

Title: NTG-102: A Refined Molecular Therapeutic to Treat Degenerative Disc Disease

Authors: Lori Moffat PhD², Hoda Gerami BSc², Bettina Benigno BSc², Ajay Matta PhD², Muhammad Zia Karim DVM, MSc(hons)², MPhil, W. Taylor MD, W Mark Erwin DC PhD^{1,2}

Affiliations: ¹Department of Surgery, University of Toronto, Toronto, Ontario, Canada.

²Notogen Inc., Toronto, Ontario, Canada.

Corresponding Author: *W. Mark Erwin DC, PhD

Email: mark.erwin@utoronto.ca; Tel: 1-721-4834

Short Title: NTG-102 novel therapeutic for degenerative disc disease

Key words: TGF- β 1, Degenerative Disc Disease, Nucleus pulposus, NTG-102, Inflammation

Competing interests: None

Funding Source: Study financed by Notogen Inc., funding

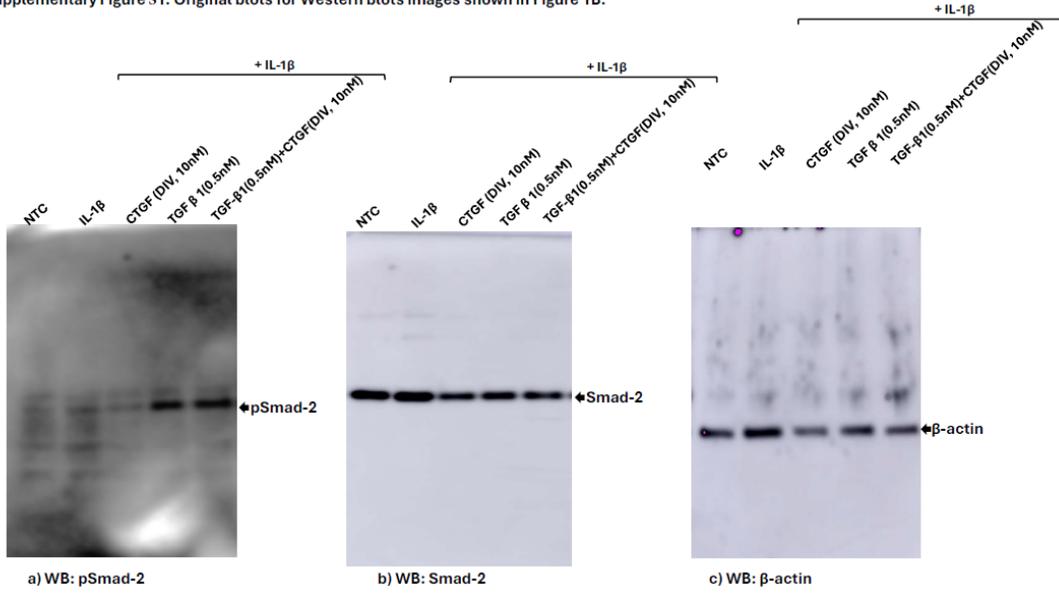
SUPPLEMENTARY DATA

Supplementary Table S1.

S. No.	Bovine- Primer Name	Primer Sequence
1	HPRT (F)	TGTCAGTTGCTGCATTCCCG
2	HPRT (R)	TTTCCAGTCAATAGTGGTGTGGTT
3	Aggrecan (F)	CTCCAGAGGGGCTCGCAGGT
4	Aggrecan (R)	GGCGTCTGGGTAGCGGAGTC
5	Col2A1 (F)	GCCGCTGTCCTTCGGTGTCA
6	Col2A1 (R)	GGGCTCGGGCTTCCACACAT
7	Cox2 (F)	CCTGATGACTGCCCAACACCCA
8	Cox2 (R)	TGTGCCCTGGGGATCAGGAATG
9	MMP-13 (F)	TGATGCCGCCTATGAGCACCC
10	MMP-13 (R)	AAAGTGAAGGGCTGCGCTGA

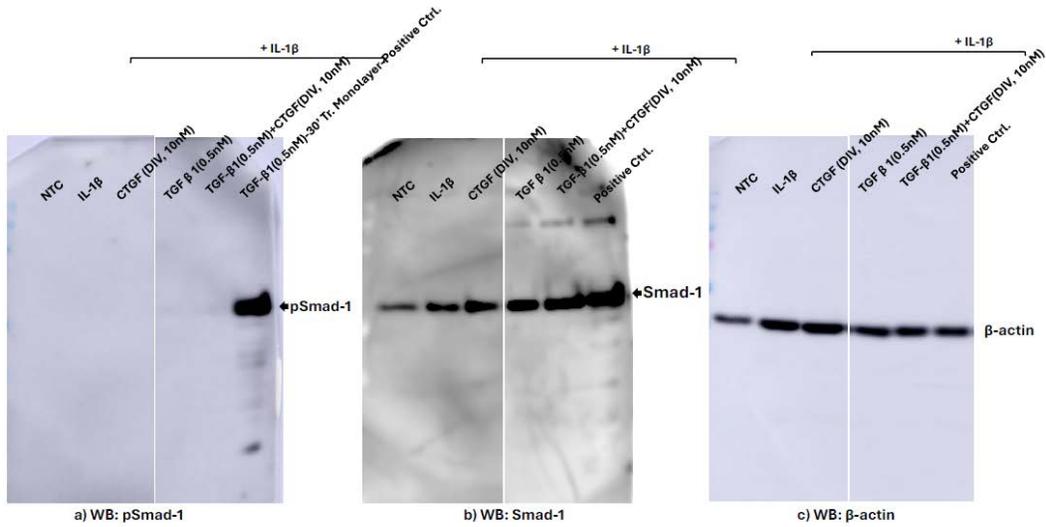
Supplementary Figure S1.

