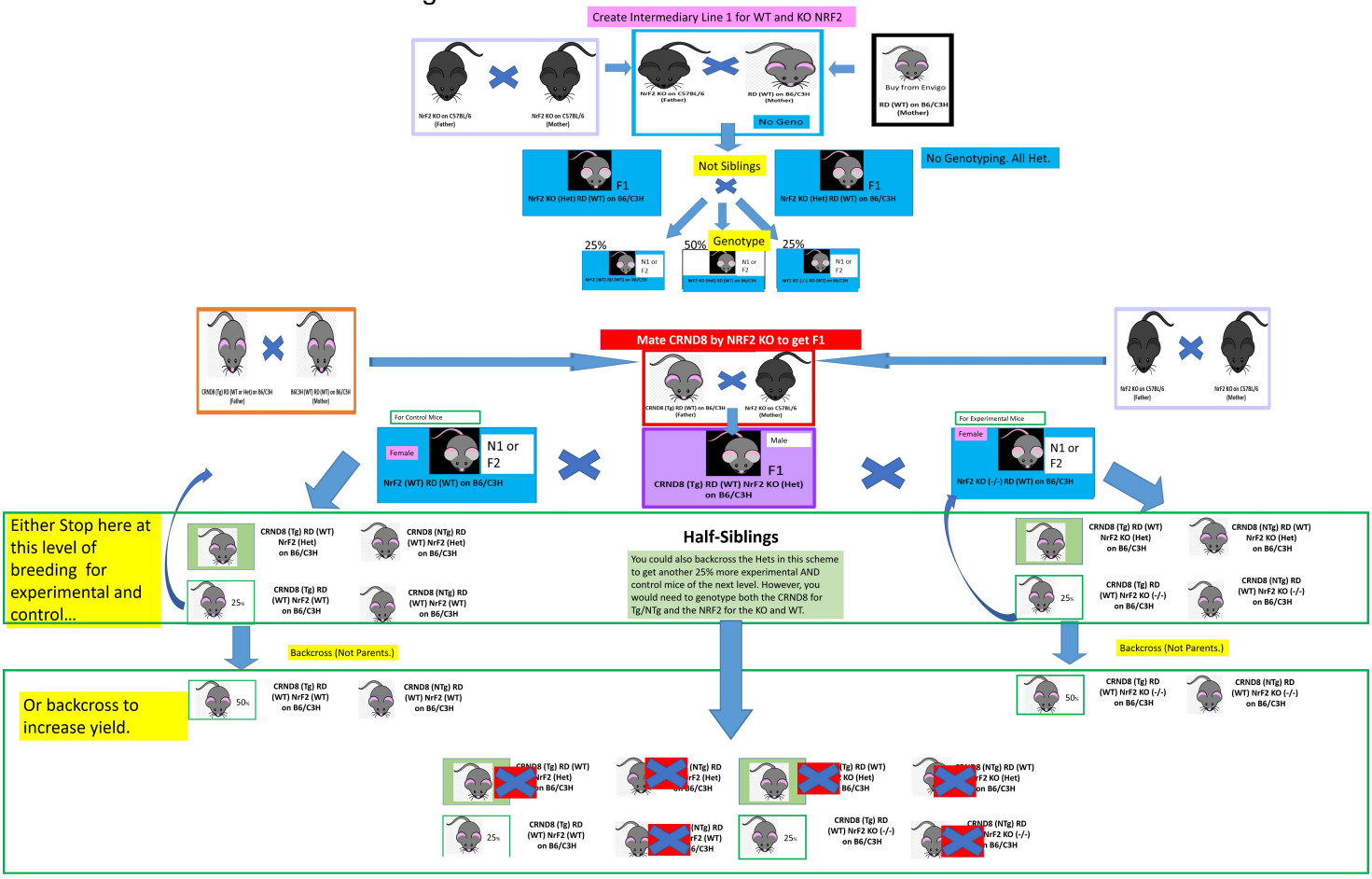

Figure 1: Breeding Scheme 5.0 to boost experimental mouse production and correct for the blindness (i.e., Rb gene) of the mice.

Table 1: Inventory of most mice being maintained exclusively for this research protocol.

