

Cdh1^{+/-} as a mouse model for BPH and LUTS

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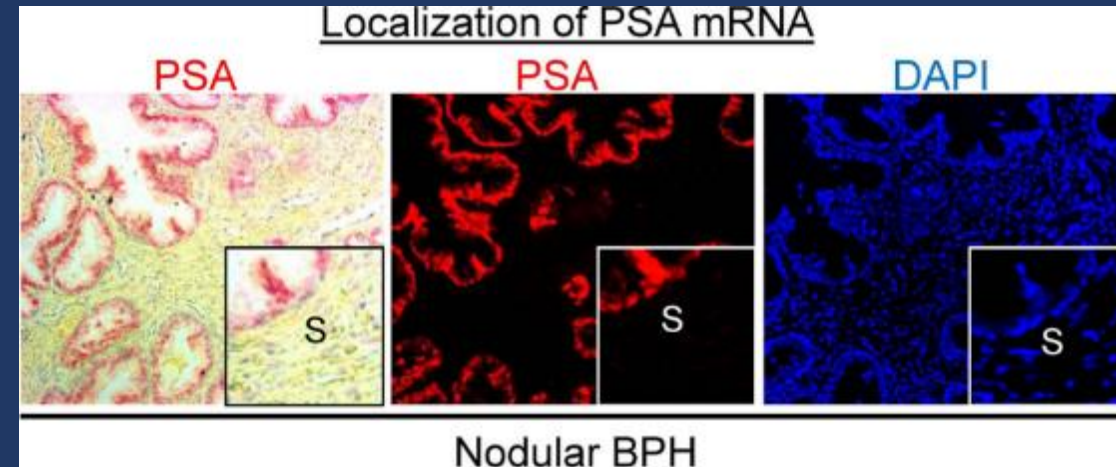
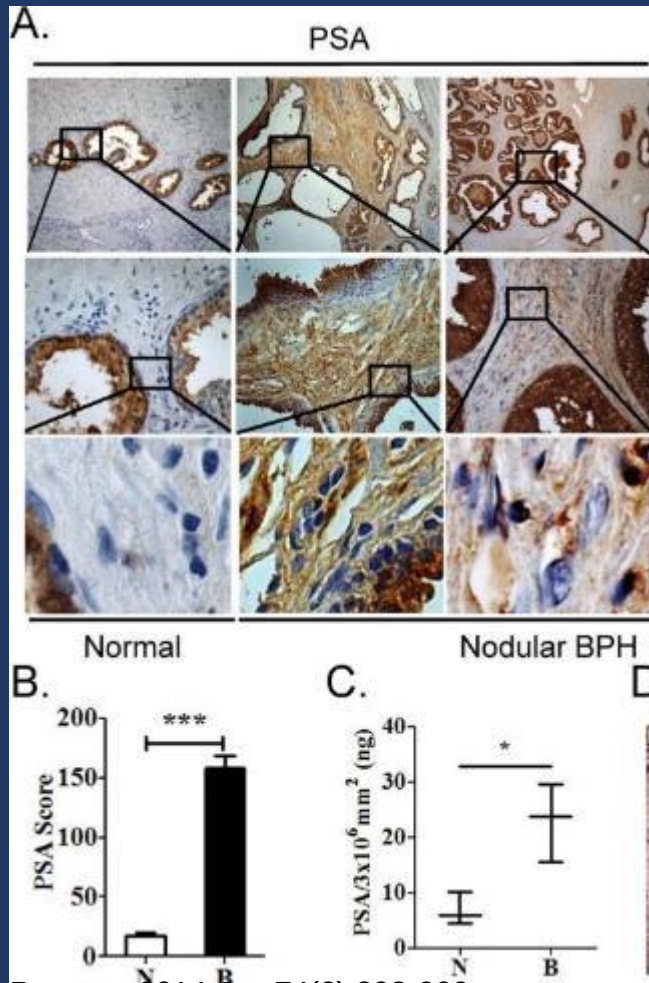


CAIRIBU as a force in developing and utilizing a mouse model for BPH/LUTS

1. Idea development
2. Experienced advice/insights
3. Resources
4. Related studies



Idea development – Stromal PSA?



