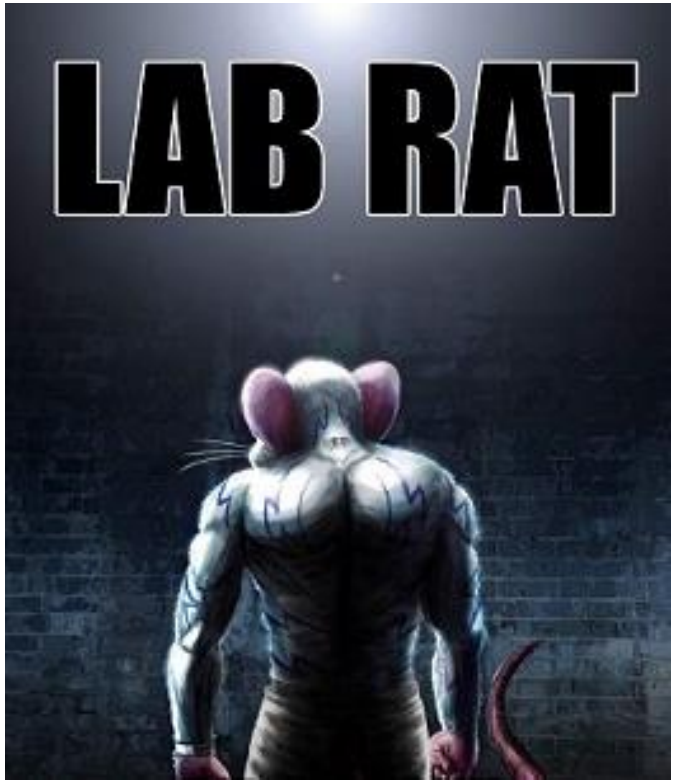
Curso avançado em Modelos Animais de Doenças Humanas

Experimentação animal translacional em urologia



Edgar Tavares da Silva

FMUC FACULDADE DE MEDICINA UNIVERSIDADE DE COIMBRA
CHUC CENTRO HOSPITALAR E UNIVERSITÁRIO DE COIMBRA
Serviço de Urologia e Transplantação Renal
NESU

Investigação Translacional

- Investigação translaccional
  - European Society for Translational Medicine (EUSTM) interdisciplinary branch of the biomedical field supported by three main pillars: bench-side, bedside and community

- Requer conhecimentos e capacidades tanto de investigação fundamental (“laboratório”) como de prática clínica (“cabeceira do doente”)

Urologia

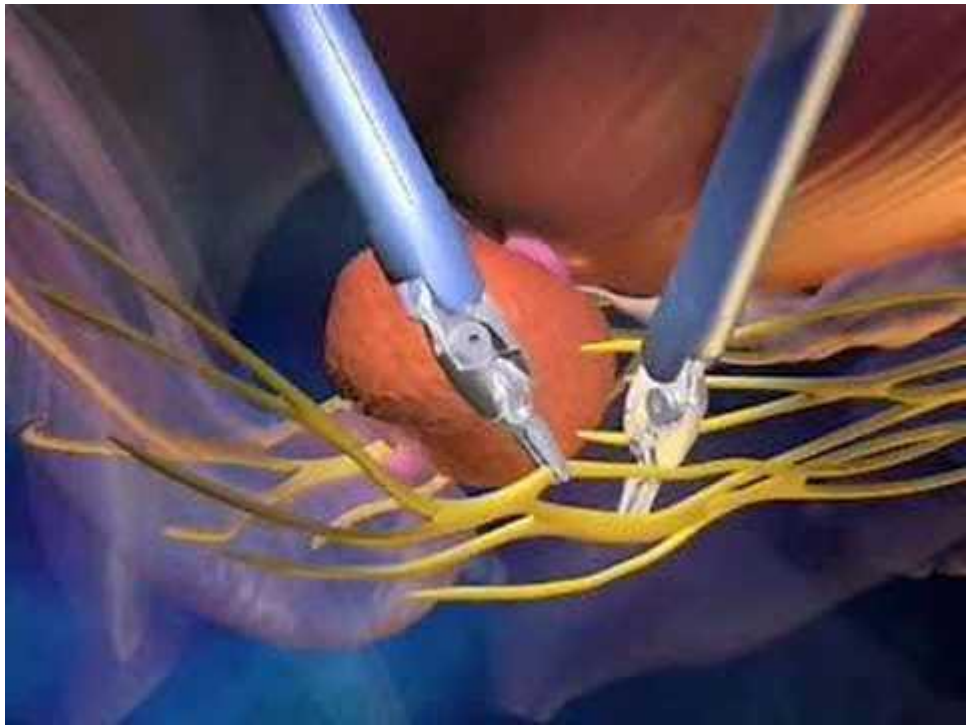
- Especialidade médica que estuda e trata a patologia do aparelho génito-urinário

  - Urologia Geral
  - Oncologia Urológica
  - Andrologia
  - Litíase Urinária
  - Urologia Funcional e Neuro-Urologia
  - Urologia Pediátrica
  - Transplantação Renal

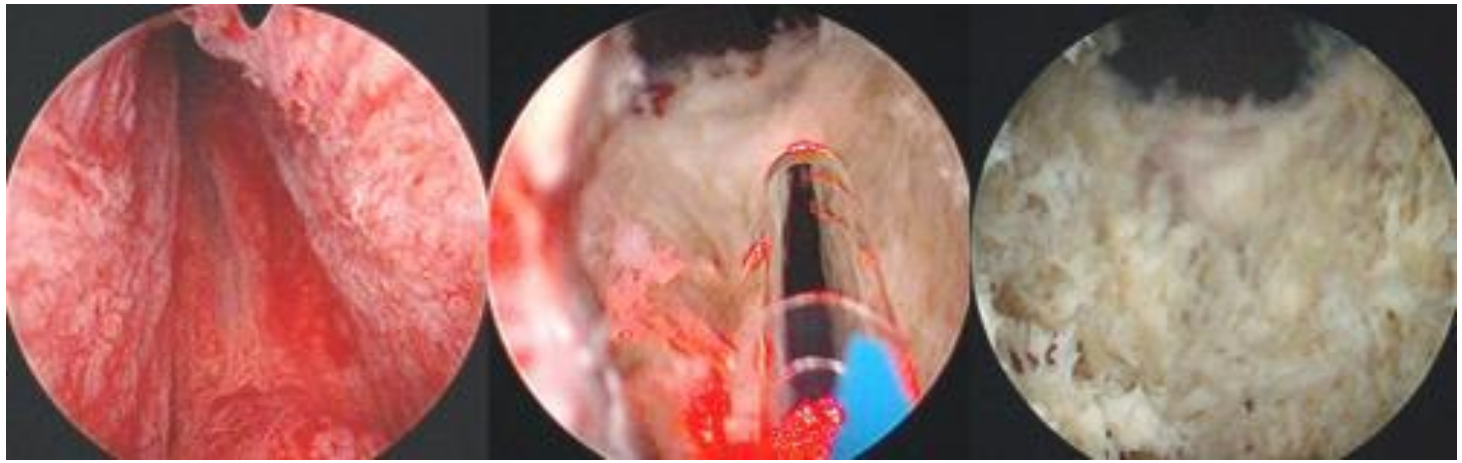
Hot Topics em Urologia

- Oncologia
  - Neoplasia da Próstata
  - Neoplasia da Bexiga
  - Neoplasia do Rim
- Bexiga Hiperactiva
- Disfunções Sexuais
  - Líbido, Erecção, Orgasmo e Ejaculação
- Cirurgia minimamente invasiva
  - Laparoscópica/Robótica, Endoscópica e Percutânea