Cage Card #	SSB	Birth Date	Sex	# Animals
1311055	Nrf2$^{-/-}$ X B6C3H F1	02/08/23	Male	2
1310835	Nrf2$^{-/-}$ X CRND8 F1	02/06/23	Male	4
1327893	Nrf2$^{-/-}$ X B6C3H F1	04/13/23	Male	4
1327992	Nrf2$^{-/-}$ X CBND8 F1	04/13/23	Male	3
1298655	Nrf2$^{-/-}$	10/31/22	Both	2
1302086	Nrf2$^{-/-}$ X B6C3H	08/08/22	Both	2
1324696	Nrf2$^{-/-}$ X B6C3H F1	04/03/23	Male	5
1300244	Nrf2$^{-/-}$ X B6C3H	08/25/22	Both	2
1300245	Nrf2$^{-/-}$ X B6C3H	09/25/22	Both	2
1300246	Nrf2$^{-/-}$ X B6C3H	08/25/22	Both	2
1300319	Nrf2$^{-/-}$ X B6C3H	11/10/22	Both	2
1300320	Nrf2$^{-/-}$ X B6C3H	08/08/22	Both	2
1300321	Nrf2$^{-/-}$ X B6C3H	11/10/22	Both	2

1300322	Nrf2$^{-/-}$ X B6C3H	11/10/22	Both	2
1300323	Nrf2$^{-/-}$ X B6C3H	08/08/22	Both	2
1300324	Nrf2$^{-/-}$ X B6C3H	11/10/22	Both	2
1300326	Nrf2$^{-/-}$ X B6C3H	08/08/22	Both	2
1302087	Nrf2$^{-/-}$ X B6C3H	08/08/22	Both	2
1302088	Nrf2$^{-/-}$ X B6C3H	09/21/22	Both	2
1302089	Nrf2$^{-/-}$ X B6C3H	08/25/22	Both	2
1302090	Nrf2$^{-/-}$ X B6C3H	08/25/22	Both	2
1302091	Nrf2$^{-/-}$ X B6C3H	08/08/22	Both	2
1327894	Nrf2$^{-/-}$ X B6C3H	04/13/23	Female	5
1300247	Nrf2$^{-/-}$ X B6C3H	01/24/23	Both	2
1298638	Nrf2$^{-/-}$ X B6C3H	08/08/22	Both	2
1298639	Nrf2$^{-/-}$ X B6C3H	08/08/22	Both	2
1298640	Nrf2$^{-/-}$ X B6C3H	08/08/22	Both	2
1298641	Nrf2$^{-/-}$ X B6C3H	09/21/22	Both	2
1298642	Nrf2$^{-/-}$ X B6C3H	08/25/22	Both	2
1298643	Nrf2$^{-/-}$ X B6C3H	08/25/22	Both	2
1298644	Nrf2$^{-/-}$ X B6C3H	08/25/22	Both	2
1298645	Nrf2$^{-/-}$ X B6C3H	08/25/22	Both	2
1298646	Nrf2$^{-/-}$ X B6C3H	11/10/22	Both	2
1298647	Nrf2$^{-/-}$ X B6C3H	11/10/22	Both	2
1298648	Nrf2$^{-/-}$ X B6C3H	11/10/22	Both	2
1298649	Nrf2$^{-/-}$ X B6C3H	11/10/22	Both	2
1300223	Nrf2$^{-/-}$ X B6C3H	08/25/22	Both	2
1322407	Nrf2$^{-/-}$ X B6C3H	08/08/22	Male	1
1317055	Nrf2$^{-/-}$ X B6C3H F1	03/09/23	Male	4
1317056	Nrf2$^{-/-}$ X B6C3H F1	03/09/23	Female	3
1317057	Nrf2$^{-/-}$ X B6C3H F1	03/12/23	Female	5
1317058	Nrf2$^{-/-}$ X B6C3H F1	03/12/23	Male	5
1317059	Nrf2$^{-/-}$ X B6C3H F1	03/09/23	Female	4
1317060	Nrf2$^{-/-}$ X B6C3H F1	03/09/23	Female	4
1317061	Nrf2$^{-/-}$ X B6C3H F1	03/09/23	Male	3
1318691	Nrf2$^{-/-}$ X B6C3H F1 X F1	02/16/23	Both	2
1318692	Nrf2$^{-/-}$ X B6C3H F1 X F1	02/16/23	Both	2
1318693	Nrf2$^{-/-}$ X B6C3H F1 X F1	02/16/23	Both	2
1318694	Nrf2$^{-/-}$ X B6C3H F1 X F1	02/16/23	Both	2