Katie Willett



Will Ricke

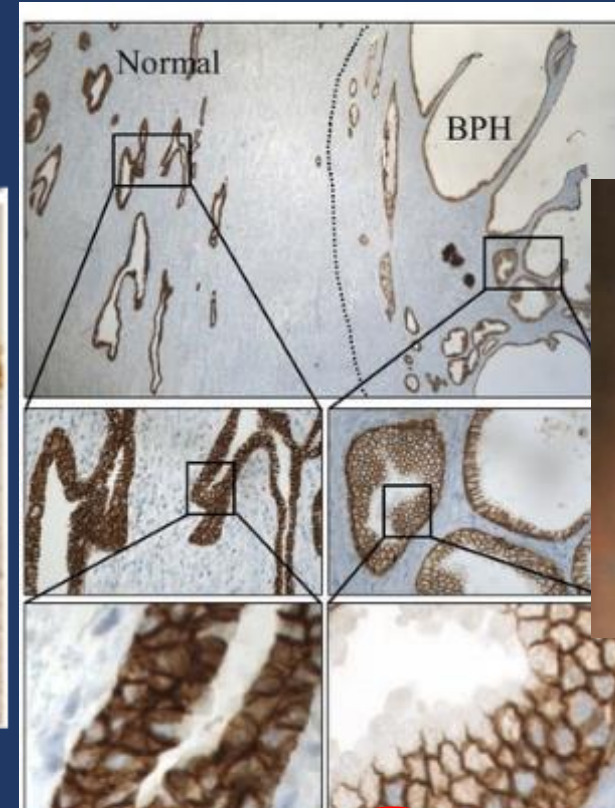
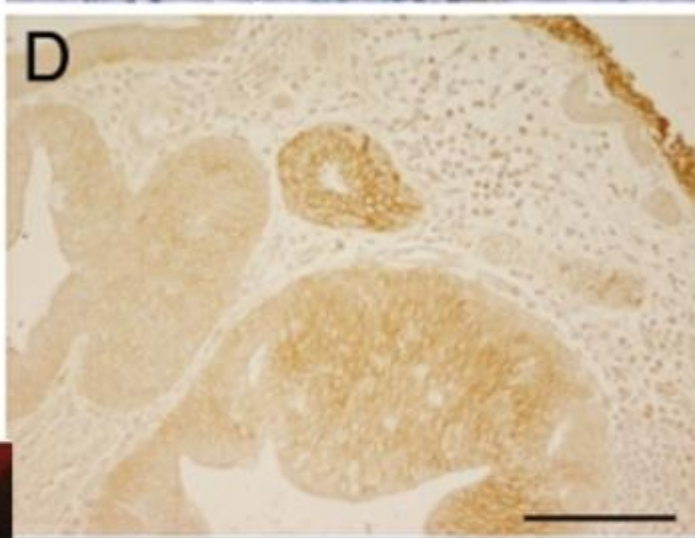
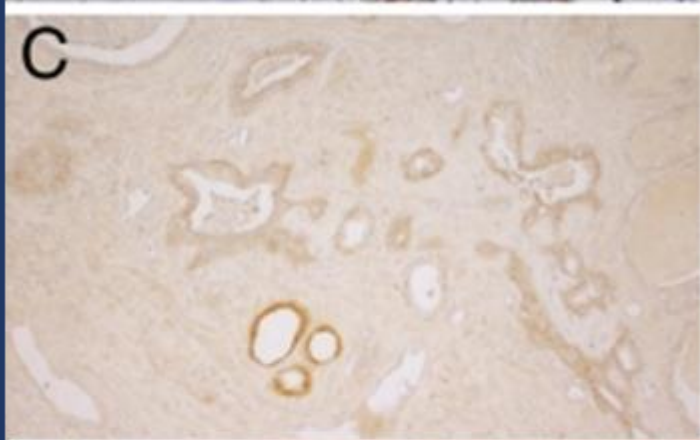
Prostate 2014 Jun;74(8):892-900.

Proteomic analysis of patient tissue reveals PSA protein in the stroma of benign prostatic hyperplasia

[Katherine J O'Malley](#)¹, [Kurtis Eisermann](#), [Laura E Pascal](#), [Anil V Parwani](#), [Tsuyoshi Majima](#), [Lara Graham](#), [Katherine Hrebinko](#), [Marie Acquafondata](#), [Nicolas A Stewart](#), [Joel B Nelson](#), [Naoki Yoshimura](#), [Zhou Wang](#)



Experienced insights and Resources



Simon Hayward



Jan-Ake Gustafsson



Li Feng

Proc Natl Acad Sci U S A. 2009 Feb 24; 106(8): 2859-2863. PMID: 19196965

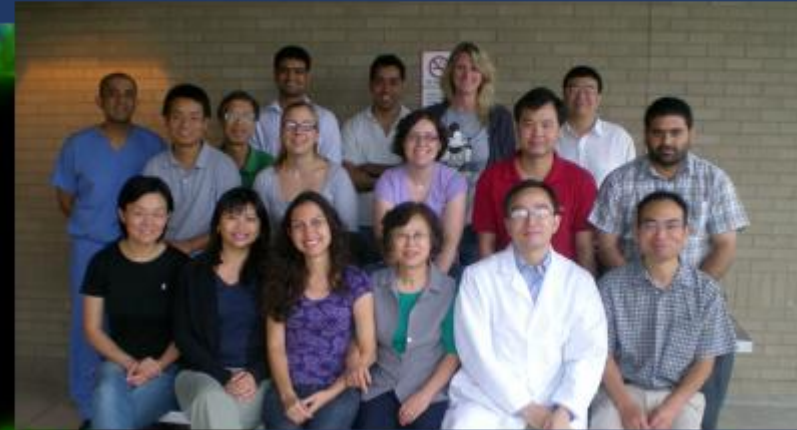
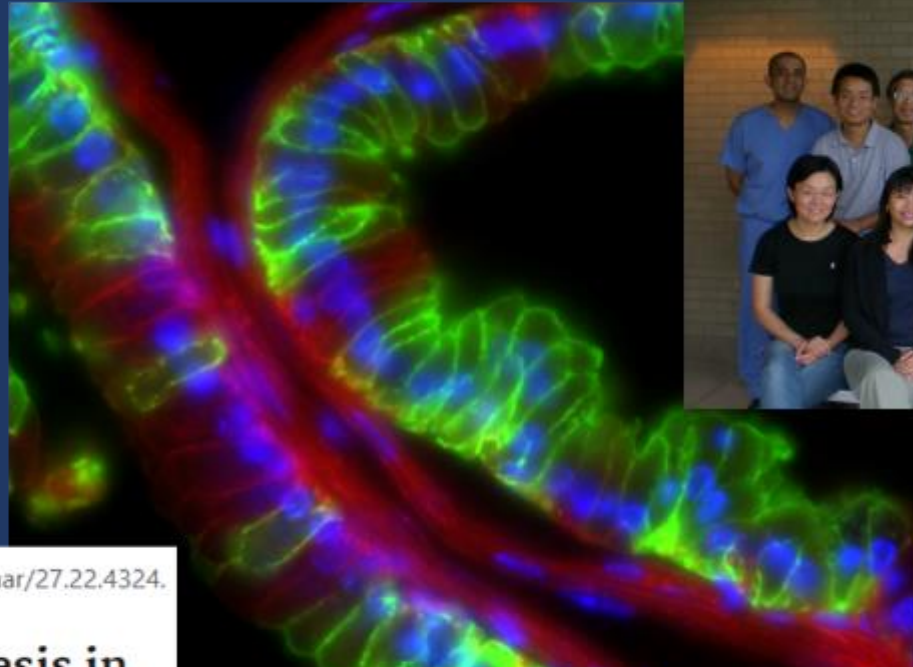
Prostate. 2019 Aug;79(11):1226-1237. Jun 18. PMID: 31212263