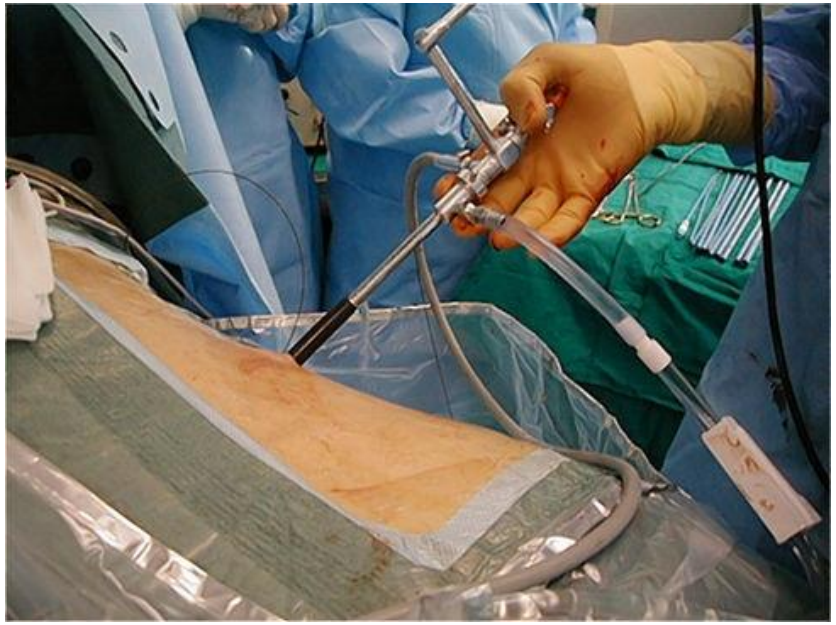
Cirurgia Robótica

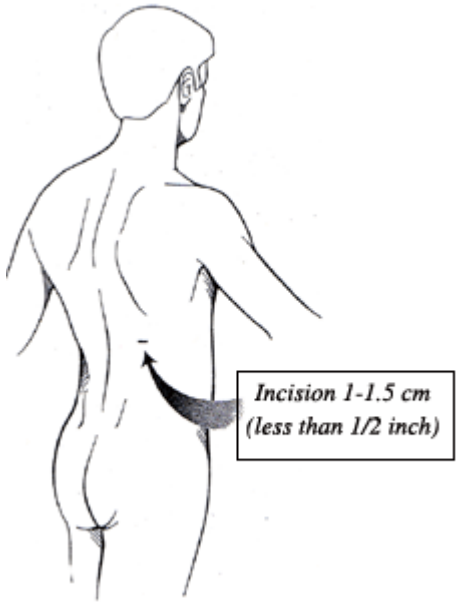


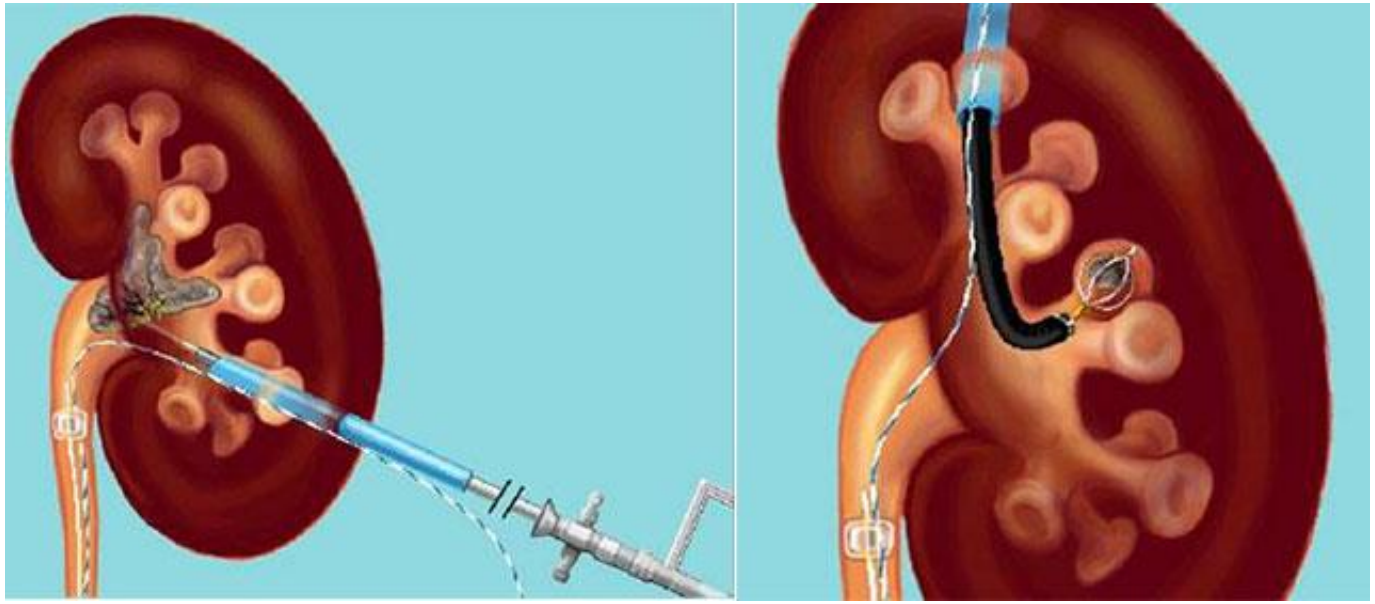
Cirurgia Endoscópica



Cirurgia Percutânea

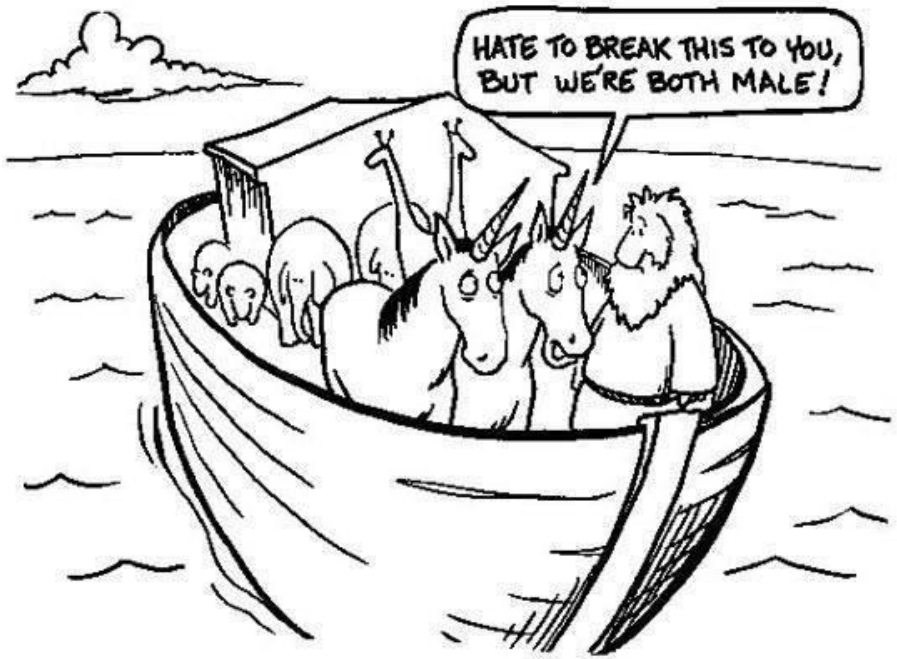






Modelos Animais em Urologia

1. Patologia oncológica
2. Disfunções Vesicais
3. HBP
4. Litíase
5. Transplantação Renal
6. Outros



What really happened to unicorns.

Modelos animais de patologia oncológica

Tumor da próstata

Tumor da próstata

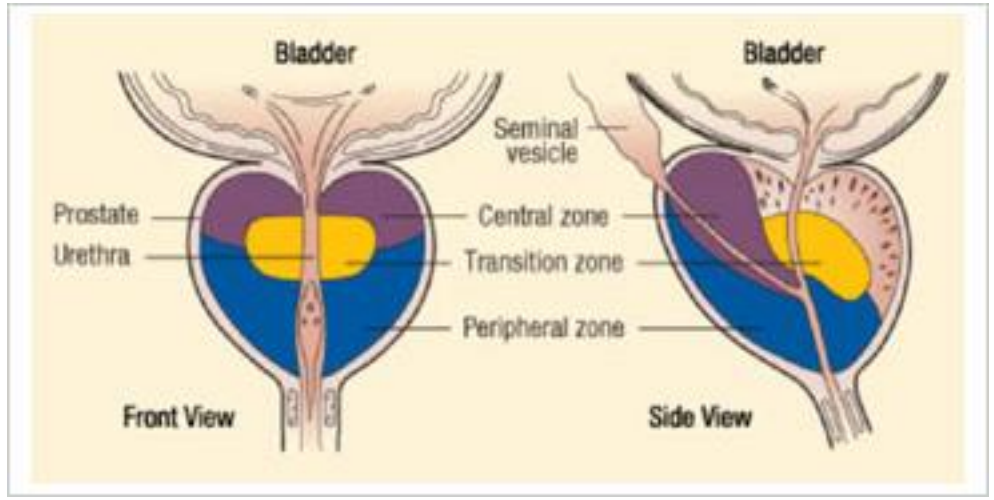
- Tipos de modelos:
  - Heterotópicos
  - Ortotópicos
    - Espontâneos
    - Xenoenxertos
    - Indução hormonal
    - Indução química
  - Metastáticos

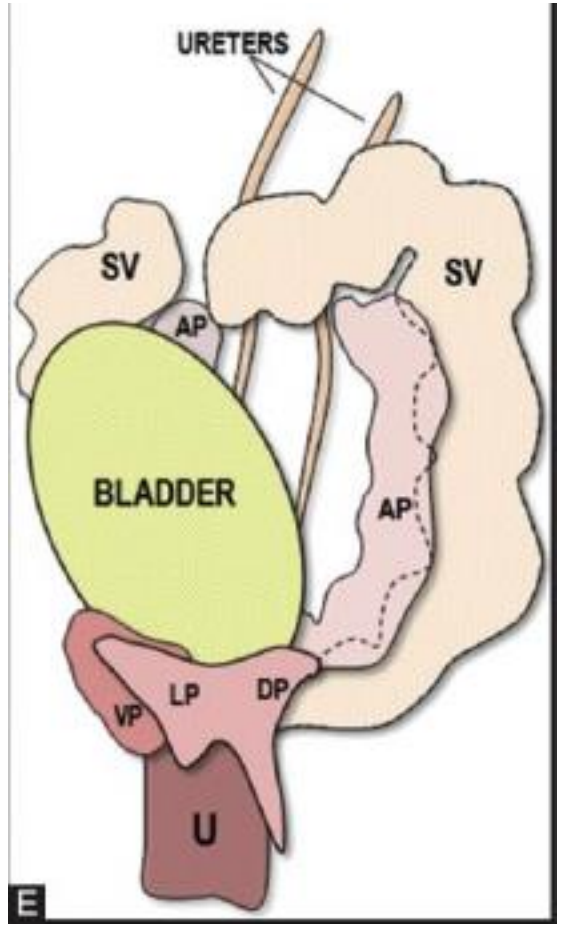
Tumor da próstata

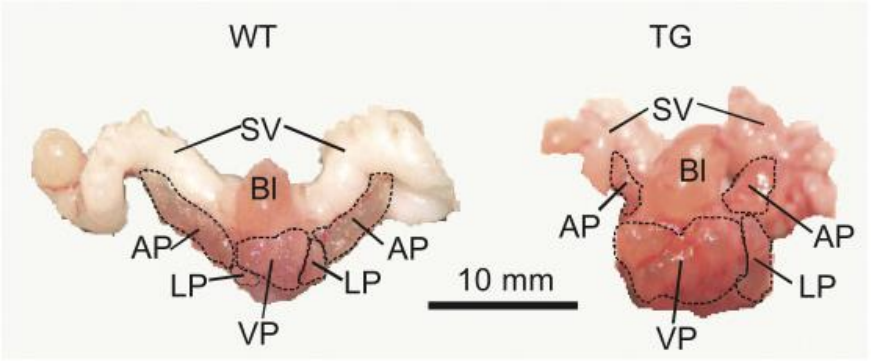
- Tipos de modelos:
  - Heterotópicos
    - Mais simples
    - Fácil seguimento
    - Sem necessidade de cirurgia de implantação
    - Não metastizam

Tumor da próstata

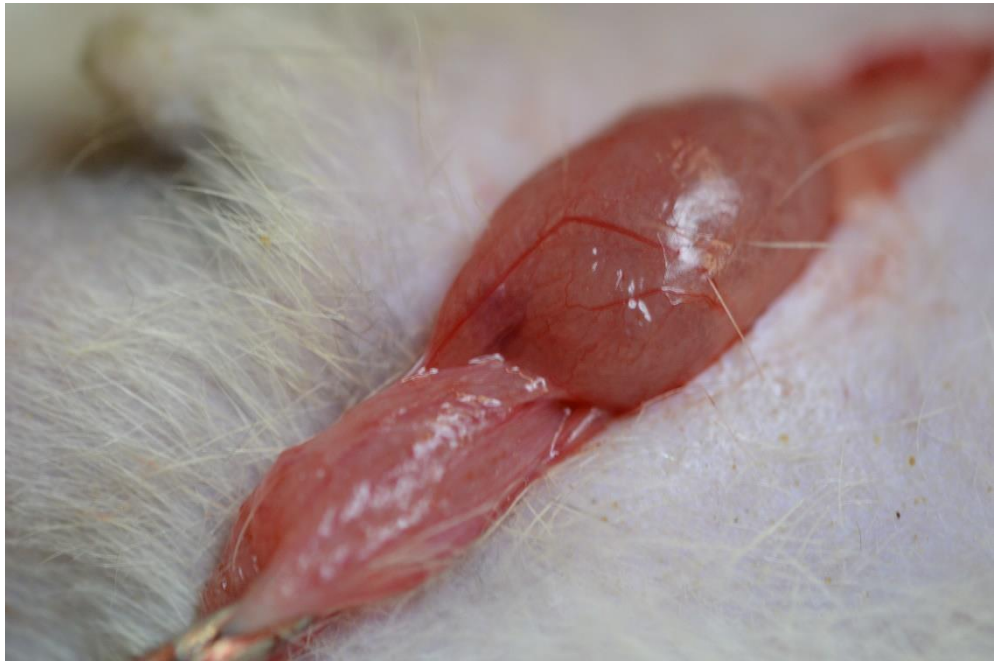
- Tipos de modelos:
  - Ortotópicos
    - Próstata animal
      - Não produz PSA
      - Lobos separados
        - Anterior, Ventral, Lateral, Dorsal
      - Partilha 95% dos genes com a humana