1318695	Nrf2$^{-/-}$ X B6C3H F1 X F1	02/08/23	Both	2
1318696	Nrf2$^{-/-}$ X B6C3H F1 X F1	02/08/23	Both	2
1318697	Nrf2$^{-/-}$ X B6C3H F1 X F1	02/14/23	Both	2
1318698	Nrf2$^{-/-}$ X B6C3H F1 X F1	02/14/23	Both	2
1318699	Nrf2$^{-/-}$ X B6C3H F1 X F1	02/14/23	Both	2
1318700	Nrf2$^{-/-}$ X B6C3H F1 X F1	02/14/23	Both	2
1318701	Nrf2$^{-/-}$ X B6C3H F1 X F1	02/14/23	Both	2
1318702	Nrf2$^{-/-}$ X B6C3H F1 X F1	02/14/23	Both	2
1318703	Nrf2$^{-/-}$ X B6C3H F1 X F1	02/14/23	Both	2
1318704	Nrf2$^{-/-}$ X B6C3H F1 X F1	02/14/23	Both	2
1318705	Nrf2$^{-/-}$ X B6C3H F1 X F1	02/16/23	Both	2
1325090	Nrf2$^{-/-}$ X B6C3H F1	04/01/23	Male	4
1316588	Nrf2$^{-/-}$ X B6C3H F1	03/09/23	Male	5
1324436	Nrf2$^{-/-}$ X B6C3H F1	03/30/23	Female	3
1325088	Nrf2$^{-/-}$ X B6C3H F1	04/01/23	Female	3
1325445	Nrf2$^{-/-}$ X B6C3H F1	04/14/23	Female	2
1324434	Nrf2$^{-/-}$ X B6C3H F1	04/27/23	Male	4
1319431	Nrf2$^{-/-}$ X B6C3H F1 X F1	02/10/23	Both	2
1318137	Nrf2$^{-/-}$ X B6C3H F1 X F1	02/07/23	Both	2
1318138	Nrf2$^{-/-}$ X B6C3H F1 X F1	02/07/23	Both	2
1318139	Nrf2$^{-/-}$ X B6C3H F1 X F1	02/08/23	Both	2
1318140	Nrf2$^{-/-}$ X B6C3H F1 X F1	02/08/23	Both	2
1318141	Nrf2$^{-/-}$ X B6C3H F1 X F1	02/08/23	Both	2
1318142	Nrf2$^{-/-}$ X B6C3H F1 X F1	02/08/23	Both	2
1318143	Nrf2$^{-/-}$ X B6C3H F1 X F1	02/08/23	Both	2
1318144	Nrf2$^{-/-}$ X B6C3H F1 X F1	02/08/23	Both	2
1318145	Nrf2$^{-/-}$ X B6C3H F1 X F1	02/08/23	Both	2
1318146	Nrf2$^{-/-}$ X B6C3H F1 X F1	02/08/23	Both	2
1318147	Nrf2$^{-/-}$ X B6C3H F1 X F1	02/08/23	Both	2
1318148	Nrf2$^{-/-}$ X B6C3H F1 X F1	02/08/23	Both	2
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1318150	Nrf2$^{-/-}$ X B6C3H F1 X F1	02/07/23	Both	2
1318151	Nrf2$^{-/-}$ X B6C3H F1 X F1	02/08/23	Both	2
1318152	Nrf2$^{-/-}$ X B6C3H F1 X F1	02/16/23	Both	2
1318153	Nrf2$^{-/-}$ X B6C3H F1 X F1	02/16/23	Both	2
1318154	Nrf2$^{-/-}$ X B6C3H F1 X F1	02/16/23	Both	2