Resources

Pierre Chambon



Daniel Metzger



Comparative Study > [Nucleic Acids Res.](#) 1999 Nov 15;27(22):4324-7. doi: 10.1093/nar/27.22.4324.

Temporally-controlled site-specific mutagenesis in the basal layer of the epidermis: comparison of the recombinase activity of the tamoxifen-inducible Cre-ER(T) and Cre-ER(T2) recombinases

A K Indra¹, X Warot, J Brocard, J M Bornert, J H Xiao, P Chambon, D Metzger

Regenerated Luminal Epithelial Cells Are Derived from Preexisting Luminal Epithelial Cells in Adult Mouse Prostate FREE

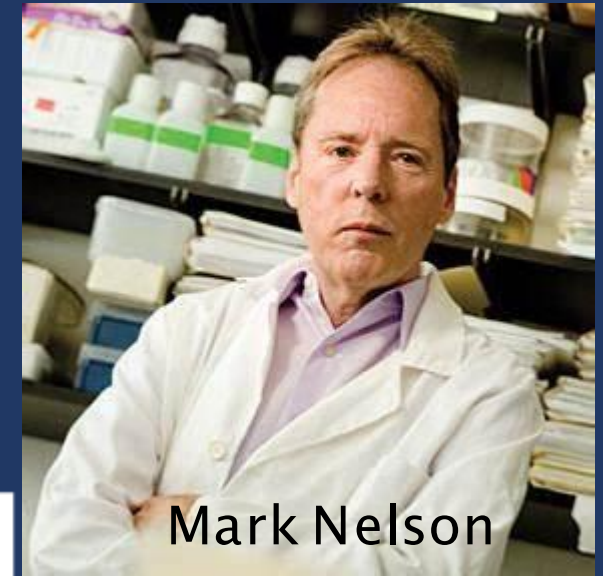
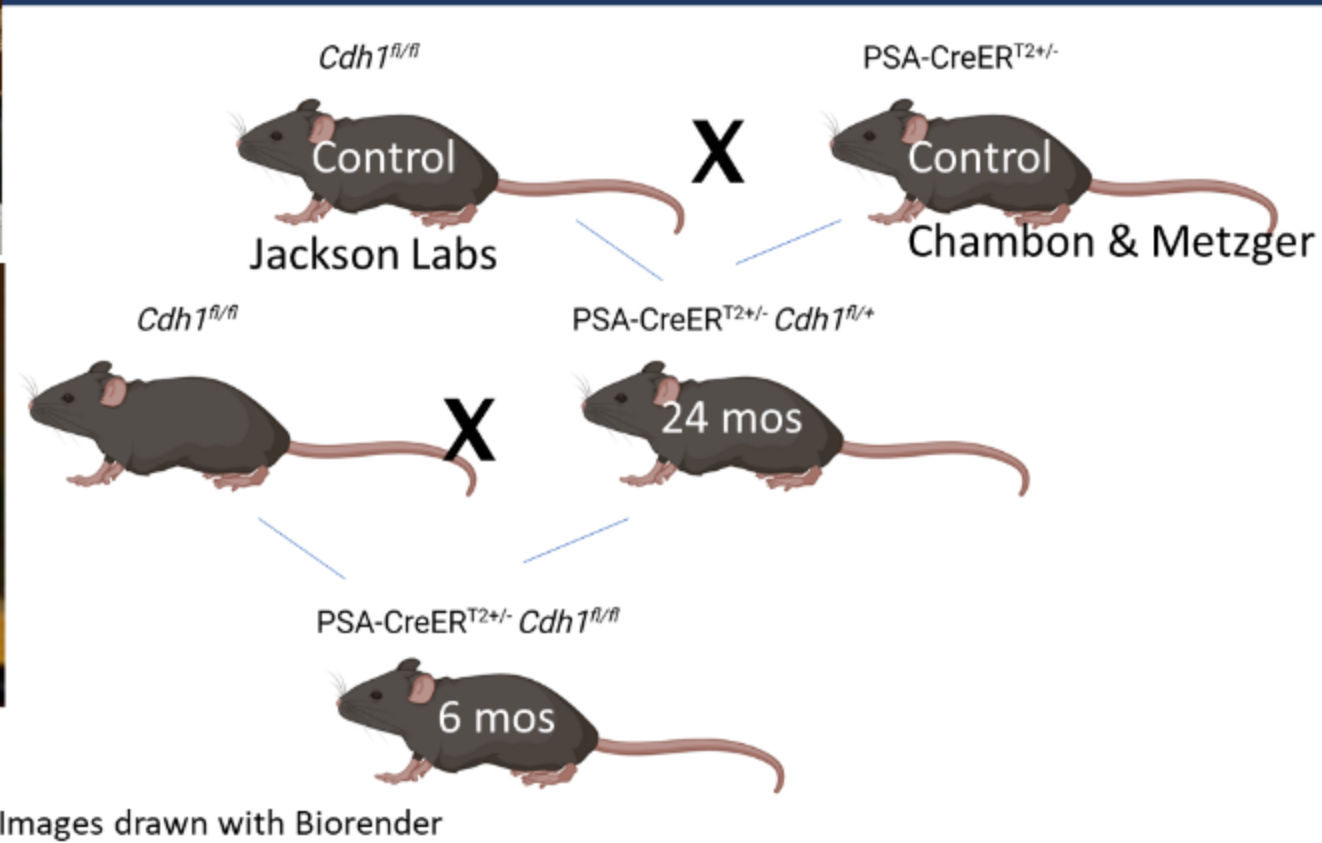
June Liu, Laura E. Pascal, Sudhir Isharwal, Daniel Metzger, Raquel Ramos Garcia, Jan Pilch, Susan Kasper, Karin Williams, Per H. Basse, Joel B. Nelson ... [Show more](#)
[Author Notes](#)