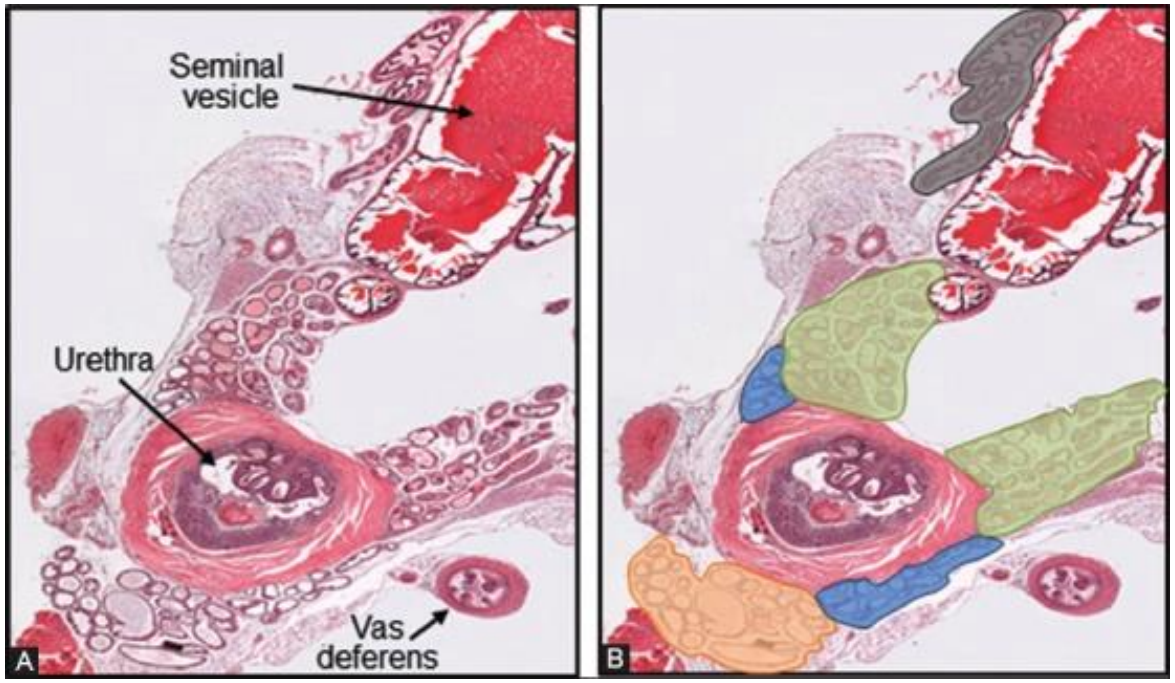






Tumor da próstata



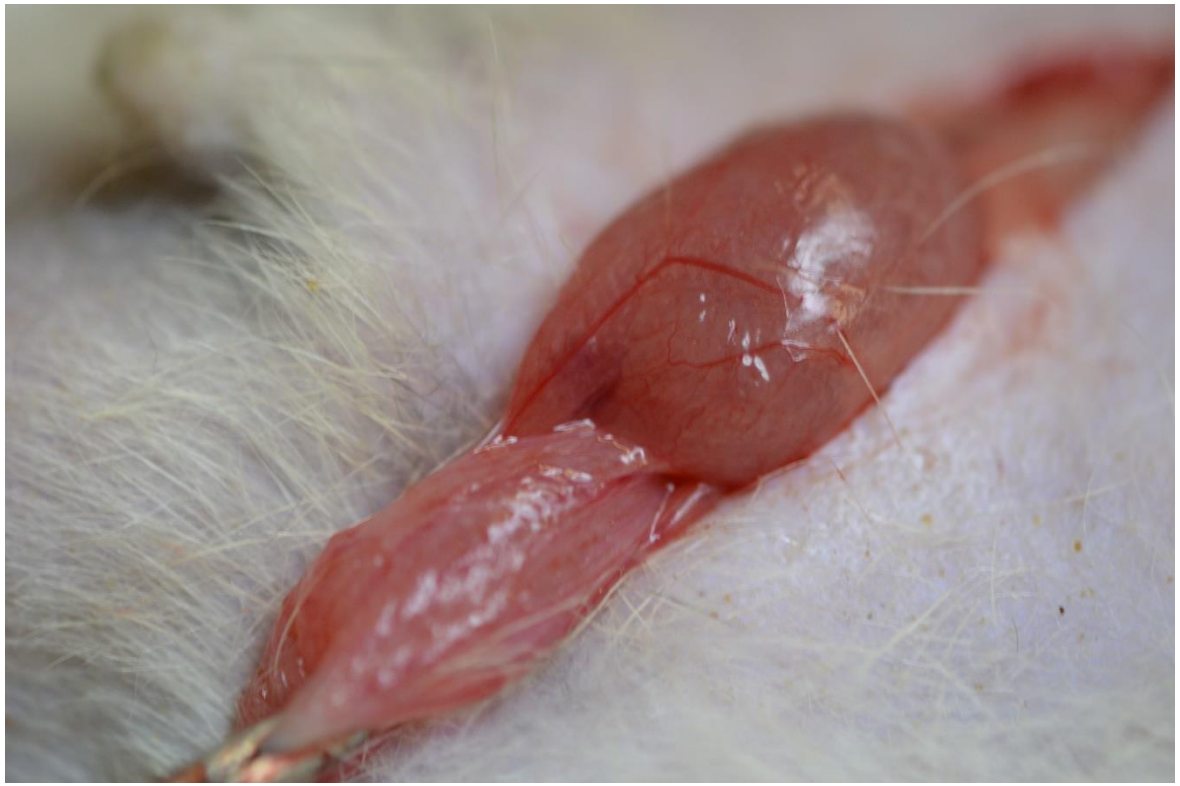


Tumor da próstata

- Tipos de modelos:
  - Ortotópicos
    - Espontâneos
      - Lobund-Wistar – 10% aos 26 meses
      - ACI/Seg – 70% aos 36 meses
        - 16% são macroscópicos
    - Xenoenxertos
      - Linhas celulares
    - Indução hormonal
      - Lobund-Wistar – protocolos com testosterona ou testosterona e estrogénios
    - Indução química
      - N-metil-N-nitrosureia (MNU), N-nitrosobis-2-oxopropil-amina (BOP), 3,2'-dimetil-4-aminobifenil (DMAB)
    - Transgénicos
      - Oncogenes virais
      - Knockout de genes supressores tumorais