1318155	Nrf2$^{-/-}$ X B6C3H F1 X F1	02/16/23	Both	2
1318156	Nrf2$^{-/-}$ X B6C3H F1 X F1	02/16/23	Both	2
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1325089	Nrf2$^{-/-}$ X B6C3H F1	04/01/23	Male	4
1324438	Nrf2$^{-/-}$ X CRND8 F1	03/30/23	Male	4
1285661	Nrf2$^{-/-}$ X CRND8 F1 X F1	10/31/22	Female	5
1307179	Nrf2$^{-/-}$ X CRND8	11/03/22	Both	3
1327990	Nrf2$^{-/-}$ X CRND8	05/11/23	Female	4
1314661	Nrf2$^{-/-}$ X CRND8	09/22/22	Both	3
1298652	Nrf2$^{-/-}$ X CRND8	10/30/22	Both	2
1313053	Nrf2$^{-/-}$ X CRND8	08/08/22	Female	1
1314660	Nrf2$^{-/-}$ X CRND8	11/03/22	Both	3
1316236	Nrf2$^{-/-}$ X CRND8	11/10/22	Female	1
1321050	Nrf2$^{-/-}$ X CRND8	09/21/22	Female	1
1325695	Nrf2$^{-/-}$ X CRND8 F1	04/12/23	Female	2
1321046	Nrf2$^{-/-}$ X CRND8 F1	03/17/23	Male	3
1324437	Nrf2$^{-/-}$ X CRND8 F1	03/30/23	Male	4
1324439	Nrf2$^{-/-}$ X CRND8 F1	03/30/23	Female	1
1325696	Nrf2$^{-/-}$ X CRND8 F1	04/12/23	Male	4
1326967	Nrf2$^{-/-}$ X CRND8 F1	02/18/23	Male	1
1326968	Nrf2$^{-/-}$ X CRND8 F1	04/13/23	Male	3
1326969	Nrf2$^{-/-}$ X CRND8 F1	04/10/23	Female	5
1326970	Nrf2$^{-/-}$ X CRND8 F1	04/10/23	Male	3
1289365	Nrf2$^{-/-}$ X CRND8 F1 X F1	11/14/22	Female	5
1291140	Nrf2$^{-/-}$ X CRND8 F1 X F1	09/08/22	Both	2
1295297	Nrf2$^{-/-}$ X CRND8 F1 X F1	12/16/22	Male	4
1275031	Nrf2$^{-/-}$ X CRND8 F1 X F1	06/10/22	Both	2
1325444	Nrf2$^{-/-}$ X BGC3H F1	04/14/23	Male	2
1313052	Nrf2$^{-/-}$ X CRND8	11/03/22	Both	3
1323409	Nrf2$^{-/-}$ X CRND8	11/10/22	Female	1

1324694	Nrf2$^{-/-}$ X B6C3H F1	04/03/25	Female	5
1286645	Nrf2$^{-/-}$ X CRND8	11/05/22	Male	5
1314480	Nrf2$^{-/-}$ X CRND8	12/08/22	Male	1
1314481	Nrf2$^{-/-}$ X CRND8 F1	02/18/23	Male	2
1321496	Nrf2$^{-/-}$ X CRND8 F1	03/20/23	Male	3

AIM 3

Major Task 4: Continue characterization of our cre mice and pursue the breeding process for CRND8-Gfap^{cre}-Nrf2$^{fl/fl}$ mice.

We used a tamoxifen-inducible cre-ERT2 system to allow cell and time-specific deletion of Nrf2 in adult astrocytes and plan to extend this characterization to microglia and neurons. Furthermore, we have begun breeding transgenic CRND8 to Gfap-cre mice to generate specific models for this study. We will continue to validate the knockout via Western blots and test their phenotypes using tissue analysis and behavioral tests. Here, we have continued to characterize astrocytes in Nrf2-mediated neuroprotection:

Astrocytic Nrf2 attenuates brain injury-induced reactive gliosis. We examined the effect of astrocytic Nrf2 on reactive gliosis, the response of glial cells to cerebral insults, and the peri-infarct areas of the cortex after injury by immunostainings with the astrocyte marker GFAP and the microglial marker Iba1. As shown in the sham mice in Fig. 2A and B, astrocytes tiled the whole cortex in a regular distribution pattern in both genotypes, most of which display a nonreactive state with small somas and fine processes. In contrast, acute cerebral insults evoked the activation and proliferation of astrocytes in both genotypes, as indicated by the increased number of astrocytes with a larger proportion of reactive astrocytes that feature hypertrophic somas and highly stained processes. Notably, the extent of this reactive astrogliosis was more severe in $Gfap^{CreERT2}$:$Nrf2^{fl/fl}$ mice than in their controls. More degenerated astrocytes with broken-down somas were observed in $Gfap^{CreERT2}$:$Nrf2^{fl/fl}$ mice, indicating the more severe deterioration was triggered by the loss of astrocytic Nrf2. Strikingly, Nrf2 activation by DMF appeared to significantly attenuate injury-caused reactive astrogliosis, which was markedly reduced under the absence of astrocytic Nrf2.