Molecular Endocrinology, Volume 25, Issue 11, 1 November 2011, Pages 1849–1857



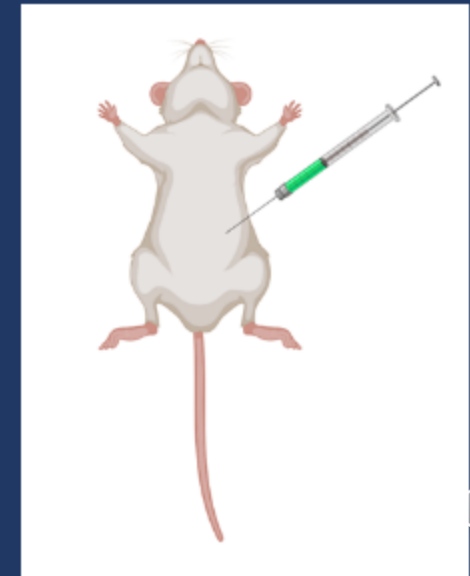
Experienced insights: generation of mice and proper controls

Dale Bjorling



Mark Nelson

Tamoxifen
@ 7 weeks



Impact of E-cadherin deletion @ 6 mos:

Homozygous

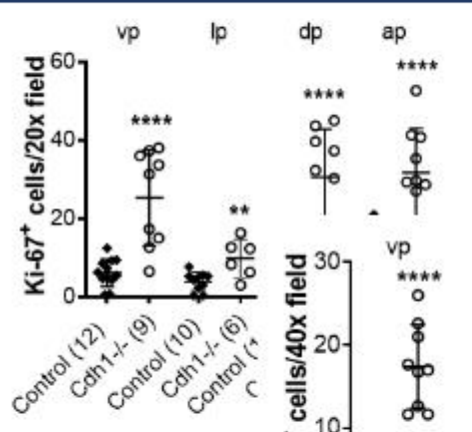
Prostate

Bladder

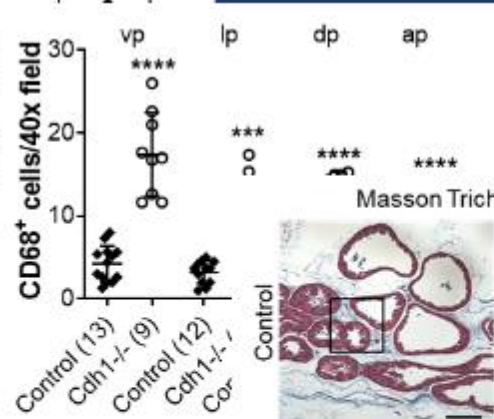
PSA-CreER^{T2+/-} *Cdh1*^{fl/fl}



Proliferation

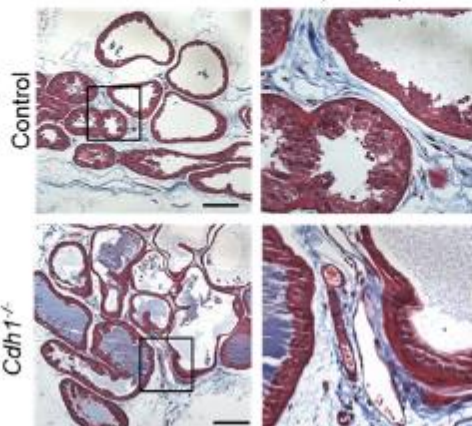


Inflammation

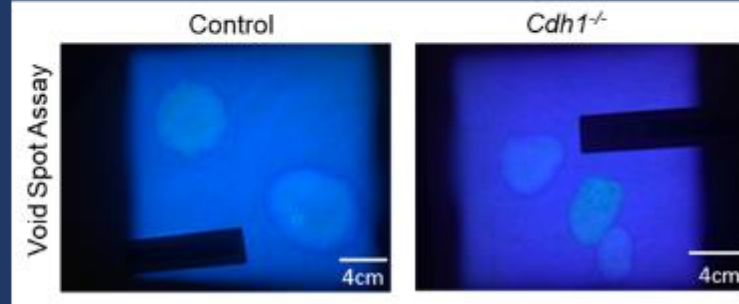


>ECM

Masson Trichrome (ventral)