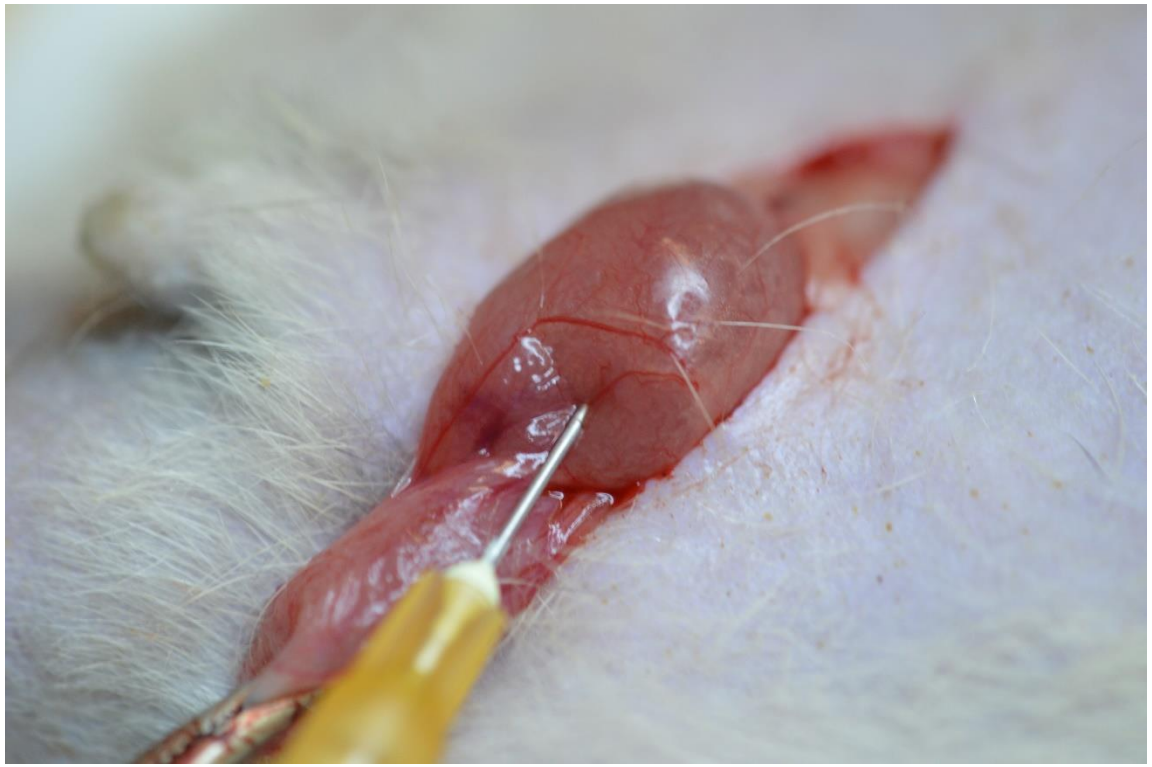
Tumor da próstata

- Tipos de modelos:
  - Ortotópicos



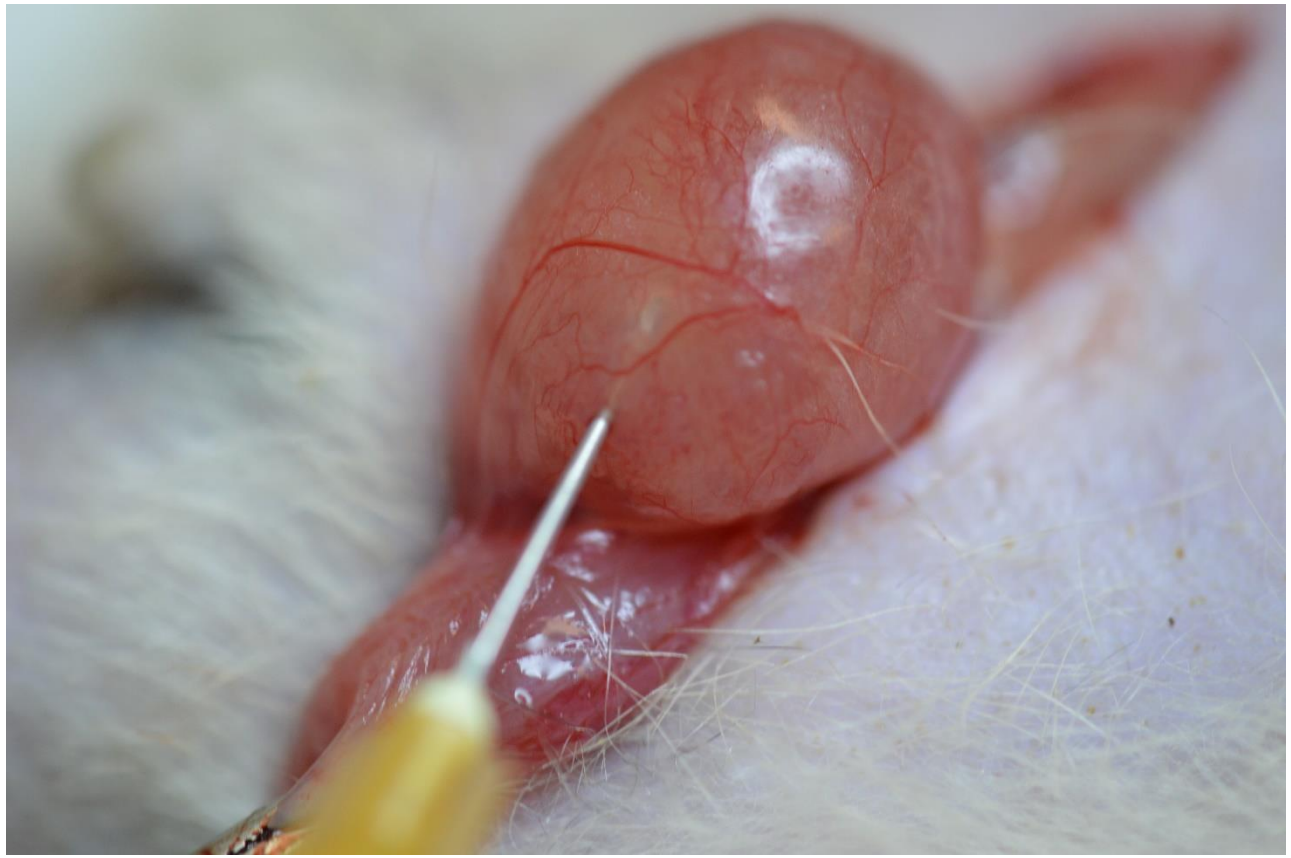
Tumor da próstata

- Tipos de modelos:
  - Ortotópicos



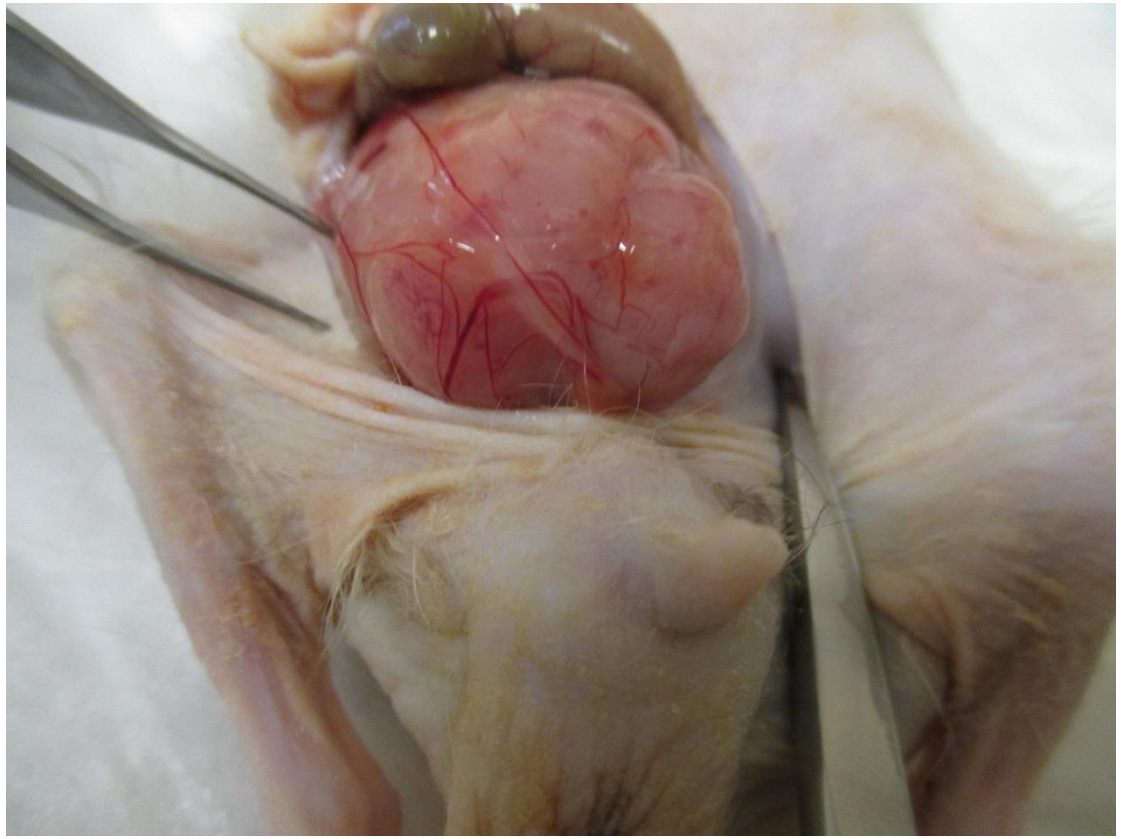
Tumor da próstata

- Tipos de modelos:
  - Ortotópicos



Tumor da próstata

- Tipos de modelos:
  - Ortotópicos

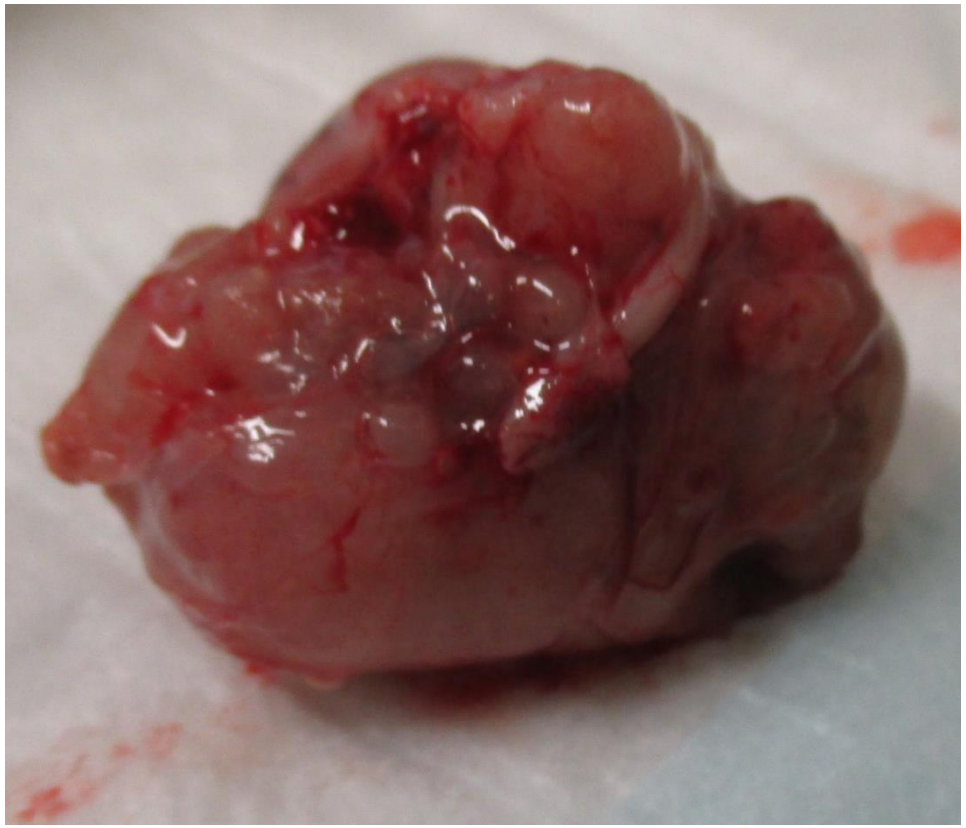


Tumor da próstata

- Tipos de modelos:
  - Ortotópicos

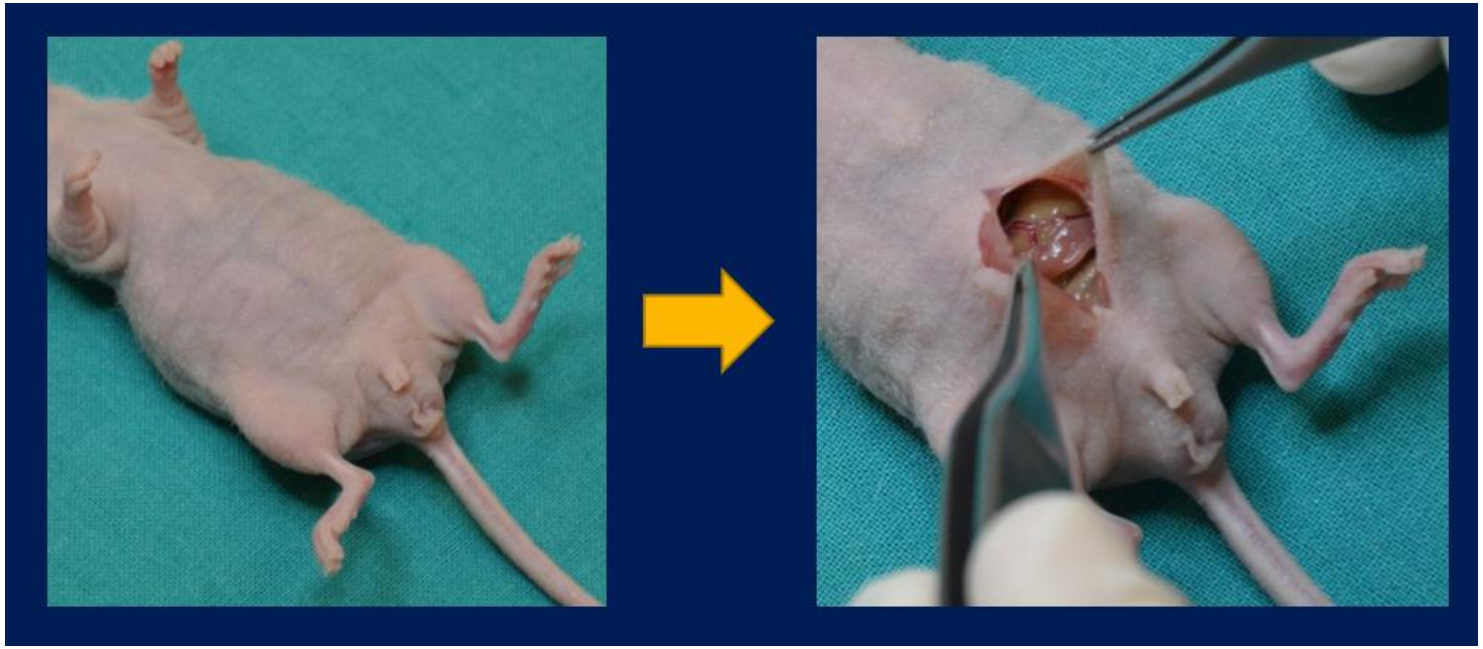
Tumor da próstata

- Tipos de modelos:
  - Ortotópicos



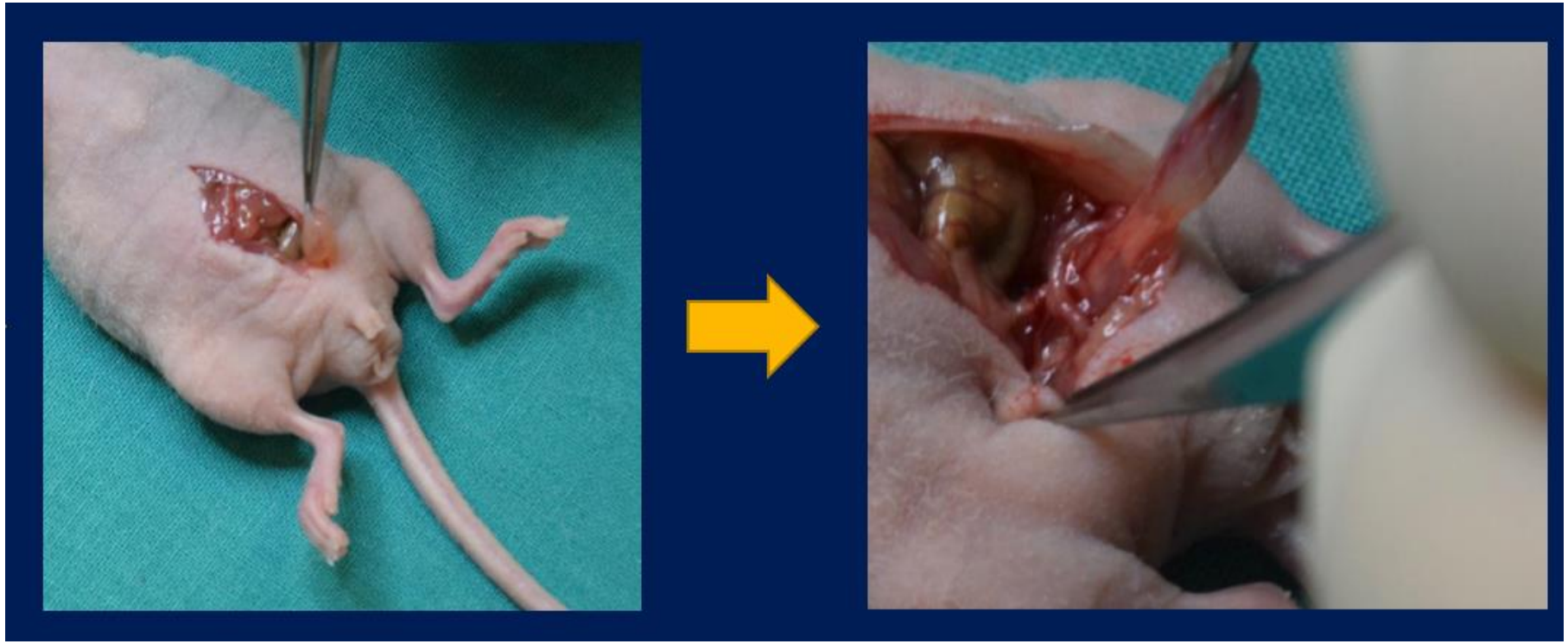
Tumor da próstata

- Tipos de modelos:
  - Ortotópico localmente avançado
    - Desenvolvido no nosso instituto
    - Simular um estadio avançado da doença
    - Aumentar a probabilidade de metastização



Tumor da próstata

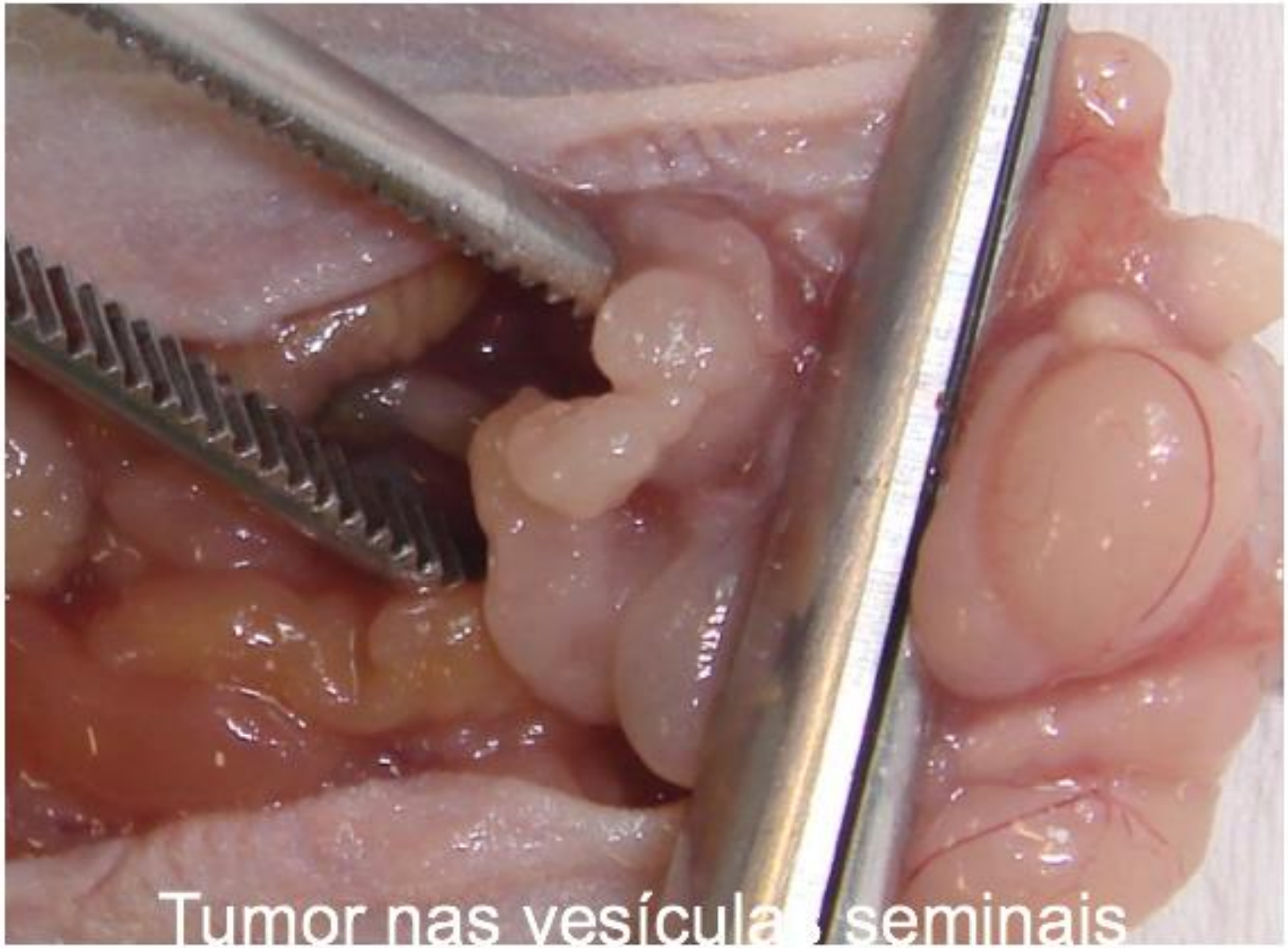
- Tipos de modelos:
  - Ortotópico localmente avançado