We also examined the effect of astrocytic Nrf2 on microglia activation (Fig. 2C). No significant difference was observed between sham groups. In contrast, injury evoked significant microglial activations in both genotypes, as characterized by hypertrophic soma with thickened and retracted processes. Similar to our observation of reactive astrocytes, Iba1-positive microglia exhibited significantly higher expression levels in injured $Gfap^{CreERT2}$:$Nrf2^{fl/fl}$ mice than in injured $Nrf2^{fl/fl}$ control mice. However, the injury-triggered reactive microgliosis was significantly attenuated in DMF-treated $Nrf2^{fl/fl}$ but not in $Gfap^{CreERT2}$:$Nrf2^{fl/fl}$ mice. Together, these findings indicated that astrocytic Nrf2 plays a substantial role in reactive gliosis in astrocytes and microglia, impacting tissue preservation and functional outcomes.

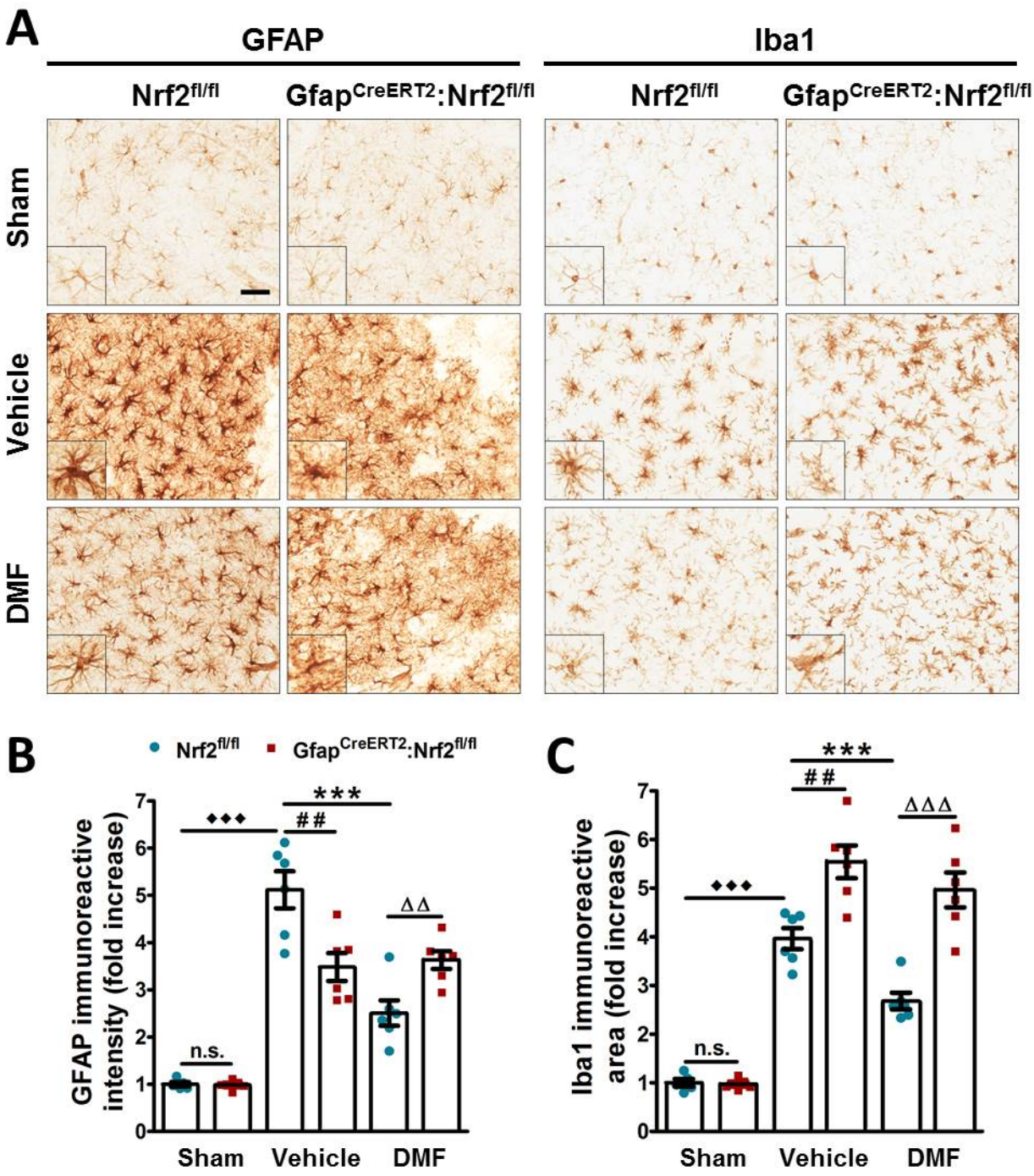

Figure 2. Astrocyte-restricted absence of Nrf2 exacerbates injury-induced reactive gliosis and eliminates the attenuation by Nrf2 activation. In both genotypes, acute insults triggered astrocytic activation and proliferation, revealed by the increased number of reactive astrocytes with hypertrophic somas and highly stained branches. Much more degenerated reactive astrocytes with breakdown cell bodies were detected in injured Gfap^{CreERT2}:Nrf2$^{fl/fl}$ but not injured Nrf2$^{fl/fl}$ mice, suggesting that astrocytic Nrf2 may protect against the deteriorative progression. DMF significantly attenuated reactive astrogliosis progression in injured Nrf2$^{fl/fl}$ but not Gfap^{CreERT2}:Nrf2$^{fl/fl}$ mice, suggesting the important role of astrocytic Nrf2 in this process. In both genotypes, acutely injured insult evoked significant activation of microglia characterized by hypertrophic soma with thickened and retracted processes, which was more obvious in Gfap^{CreERT2}:Nrf2$^{fl/fl}$ mice. Nrf2 activation by DMF significantly reduced the Iba1-positive signals in Nrf2$^{fl/fl}$ mice but not Gfap^{CreERT2}:Nrf2$^{fl/fl}$ mice. n=5–6 per group. ***P < 0.001, $^{\#\#}$P < 0.01, $^{\Delta\Delta}$P < 0.01, $^{\Delta\Delta\Delta}$P < 0.001.