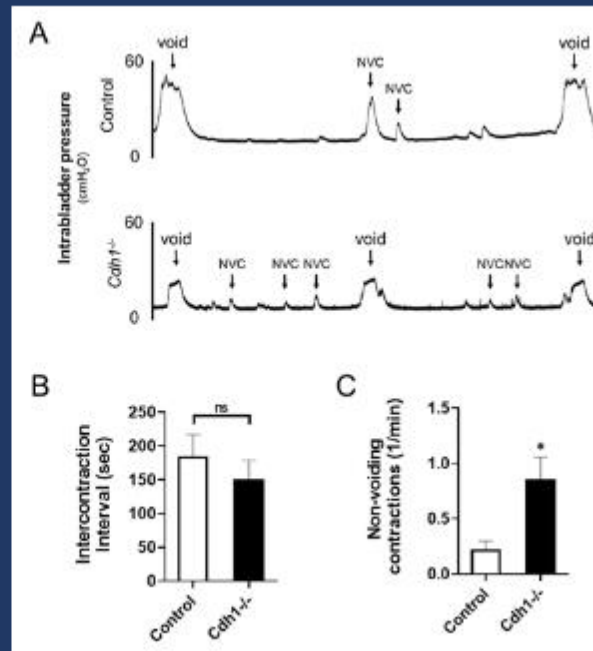


Chad Vezina



Heterozygous

PSA-CreER^{T2+/-} *Cdh1*^{fl/+}

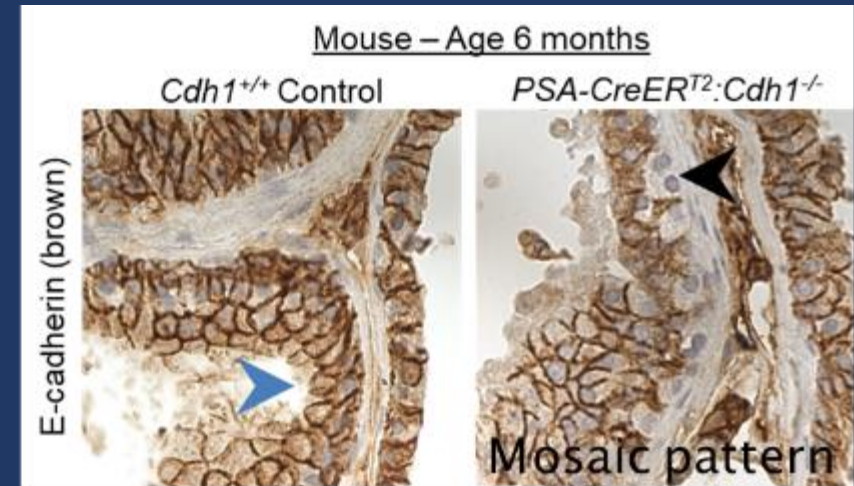
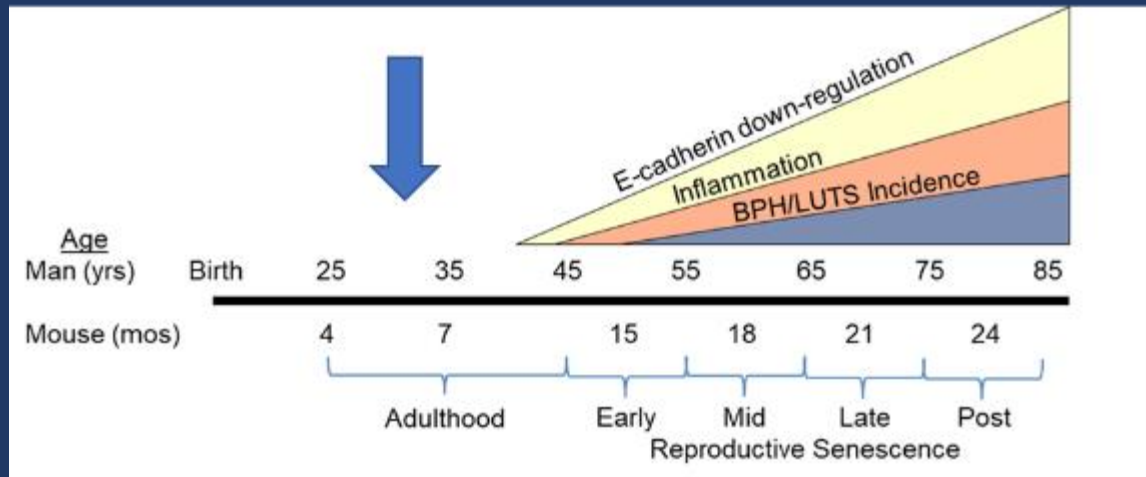


> Endocrinology. 2021 Jan 1;162(1):bqaa212. doi: 10.1210/endo/bqaa212.