Modelo completamente ortotópico

Modelo localmente avançado

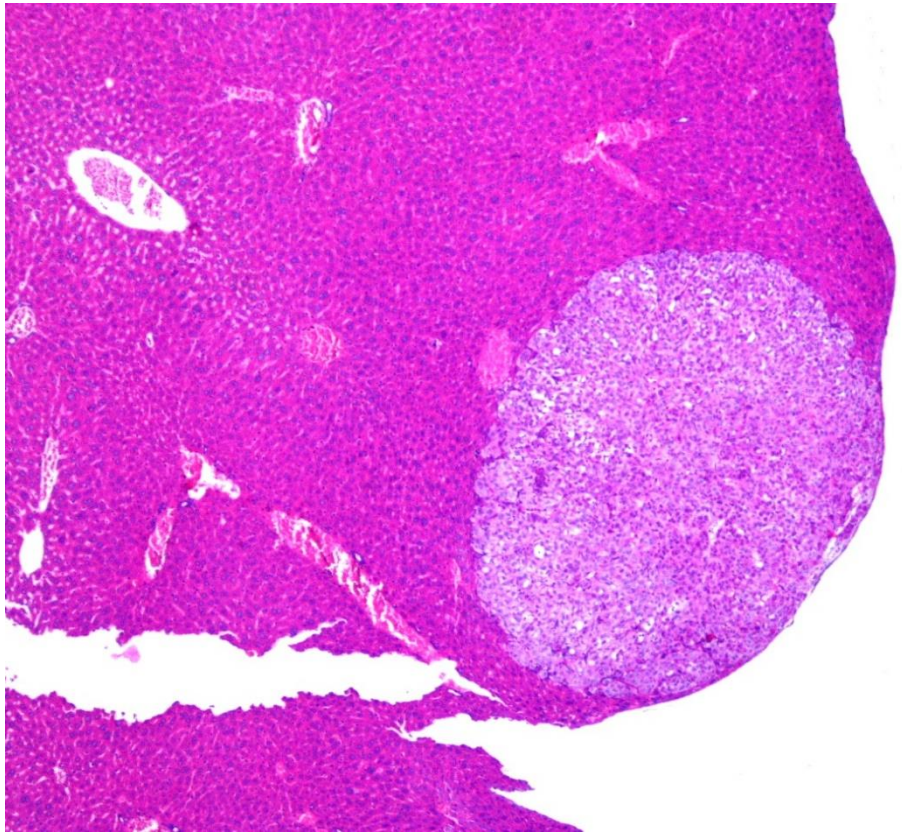
Tumor da próstata



Tumor da próstata

Tumor da próstata

- Tipos de modelos:
  - Ortotópico localmente avançado



Tumor da próstata

- Tipos de modelos:
  - Metastáticos
    - Presentem responder à dificuldade em obter metastização a partir de modelos ortotópicos
    - Tipos
      - Injecção intra-cardíaca
        - Metástases ganglionares
        - Extremidades de ossos longos
      - Injecção intra-óssea
      - Injecção veia dorsal da cauda

Modelos animais de patologia oncológica

Tumor da bexiga

Tumor da bexiga

- Tipos de modelos:
  - Heterotópicos
  - Ortotópicos
    - Indução química
    - Enxertos
      - Singénicos
      - Xenoenxertos
    - Genéticamente modificados

Tumor da bexiga

- Tipos de modelos:
  - Ortotópicos
    - Indução química
      - Usados para estudos de quimioprevenção
      - Levam 8 a 14 meses a desenvolverem-se
      - Químicos usados
        - BBN (N-butil-N-(4-hidroxibutil)nitrosamina)
          - É o agente mais usado porque lembra um TCT de alto grau
          - Começa com atipia, passa a cis e finalmente MIBC
        - FANFT (N-[4-(5-nitro-2-furyl)-2-tiazol]formamido)
          - Tumores predominantemente uroteliais, com algum grau de diferenciação escamosa
          - Também já se descreveu hiperplasia, displasia e *cis*
        - MNU (N-metil-N-nitrosureia)
          - Dá alterações neoplásicas progressivas, tornando-se cada vez menos diferenciadas
          - Começa com cis, passa a papilar e depois MIBC volumosos

Tumor da bexiga

- Tipos de modelos:
  - Ortotópicos
    - Enxertos
      - Xenoenxertos – requerem ratos imunocomprometidos
        - Não dá para avaliar o papel da imunidade
        - Problemas – sucesso de implantação e seguimento oncológico
      - Singénicos – tumor de rato em ratos imunocompetentes
        - MB49 e as MBT-2
        - A taxa de tumor varia de 30-100%, dependendo se há pré-tratamento
    - Ratos geneticamente modificados
      - Os tumores destes modelos são menos heterogéneos – influencia a progressão e metastização
      - A célula de origem pode não reflectir as dos tumores humanos
      - Limitações – longos períodos de latência, penetrância incompleta e requerem um elemento genético artificial

Tumor da bexiga

- Sucesso na implantação
  - Depende de técnica e do pré-tratamento

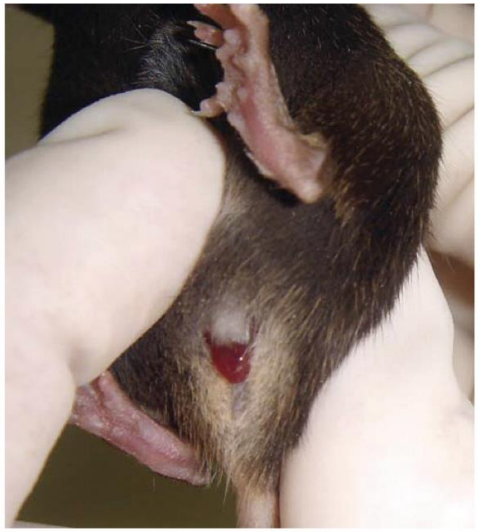
  - Sem pré-tratamento só surge tumor em 6 a 50% dos ratos
    - Com o pré-tratamento surge em 80-100%
    - Tipos de pré-tratamento - ácido clorídrico, tripsina, coagulação da mucosa com corrente eléctrica, traumatismo com catéter
    - Visa lesar a barreira de GAGs

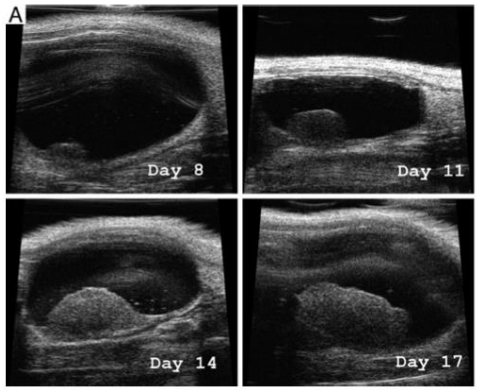
  - Técnica de instilação
    - Implantar uma concentração maior
    - Aumentar o tempo de contacto
      - Cerclagem em redor da uretra para impedir a saída das células
      - 30 min-3 horas
    - Mas o aumento do tempo de contacto aumenta:
      - Tumores do urotélio alto
      - Estenoses da uretra/perfuração vesical
      - Mortalidade animal (pode chegar aos 20%)

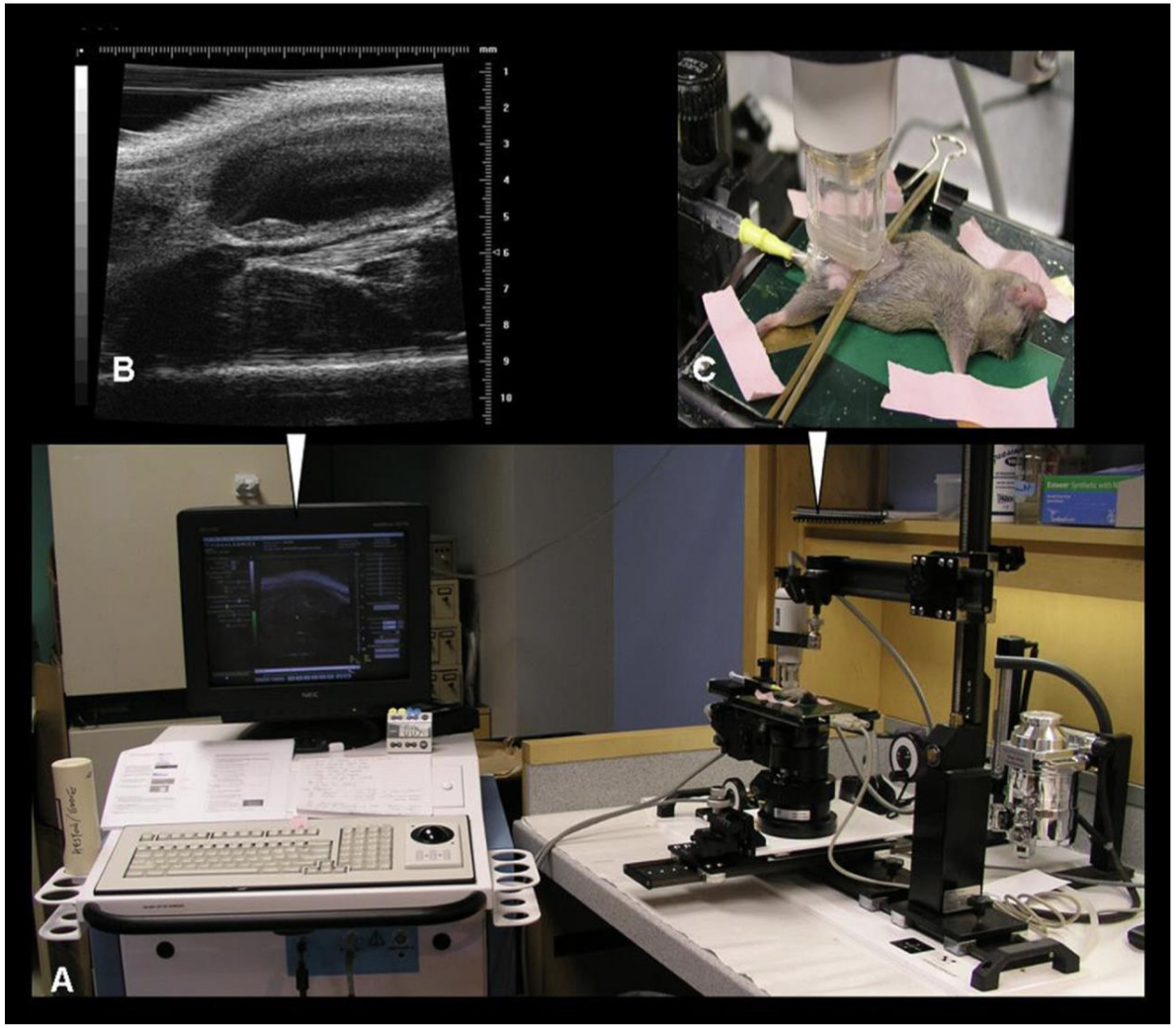
Tumor da bexiga

- Seguimento do tumor
  - Clínico
  - Cistoscopia ultra-fina – sensibilidade e especificidade >90%
  - Ecografia – transluminal ou transabdominal
    - Valor preditivo do estadio de 95%
    - Requer treino
  - RMN – tem mau poder de resolução para lesões pequenas e iniciais
  - Todos requerem anestesia e cateterização, o que leva a perdas de animais

Tumor da bexiga





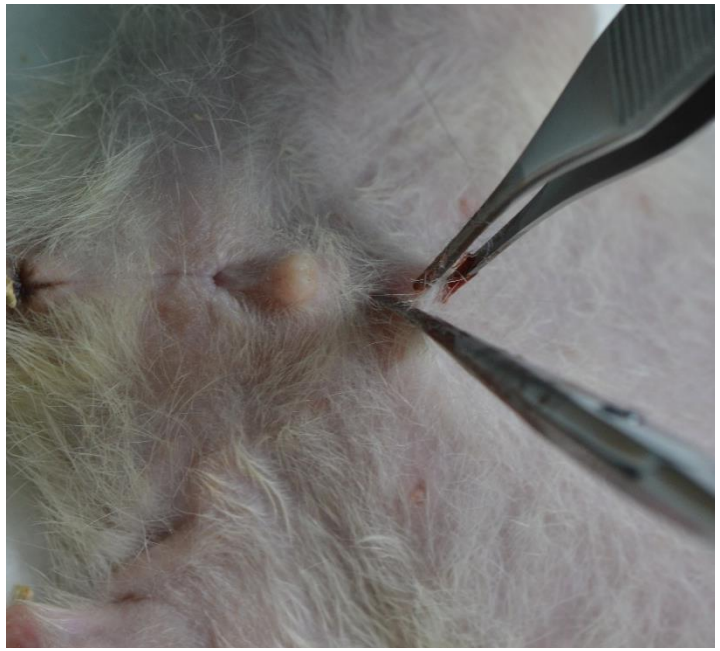


Tumor da bexiga

- Modelo ortotópico com cistostomia fechada
  - Procurava resolver o problema do seguimento
  - Baseava-se na experiência dos modelos heterotópicos com sucesso de implantação de ~80%