- What opportunities for training and professional development has the project provided?

During the past quarter, SD has supervised ~36 undergraduate students taking Medical Sciences Senior Research at UF (BMS4905). These students have had remote or in-person opportunities to learn more about the fields of neurology and biochemistry through participation in our lab's ongoing research, including this project.

We have trained our undergraduate volunteers to perform statistical analysis on the raw data obtained from this project using JMP. Specifically, the tests taught include: Chi-Square Goodness-of-Fit, Levene Test for Equality of Variances, and Welch's Correction

- How were the results disseminated to communities of interest?

Nothing to Report.

- What do you plan to do during the next reporting period to accomplish the goals?

AIM 1

Subtask 4: Continue quantification analysis.

Subtask 5: Monitor toxicity at the different doses

As a final task for aim 1, we will evaluate the toxicity of DMF and MMF at various doses in CRND8 mice after TBI and determine their respective roles in attenuating AD and CAA neurobehavioral and pathophysiological outcomes. We will examine groups of TgCRND8 mice: sham, TBI, TBI+DMF (low, medium, high dose), and TBI+MMF (low, medium, high dose), and monitor for signs of drug toxicity or adverse effects. To assess the impact of DMF and MMF on neurobehavioral outcomes, we will perform cognitive and motor function tests on all mice at predetermined time points post-TBI, then harvest tissues for analysis.

AIM 2

Major Task 2: Repeat the optimal conditions in the Nrf2-/- mice

Subtask 5: We will be able to generate experimental mice. We plan to do the LFAO injections at P0, let them age, and perform the behavioral experiments and surgeries.