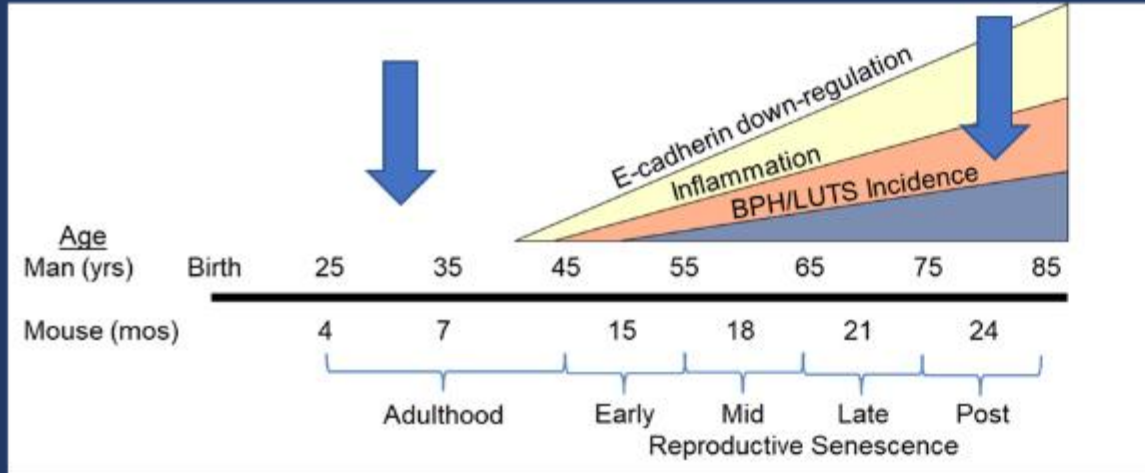
Prostate-Specific Deletion of *Cdh1* Induces Murine Prostatic Inflammation and Bladder Overactivity

Laura E Pascal¹, Shinsuke Mizoguchi¹, Wei Chen¹, Lora H Rigatti², Taro Igarashi¹, Rajiv Datta¹, Pradeep Tyagi¹, Zeyu Wu¹, Zhenyu Yang¹, William C de Groat⁴, Donald B DeFranco¹, Naoki Yoshimura¹, Zhou Wang^{1,4,5}

Limitations to the *Cdh1^{flox/flox}* mouse...



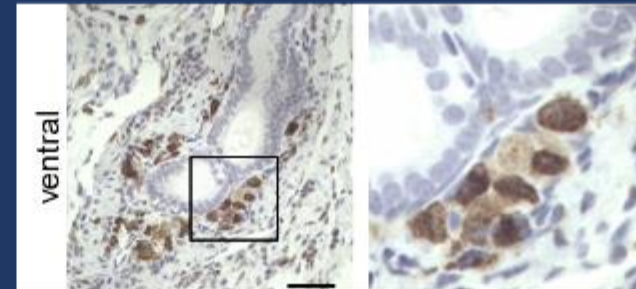
Examination of *Cdh1^{flox/+}* mouse...



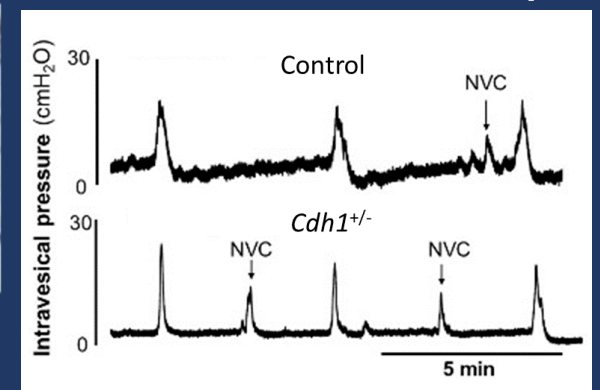
PSA-CreER^{T2+/-} *Cdh1^{fl/+}*



Prostate Inflammation



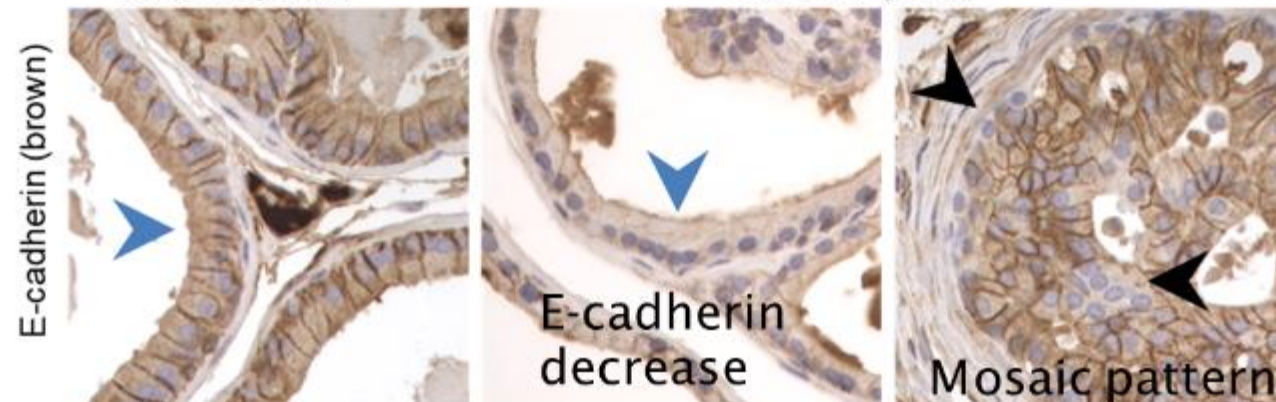
Bladder overactivity



Mouse – Age 24 months

PSA-Cre⁻; *Cdh1^{flox/flox}*

PSA-Cre⁺; *Cdh1^{flox/+}*



Related studies

What happens to aging mouse prostate and bladder function?