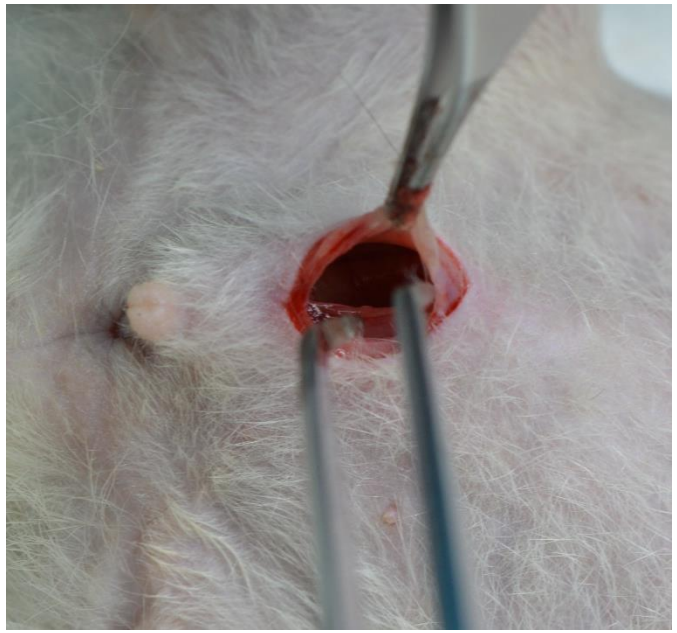
Tumor da bexiga

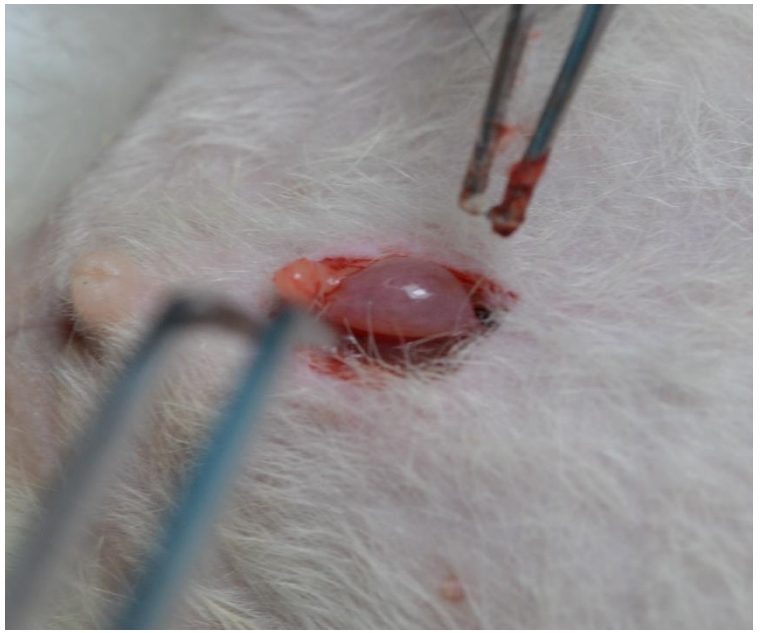
- Modelo ortotópico com cistostomia fechada



Tumor da bexiga

- Modelo ortotópico com cistostomia fechada





Tumor da bexiga

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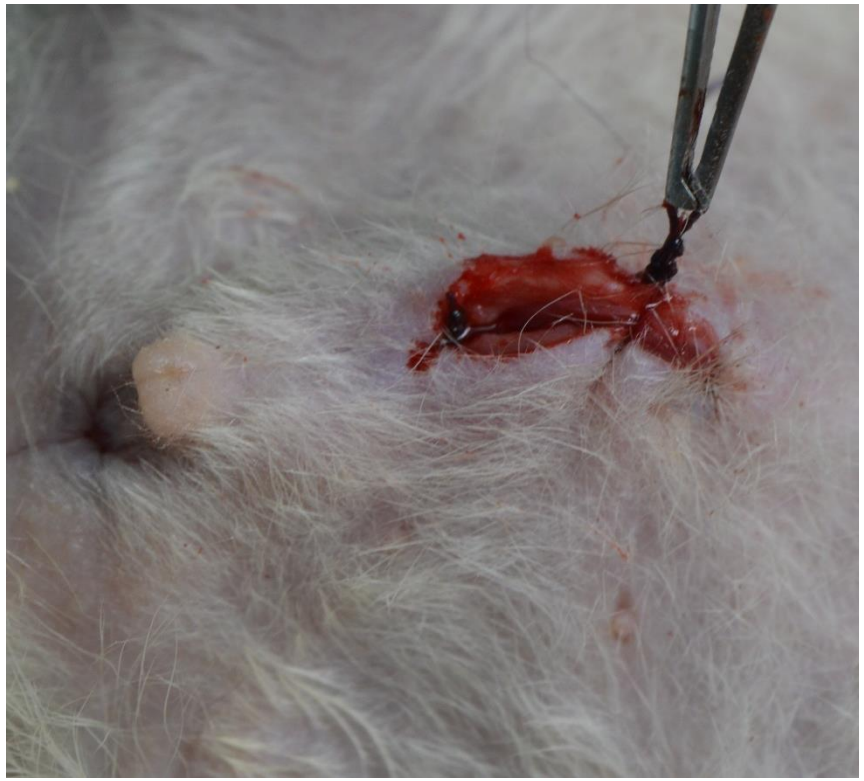

Tumor da bexiga

- Modelo ortotópico com cistostomia fechada

Tumor da bexiga

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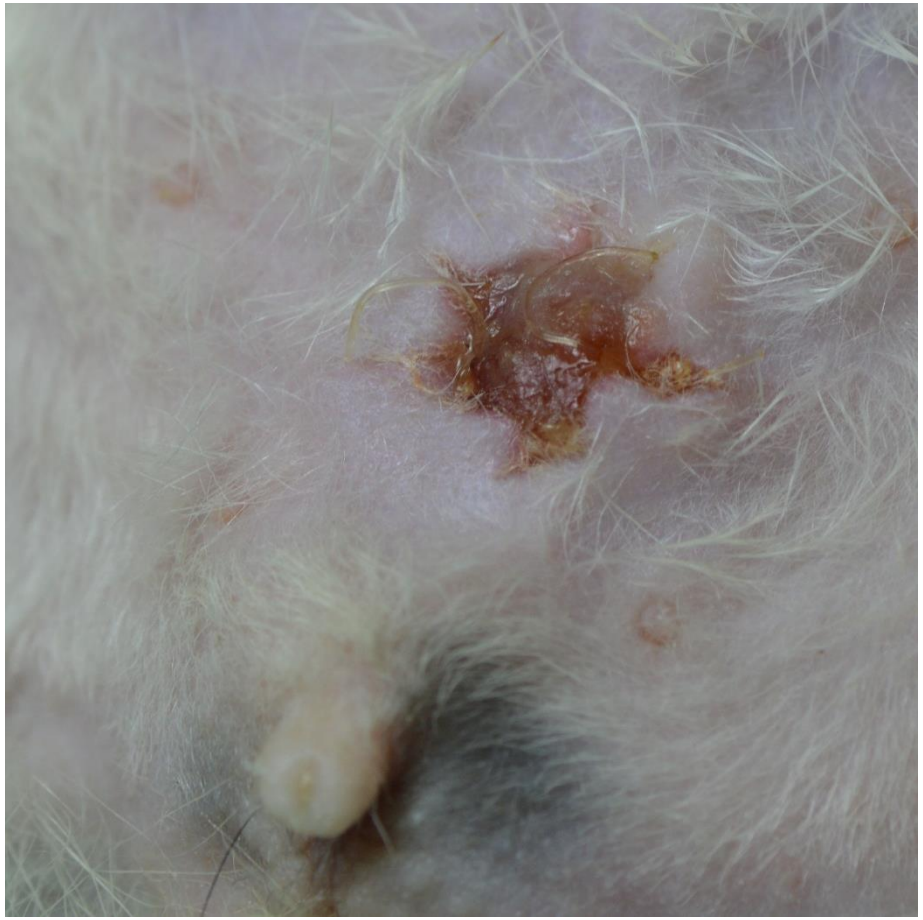
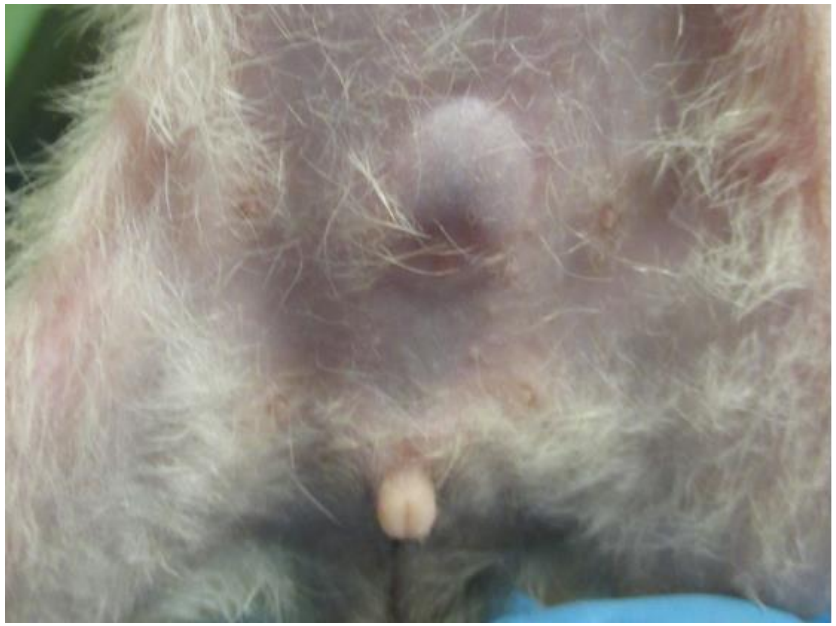
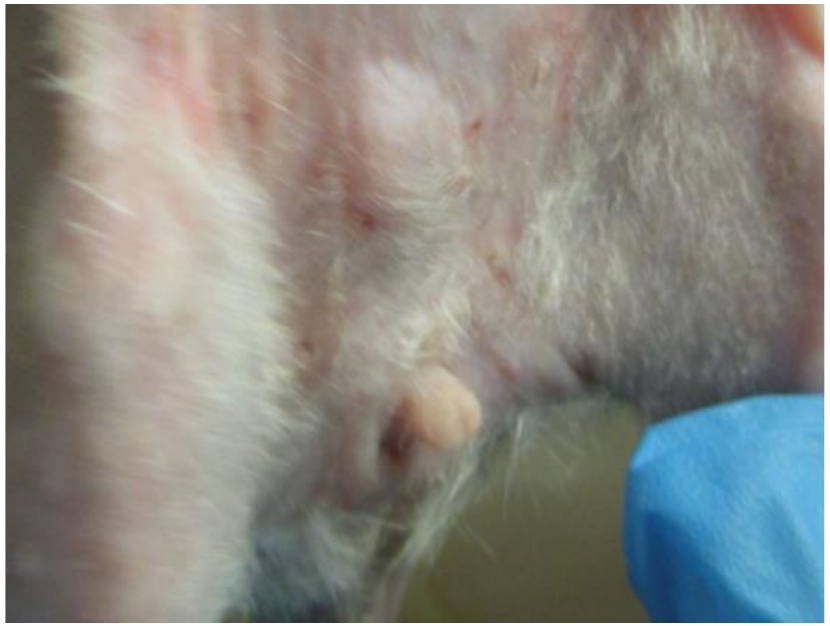
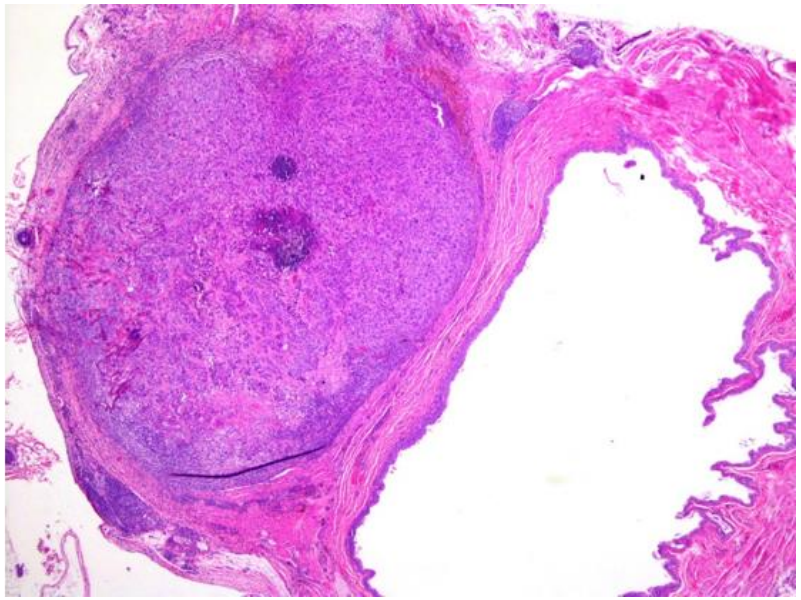