AIM 3

Major Task 3: Based on the result from Aim 2, we selected the Gfap-Cre mice to breed with the Nrf2^{fl} mice (and compare results with all the appropriate matched controls)

We will also pursue breeding and use the optimized protocol for the tamoxifen treatment in these unique cre-flox mice.

Finally, we will generate the CRND8/Gfap-Cre Nrf2$^{fl/fl}$ mice and compare them with the appropriate groups and controls.

4. Impact

- What was the impact on the development of the principal discipline(s) of the project?

Paper (acknowledging DOD funding)

1. Mohamed, B., Yarlagadda, K., Simon, A., Sohooli, M., Eisenschenk, S., **Doré, S**. Obstructive sleep apnea and stroke: Determining mechanisms behind their association and treatment options. *Translational Stroke Research*. March 2023; doi/10.1007/s12975-023-01123-x

Abstracts presented at Research Conferences (acknowledging DOD funding):

1. Trevi Perez, Olivia Edwards, Josh Lua, Diana J. Wilkie, **Sylvain Doré**, Investigation of the relevance of soluble CD163, CD36, and LRP1 receptors in the clinical assessment and treatment of sickle cell disease. *UF-Department of Anesthesiology Celebration of Research,* March 2023.
2. Kyra Carney, Yasmin Araujo, **Sylvain Doré**. Comparison of market iron chelators and HBED for treatment of iron overload post-traumatic brain injury. *UF-Department of Anesthesiology Celebration of Research,* March 2023.
3. Kanishka Ekanayake, Emily Barlow, Rakan Alshaibi, **Sylvain Doré**. The role of soluble TNF receptors in inflammation caused by ischemic stroke, intracerebral hemorrhage, and traumatic brain injury. *UF-Department of Anesthesiology Celebration of Research,* March 2023.

4. Valerie Cabrera, **Sylvain Doré**. Evidence that subarachnoid hemorrhage may be a risk factor for the etiopathology of Alzheimer's Disease *UF-Department of Anesthesiology Celebration of Research,* March 2023.
5. Ali Solhpour, Siddharth Kumar, Matthew J. Koch, **Sylvain Doré**. Impact of blood component transfusions, tranexamic acid, and Fluids on subarachnoid hemorrhage outcomes. *UF-Department of Anesthesiology Celebration of Research,* March 2023.
6. Saba Khan, **Sylvain Doré**. Potential avenues to increase tPA administration in ischemic stroke patients: A review of selective tPA combination therapies. *UF-College of Medicine: UF-Department of Anesthesiology Celebration of Research,* March 2023.
7. Maryam Sohooli, Basma Mohamed, Keerthi Yarlagadda, Zachary Self, Alexandra Simon, Frank Rigueiro, Stephan Eisenschenk, **Sylvain Doré**. Obstructive sleep apnea and stroke: Determining the mechanisms behind their association and treatment options. *UF-Department of Anesthesiology Celebration of Research,* March 2023.
8. Harini Choula, Reed Cecil, **Sylvain Doré**. Circle of Willis variants effect on traumatic brain injury (TBI). *UF-Department of Anesthesiology Celebration of Research,* March 2023.
9. Alexandra Vicini, **Sylvain Doré**. Soluble CD163, CD36, and LRP1 receptors to monitor neurological deficits in cerebral amyloid angiopathy patients. *UF-Department of Anesthesiology Celebration of Research,* March 2023.
10. Emery Perrin, **Sylvain Doré**. Status of potential protein biomarkers for neonatal hypoxic-ischemic encephalopathy. *UF-Spring Undergraduate Research Symposium,* April 2023.
11. Thabasya Veeramani, **Sylvain Doré**. Therapeutic potential of iron chelators mitigating oxidative stress and iron homeostasis dysregulation following ischemic stroke. *UF-Spring Undergraduate Research Symposium,* April 2023.
12. Harry Villanueva, **Sylvain Doré**. Potential implications of the mutant heme oxygenase 1 gene in sickle cell disease pathology. *UF-Spring Undergraduate Research Symposium,* April 2023.
13. Mohammad Naem, **Sylvain Doré**. Can haptoglobin phenotyping improve therapies against the anatomical and neurological consequences of intracerebral hemorrhage (ICH)? *UF-Spring Undergraduate Research Symposium,* April 2023.
14. Chase Comprosky, **Sylvain Doré**. Can the non-canonical/non-enzymatic activity of L-PGDS alter the consequences of chronic neurological disease? *UF-Spring Undergraduate Research Symposium,* April 2023.
15. Sebin George, **Sylvain Doré**. Investigating the potential of CRF receptor (CRFR) drugs as a therapy against the consequences of stroke. *UF-Spring Undergraduate Research Symposium,* April 2023.
16. Camille Jastrzebski, Mackenzie Williams, **Sylvain Doré**. Iron chelators as an emerging therapeutic treatment option for subarachnoid hemorrhage. *UF-Spring Undergraduate Research Symposium,* April 2023.
17. Kyra Carney, Yasmin Araujo, **Sylvain Doré**. Comparison of market iron chelators and HBED for treatment of iron overload post-traumatic brain injury. *UF-Spring Undergraduate Research Symposium,* April 2023.
18. Kanishka Ekanayake, Emily Barlow, Rakan Alshaibi, **Sylvain Doré**. The role of soluble TNF receptors in inflammation caused by ischemic stroke, intracerebral hemorrhage, and traumatic brain injury. *UF-Spring Undergraduate Research Symposium,* April 2023.
19. Valerie Cabrera, **Sylvain Doré**. Evidence that subarachnoid hemorrhage may be a risk factor for the etiopathology of Alzheimer's Disease. *UF-Center for Undergraduate Research: UF-Spring Undergraduate Research Symposium,* April 2023.
20. Saba Khan, **Sylvain Doré**. Potential avenues to increase tPA administration in ischemic stroke patients: A review of selective tPA combination therapies. *UF-Spring Undergraduate Research Symposium,* April 2023.