> [Aging \(Albany NY\)](#). 2019 May 13;11(9):2653-2669. doi: 10.18632/aging.101938.

Prostate enlargement and altered urinary function are part of the aging process

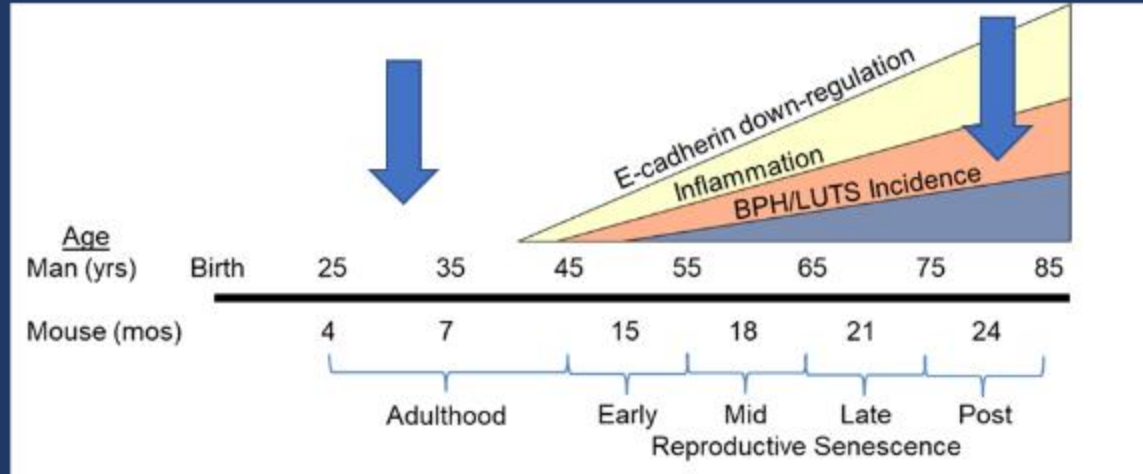
Teresa T Liu^{1 2}, Samuel Thomas³, Dalton T Mclean^{1 4}, Alejandro Roldan-Alzate^{2 5 6},
Diego Hernando^{6 7}, Emily A Ricke¹, William A Ricke^{1 8}



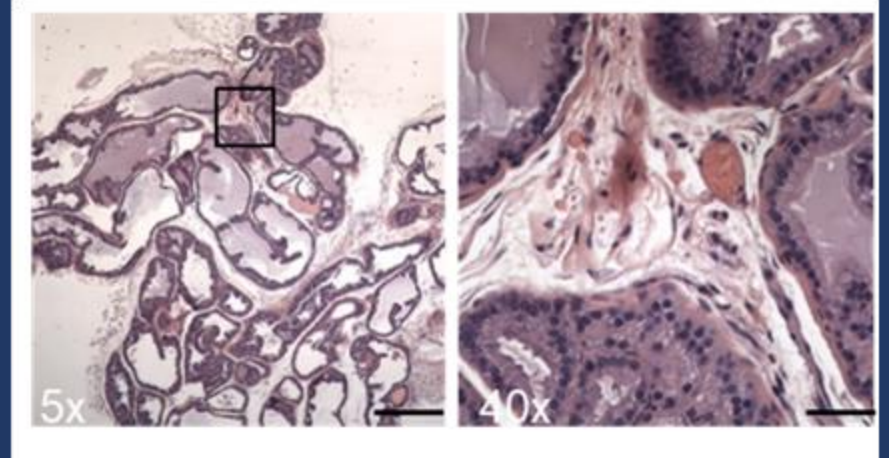
Does aging influence the impact of E-cadherin reduction?



Impact of aging on control mice...