Supplementary Figure S1. Original blots for Western blots images shown in Figure 1B.

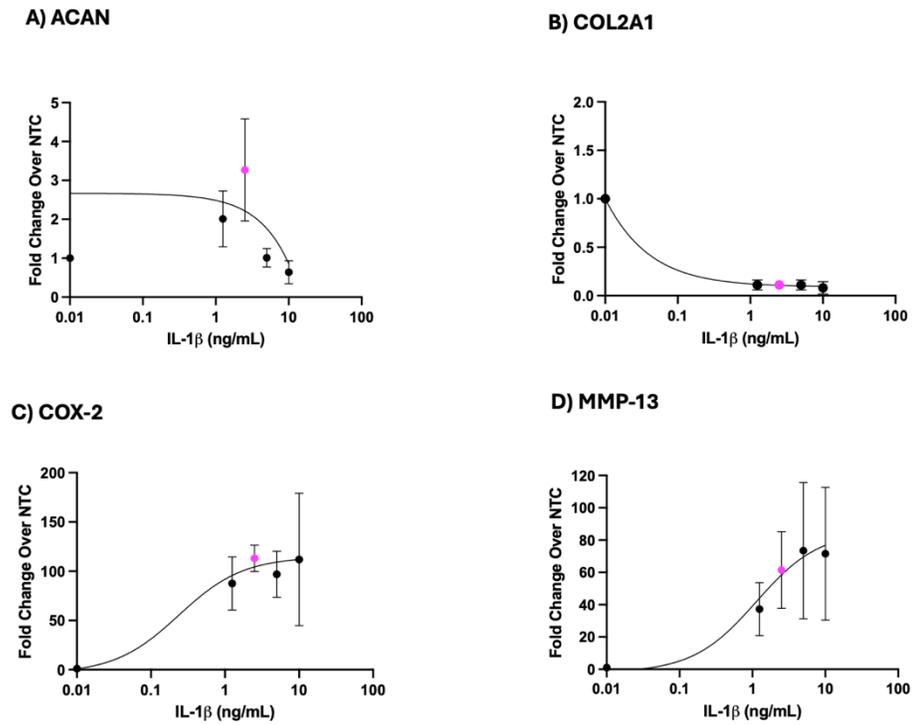


Supplementary Figure S2.

Supplementary Figure S2. Original blots for Western blots images shown in Figure 1C.



Supplementary Figure S3.



Supplementary Fig. S3: (A-D) IL-1 β Dose curve calculations leading to the conclusion that 2.5 ng/mL IL-1 β is sufficient to suppress collagen type 2 expression and increase pro-inflammatory/matrix degrading enzyme gene expression.

RIS Protocol
Number: 41495

Approval Date: 30-Aug-21

PI Name: Dr William (W. Mark)
Erwin

Division Name:

Dear Dr William (W. Mark) Erwin:

Re: Your research protocol application entitled, "Anti-degenerative/Pro-repair effects of NTG-101 upon human Intervertebral Disc Nucleus Pulposus Cells"

The Health Sciences REB has conducted a Delegated review of your application and has granted approval to the attached protocol for the period 2021-08-30 to 2022-08-29.

If this research involves face-to-face (F2F) in person research, please note that REB approval alone is not sufficient to commence research. You must wait for an approval letter from the F2F COVID-19 Review Committee. The approval letter will be sent to the Principal Investigator's email address once the Committee has deemed the F2F in-person research ready to start.

Please be reminded of the following points:

- An **Amendment** must be submitted to the REB for any proposed changes to the approved protocol. The amended protocol must be reviewed and approved by the REB prior to implementation of the changes.
- An annual **Renewal** must be submitted for ongoing research. Renewals should be submitted between 15 and 30 days prior to the current expiry date.
- A **Protocol Deviation Report (PDR)** should be submitted when there is any departure from the REB-approved ethics review application form that has occurred without prior approval from the REB (e.g., changes to the study procedures, consent process, data protection measures). The submission of this form does not necessarily indicate wrong-doing; however follow-up procedures may be required.
- An **Adverse Events Report (AER)** must be submitted when adverse or unanticipated events occur to participants in the course of the research process.
- A **Protocol Completion Report (PCR)** is required when research using the protocol has been completed. For ongoing research, a PCR on the protocol will be required after 7 years, (Original and 6 Renewals). A continuation of work beyond 7 years will require the creation of a new protocol.
- If your research is funded by a third party, please contact the assigned Research Funding Officer in Research Services to ensure that your funds are released.

Best wishes for the successful completion of your research.