Tumor da bexiga





Tumor da bexiga



Tumor da bexiga

Modelos animais de patologia oncológica

Tumor do rim

Xenoenxerto Heterotópico

EUROPEAN UROLOGY 59 (2011) 619–628

available at www.sciencedirect.com
journal homepage: www.europeanurology.com

European Association of Urology

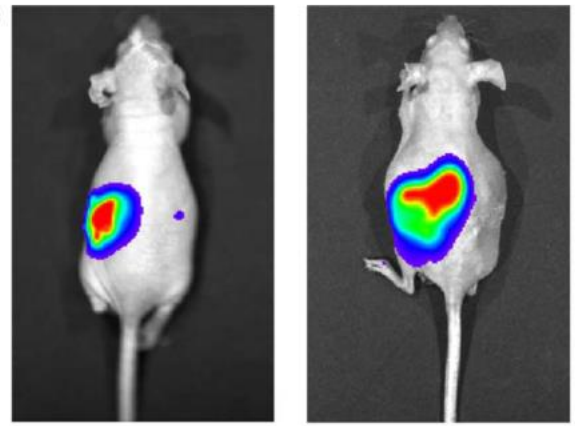
Kidney Cancer

Development and Characterization of Clinically Relevant Tumor Models From Patients With Renal Cell Carcinoma

Jose A. Karam[a], *Xiu-Ying Zhang*[a], *Pheroze Tamboli*[b], *Vitaly Margulis*[c], *Hua Wang*[d], *E. Jason Abel*[a], *Stephen H. Culp*[a], *Christopher G. Wood*[a,*]

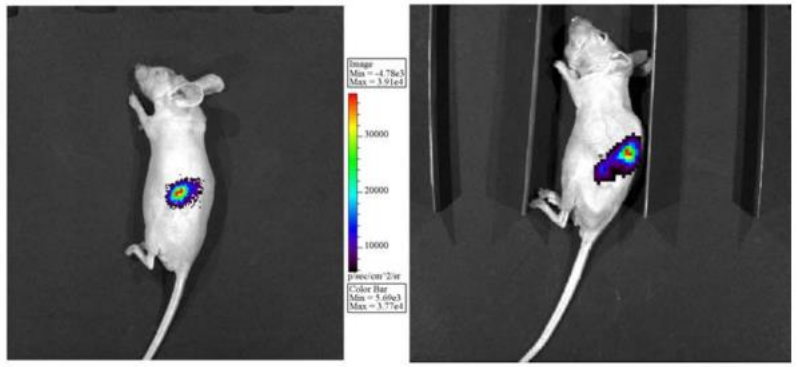
Measurements: Tumor tissues obtained during surgery were implanted into the subcutaneous space of female BALB/c nude mice and serially passaged into new mice. Tumors were characterized by histology, short tandem repeat (STR) fingerprinting, von Hippel-Lindau (VHL) gene sequencing, and single nucleotide polymorphism (SNP) analysis. Tumor-bearing mice were treated with sunitinib or everolimus. Primary cell cultures were derived from patient tumors and transfected with a lentivirus carrying the luciferase gene. Four subcutaneous xenograft mouse models were developed, representing papillary type 1, papillary type 2, clear cell, and clear cell with sarcomatoid features RCC.

(a)



MDA-RCC-55, day 27 MDA-RCC-55, day 46

(b)



MDA-RCC-80, day 13 MDA-RCC-80, day 25

Crioablação Massas Renais

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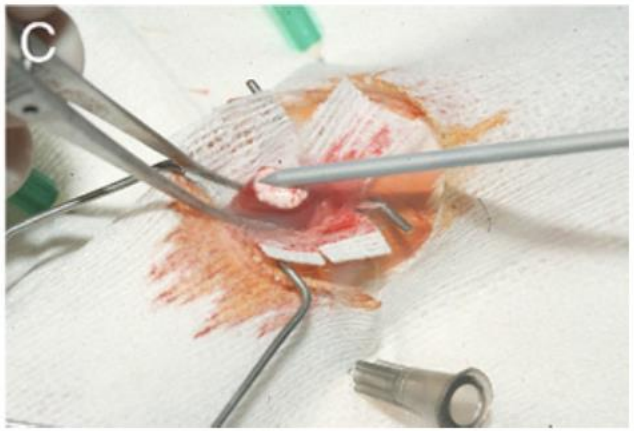
Printed in U.S.A.
DOI:10.1016/j.juro.2009.08.110

Immunological Response to Renal Cryoablation in an In Vivo Orthotopic Renal Cell Carcinoma Murine Model

Surena F. Matin,* Padmanee Sharma, Inderbir S. Gill,† Charles Tannenbaum, Michael G. Hobart, Andrew C. Novick and James H. Finke‡

From the Departments of Urology (SFM) and Genitourinary Medical Oncology (PS), University of Texas M. D. Anderson Cancer Center, Houston, Texas, Department of Urology, University of Southern California (ISG), Los Angeles, California, Glickman Urological Institute (CAN) and Lerner Research Institute (CT, JHF), Cleveland Clinic, Cleveland, Ohio, and Alberta Urology Institute (MGH), Edmonton, Alberta, Canada

Conclusions: This study shows the potential feasibility of this animal model for studying cryo-immunology. We confirm the absence of any significant immune cell infiltration in tumor bearing kidneys and report a significant inflammatory infiltrate after cryoablation, consisting primarily of neutrophils, macrophages, and CD4+ and CD8+ T cells with an increase in the T helper type 1/2 ratio. This orthotopic murine model can form the basis of future studies of additional immunological aspects of renal cryoablation.



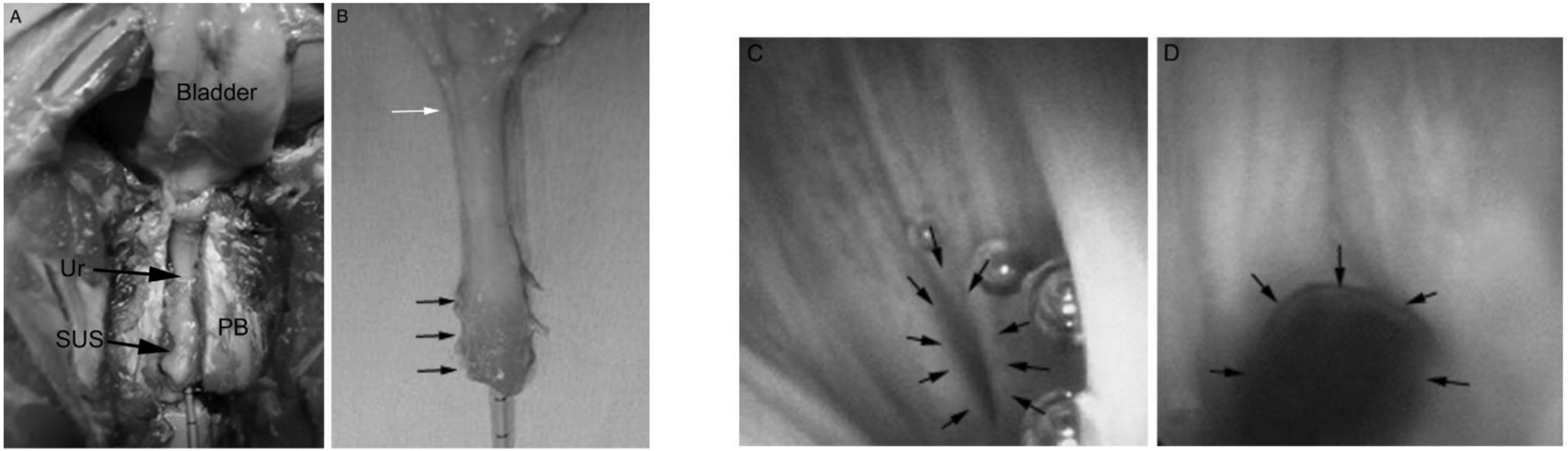
Modelos animais de disfunções vesicais

Incontinência Urinária

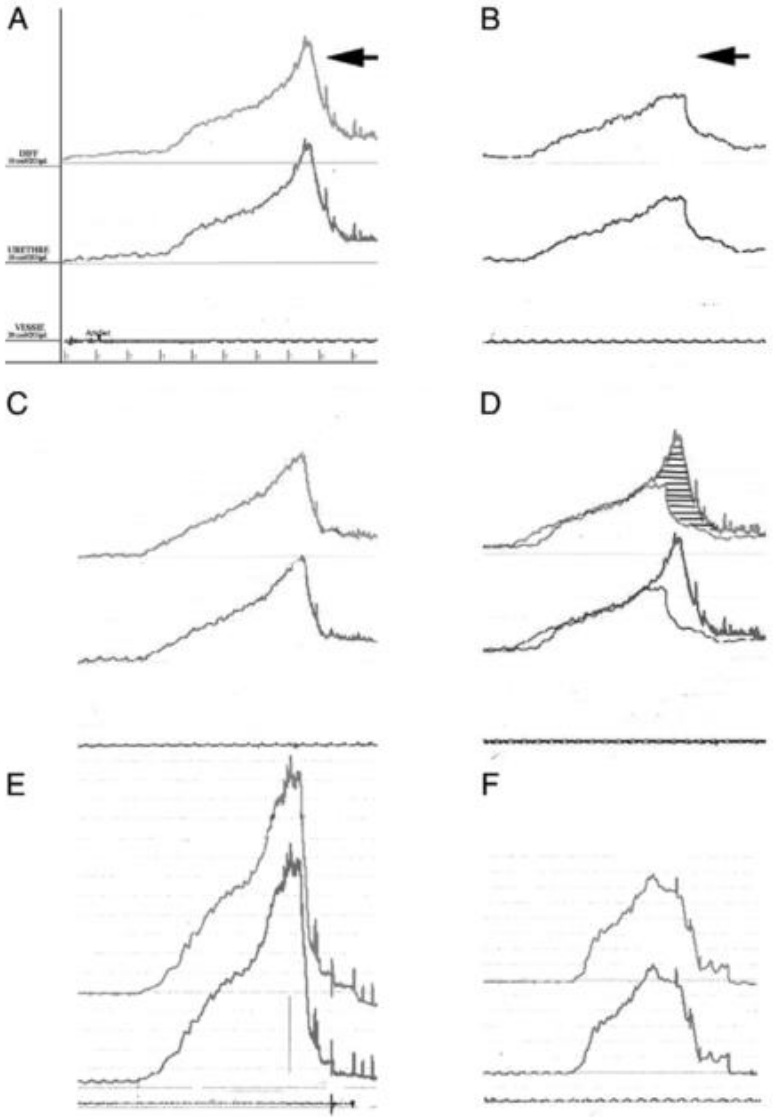
THE JOURNAL OF UROLOGY® Vol. 176, 2729-2735, December 2006

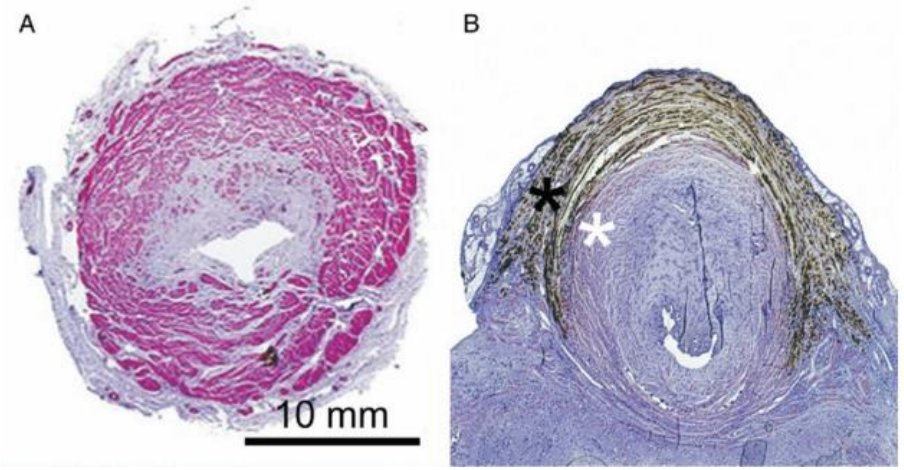
The Striated Urethral Sphincter of the Pig Shows Morphological and Functional Characteristics Essential for the Evaluation of Treatments for Sphincter Insufficiency