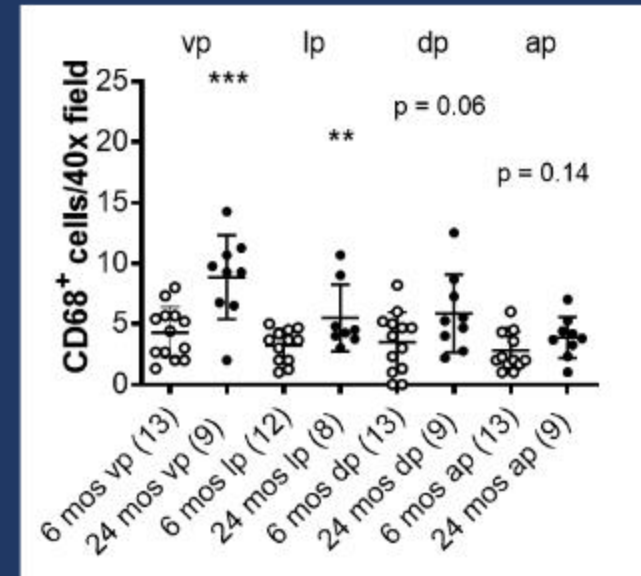
Prostate



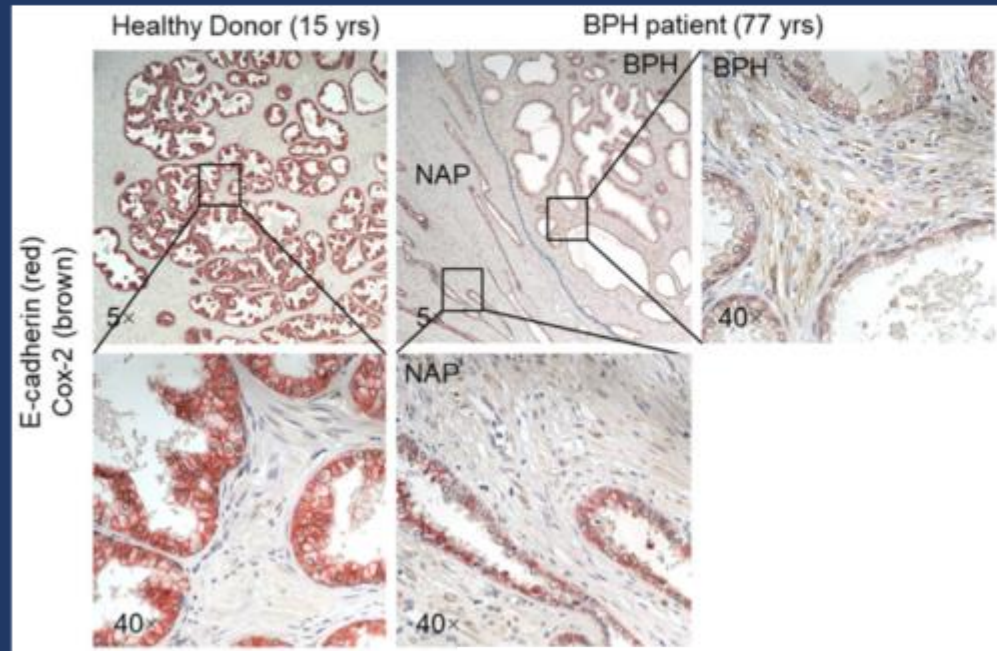
Bladder

Table 4. Bladder voiding characteristics in male *Cdh1^{flx/+}* mice 6 mos vs 24 mos.

Genotype:	6 mos <i>Cdh1^{flx/flx}</i>		24 mos <i>Cdh1^{flx/+}</i>		p-value
	Mean	S.D.	Mean	S.D.	
Non-voiding Contractions (min ⁻¹)	0.098	0.071	0.209	0.217	0.098
Urinary Frequency	1.80	0.837	2.50	1.643	0.413
Average Single Voided Volume (μl)	608	103	217.8	155.1	0.001
Total Urine (μl)	1094	534.0	567.7	348.2	0.071



Correlation of E-cadherin with aging and inflammation in human prostate



Am J Clin Exp Urol 2021;9(1):XXX-XXX
www.ajceu.us /ISSN:2330-1910/AJCEU0128120

Original Article

E-cadherin expression is inversely correlated with aging and inflammation in the prostate

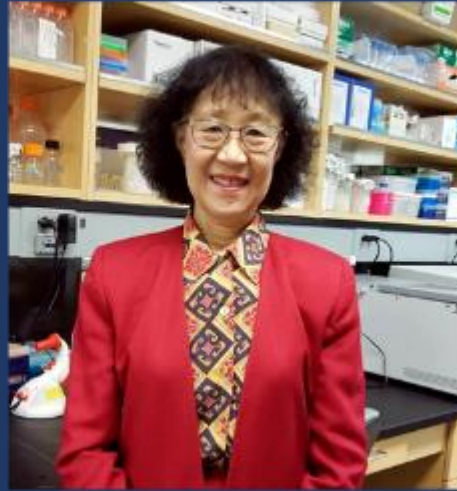
Laura E Pascal^{1,2*}, Rajiv Dhir^{3*}, Goundappa K Balasubramani⁴, Wei Chen¹, Chandler N Hudson¹, Pooja Srivastava³, Anthony Green³, Donald B DeFranco^{5,6}, Naoki Yoshimura^{1,6}, Zhou Wang^{1,2,6}

Table 5. Pearson correlation of E-cadherin and stromal COX-2 (str) immunostaining with age and inflammatory cells in prostate

E-cadherin vs.	Age	COX-2 (epi)	COX-2 (str)	CD8	CD4	CD20	CD68
Pearson r							
r	-0.56	-0.28	-0.14	-0.36	-0.29	-0.45	-0.40
95% CI	-0.78 to -0.23	-0.60 to 0.13	-0.50 to 0.26	-0.66 to 0.030	-0.61 to 0.11	-0.71 to -0.073	-0.68 to -0.015
R squared	0.32	0.076	0.020	0.13	0.083	0.20	0.16
p value							
p (two-tailed)	0.0027	0.070	0.15	0.022	0.043	0.19	0.082



Conversations because of CAIRIBU:



Future:

1. Target prostate inflammation?

2. Mechanisms of aging in the prostate and bladder that impact BPH/LUTS