- What was the impact on other disciplines?
Nothing to Report.

- What was the impact on technology transfer?
Nothing to Report.

- What was the impact on society beyond science and technology?
Nothing to Report.

5. Changes/Problems
Please be advised that the PI on this project, Dr Sylvain Dore, has recently resigned. This report was prepared by Cibele Castro who worked on the project as a post-doctoral associate.

6. Products
Nothing to Report.

7. Participants & Other Collaborating Organizations
- What individuals have worked on the project?

Name:	Sylvain Doré, PhD, FAHA
Project Role:	P.I.
Researcher Identifier (e.g., ORCID ID):	0000-0003-3771-5109
Nearest person month	2.16
Contribution to Project:	S.D. has been managing the project and coordinating the breeding, etc.
Funding Support:	Nothing to Report

Name:	Caleb Charles, BS
Project Role:	Lab Technician
Researcher Identifier (e.g., ORCID ID):	N/A
Nearest person month	6
Contribution to Project:	C.C. is providing lab support for the various protocols.
Funding Support:	Nothing to Report

Name:	Cibele Canal Castro PhD
Project Role:	Post-doctoral Associate
Researcher Identifier (e.g., ORCID ID):	0000-0001-5183-4054
Nearest person month	12
Contribution to Project:	CCC is from Brazil, and she is devoting her time to most of the surgeries for this protocol. This is essentially her 3rd postdoc, after completing one in Germany and another at Johns Hopkins under the supervision of the lab of Ted and Valina Dawson. Again, she came with the highest recommendations. She has unique mouse surgery skills.
Funding Support:	Nothing to Report

Name:	Alexandra Vicini, BS
Project Role:	Lab OPS Technician
Researcher Identifier (e.g., ORCID ID):	N/A
Nearest person month	6
Contribution to Project:	A.V. is providing lab support for the various protocols.
Funding Support:	Nothing to Report

Name:	Olivia Edwards, BS

Project Role:	Lab OPS Technician
Researcher Identifier (e.g., ORCID ID):	N/A
Nearest person month	3
Contribution to Project:	O.E. is providing lab support for the various protocols.
Funding Support:	Nothing to Report

- Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

No change from the last period.

(The PI, Dr. Doré, is still helping a co-investigator who left, and they are working together on a paper on TBI in mice.)

- What other organizations were involved as partners?

Nothing to Report.

8. Special Reporting Requirements

Nothing to Report.

9. Appendices

Quadchart