

# Notch Signaling in the regulation of TMJ Osteoarthritis

---

*2021 Grants*

*Dr Sumit Yadav*

---

syadav@unmc.edu  
O: 317-919-8765

# FollowUp Form

---

## ***Award Information***

---

*In an attempt to make things a little easier for the reviewer who will read this report, please consider these two questions before this is sent for review:*

- Is this an example of your very best work, in that it provides sufficient explanation and justification, and is something otherwise worthy of publication? (We do publish the Final Report on our website, so this does need to be complete and polished.)*
- Does this Final Report provide the level of detail, etc. that you would expect, if you were the reviewer?*

## **Title of Project\***

Notch Signaling in the regulation of TMJ Osteoarthritis

## **Award Type**

Biomedical Research Award (BRA)

## **Period of AAOF Support**

July 1, 2021 through December 31, 2022

## **Institution**

University of Nebraska Medical Center

## **Names of principal advisor(s) / mentor(s), co-investigator(s) and consultant(s)**

NA

## **Amount of Funding**

\$30,000.00

## **Abstract**

(add specific directions for each type here)

## ***Respond to the following questions:***

---

### **Detailed results and inferences:\***

If the work has been published, please attach a pdf of manuscript below by clicking "Upload a file".

OR

Use the text box below to describe in detail the results of your study. The intent is to share the knowledge you have generated with the AAOF and orthodontic community specifically and other who may benefit from your study. Table, Figures, Statistical Analysis, and interpretation of results should also be attached by clicking "Upload a file".

Final Report.pdf

Please see attached word document

### **Were the original, specific aims of the proposal realized?\***

Yes

### **Were the results published?\***

No

### **Have the results of this proposal been presented?\***

No

### **To what extent have you used, or how do you intend to use, AAOF funding to further your career?\***

The preliminary data generated from the grant was used to obtain an RO1

*Comment: The AAOF PARC commends your accomplishments in completing this project and securing additional funding. We look forward to the findings of your study being placed in the public domain for the benefit of advancing our knowledge base in TMD.*

### **Accounting: Were there any leftover funds?**

## ***Not Published***

---

### **Are there plans to publish? If not, why not?\***

Yes. We plan to publish the data after we obtain the data for single cell sequencing

## *Not Presented*

---

### **Are there plans to present? If not, why not?\***

Yes. Once, we have complete data, we will present in IADR/AADOCR

## *Internal Review*

---

### **Reviewer Comments**

Award was transferred from UConn to University of Nebraska, see refund info under the documents tab...remaining award amount transferred \$24,312.45

### **Reviewer Status\***

Approved

## File Attachment Summary

---

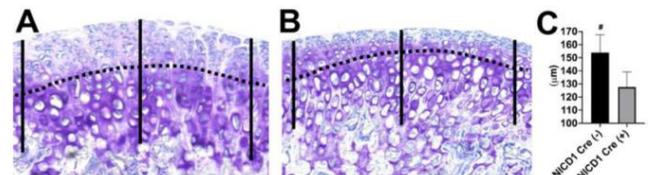
### *Applicant File Uploads*

- Final Report.pdf

Final Report:

**Conditional overexpression of NICD1 in  $\alpha$ SMA expressing cells leads to decreased cartilage thickness and altered cellular morphology:**

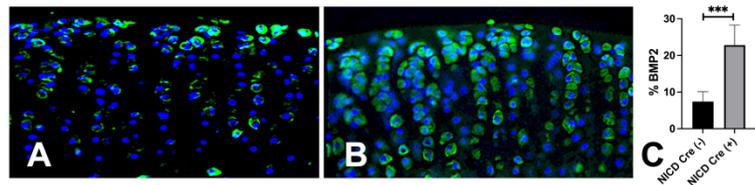
Six-week-old male (n=12; 6 per group; 6 NICD1 Cre (-) & 6 NICD Cre (+))  $\alpha$ SMA CreERT2-NICD1 (NICD1 over expressed in  $\alpha$ SMA expressing cells in the MCC and subchondral bone) mice were injected with 5 consecutive doses of tamoxifen and mice were euthanized 4 weeks later. Histological sections were stained with Toluidine Blue (TB). There was a decrease in total cartilage thickness (Fig. 1C), altered cellular morphology (Fig. 1B) and decreased matrix synthesis in NICD1 Cre (+) mice (Fig. 1B) when compared to NICD1 Cre (-) mice (Fig. 1A). We also observed that oval cells (Col10a1) in NICD1 overexpressing (Fig. 1B) mice were migrating towards the fibrous layer of the cartilage and there was decrease in the thickness of fibrous layer (see dotted line in Fig. 1B) when compared to NICD1 Cre (-) mice (Fig. 1A).



**Figure 1:** Decreased cartilage thickness with conditional over expression of NICD1 in  $\alpha$ SMA expressing cells in male mice. (A)  $\alpha$ SMA CreERT2-NICD (-); (B)  $\alpha$ SMA CreERT2- NICD (+); (C) Histogram. (n=6/gp)

**Conditional overexpression of NICD1 in  $\alpha$ SMA expressing cells leads increased protein expression of BMP2:**

Six-week-old male (n=12; 6 per group; 6 NICD1 Cre (-) & 6 NICD Cre (+))  $\alpha$ SMA CreERT2-NICD1 (NICD1 over expressed in  $\alpha$ SMA expressing cells in the MCC and subchondral bone) mice were injected with 5 consecutive doses of tamoxifen and mice were euthanized 4 weeks later. Histological sections were stained with BMP2 antibody. There was a significant increase in BMP2 positive cells in NICD1 Cre (+) mice (Figs. 2B & 2C) when compared to NICD1 Cre (-) mice. (Figs. 2A & 2C).



**Figure 2:** Increased BMP2 protein in chondrocytes. (A)  $\alpha$ SMA CreERT2-NICD (-); (B)  $\alpha$ SMA CreERT2- NICD (+); (C) Histogram. (n=6/gp)