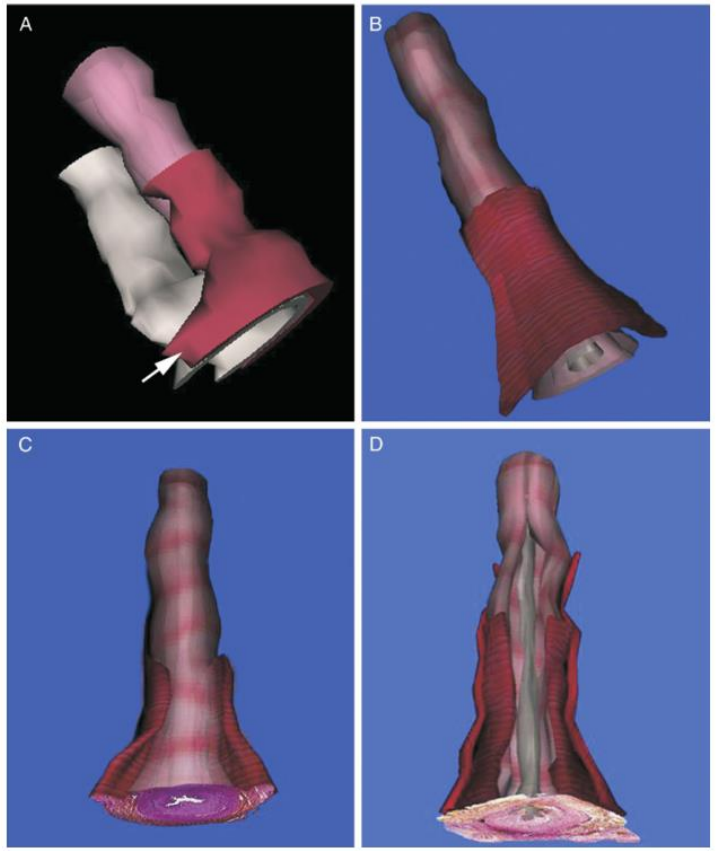
Laurent Zini,* Constant Lecoeur,* Salem Swieb, Hélène Combrisson, Vincent Delmas, Romain Ghérardi, Claude Abbou, Dominique Chopin and René Yiou†



Incontinência urinária







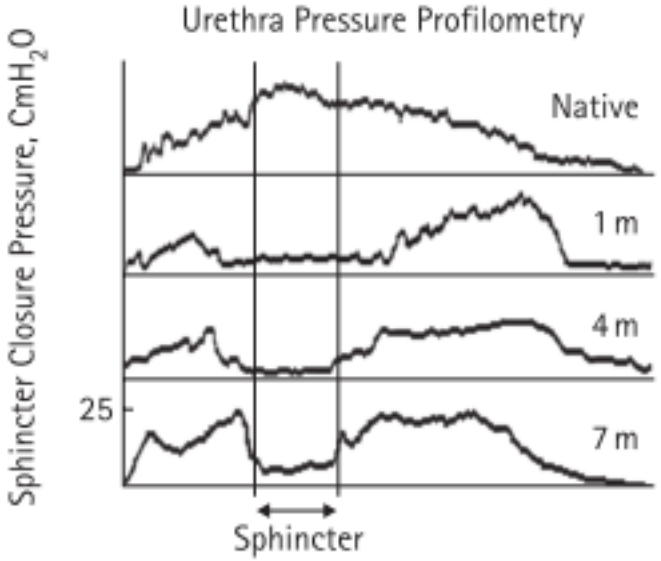
Incontinência Urinária

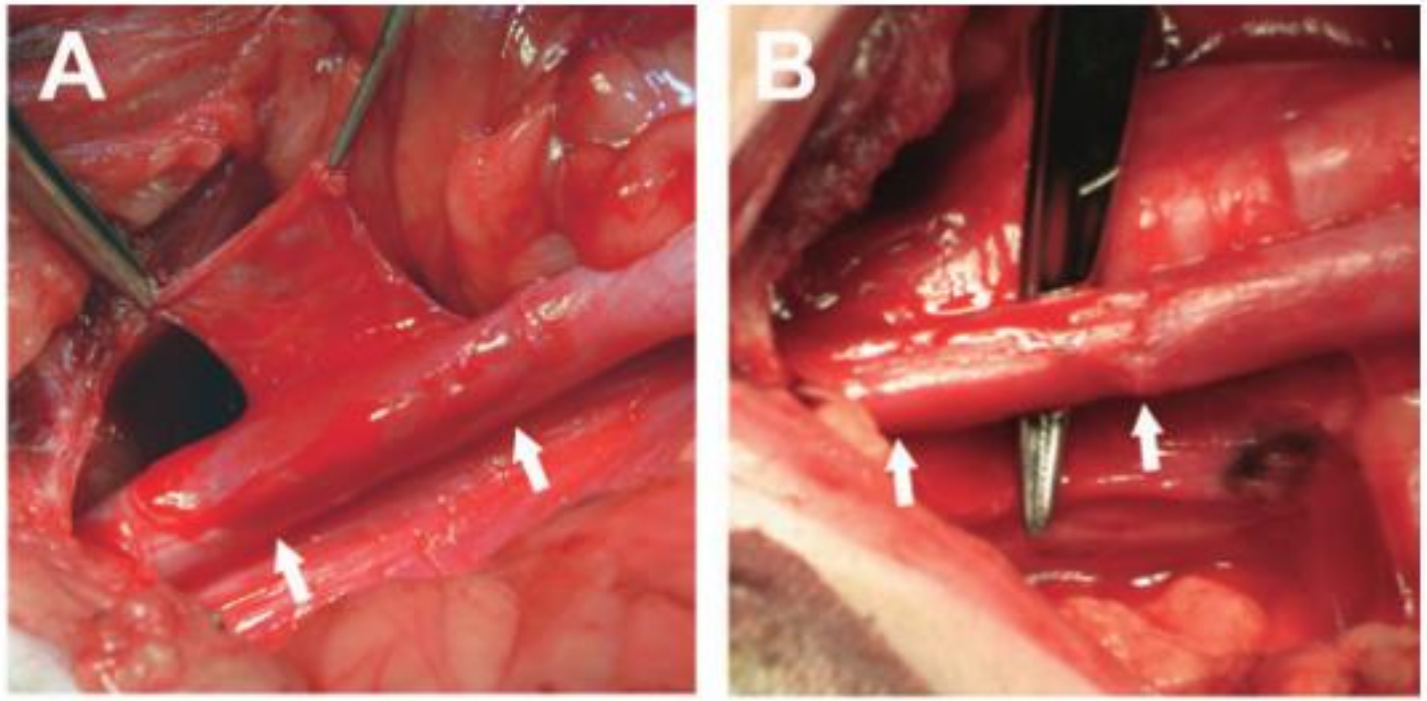
2008 BJU INTERNATIONAL | 103, 248–253 | doi:10.1111/j.1464-410X.2008.08001.x

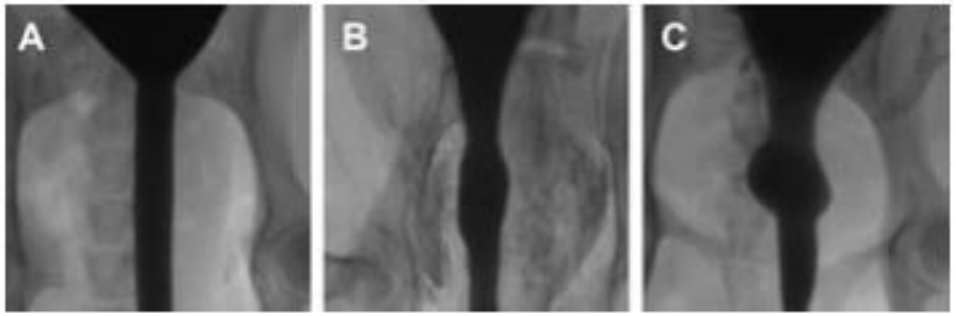
BJUI
BJU INTERNATIONAL

A canine model of irreversible urethral sphincter insufficiency

Daniel Eberli, Karl-Erik Andersson, James J. Yoo and Anthony Atala
Wake Forest Institute for Regenerative Medicine, Medical Center Boulevard, Winston-Salem, North Carolina, USA
Accepted for publication 18 June 2008







Incontinência Urinária

Advanced Drug Delivery Reviews 82–83 (2015) 106–116

Contents lists available at ScienceDirect

Advanced Drug Delivery Reviews

journal homepage: www.elsevier.com/locate/addr

Stress urinary incontinence animal models as a tool to study cell-based regenerative therapies targeting the urethral sphincter☆

Bernardo Herrera-Imbroda [a,1], María F. Lara [a,1], Ander Izeta [b], Karl-Dietrich Sievert [c,d], Melanie L. Hart [c,*]

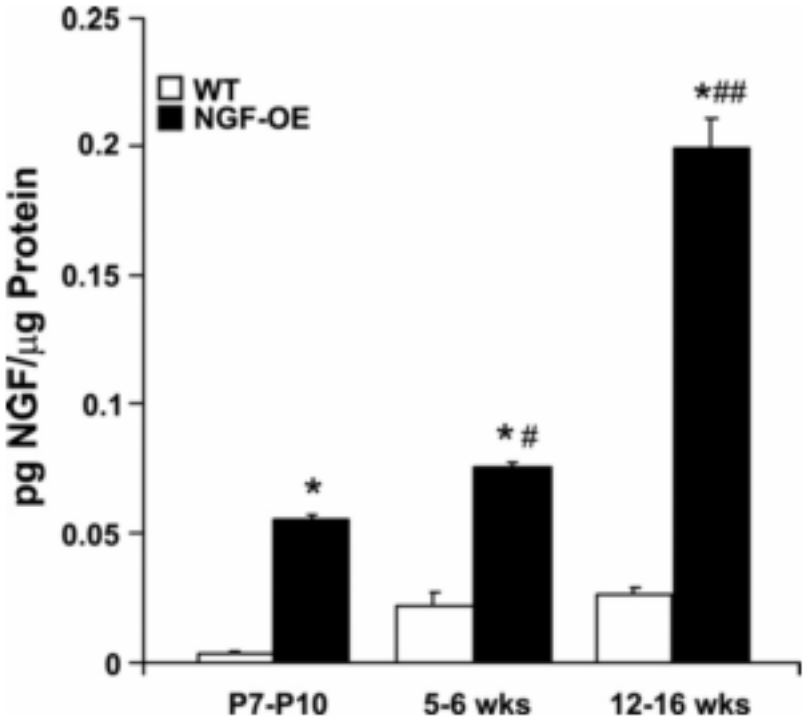
Contents

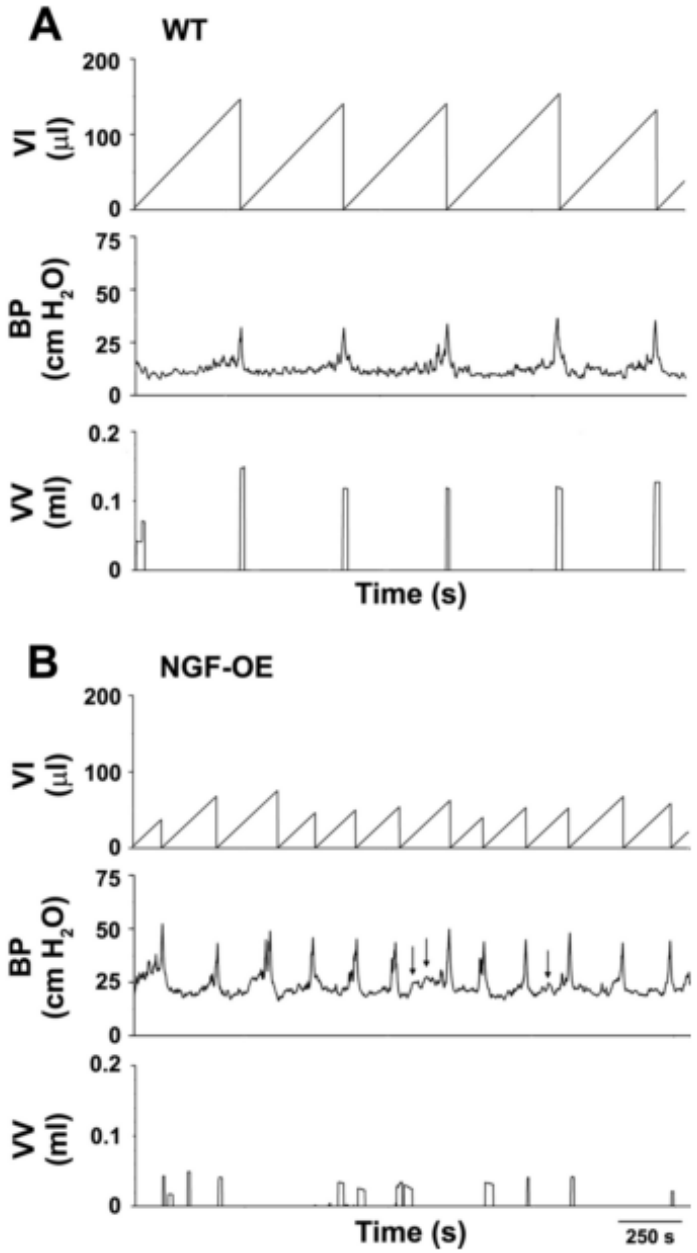
Bexiga Hiperactiva

Am J Physiol Regul Integr Comp Physiol 298: R534–R547, 2010.
First published December 23, 2009; doi:10.1152/ajpregu.00367.2009.

Overexpression of NGF in mouse urothelium leads to neuronal hyperinnervation, pelvic sensitivity, and changes in urinary bladder function

Birthe Schnegelsberg,[1] Tung-Tien Sun,[4] Gary Cain,[3] Anindya Bhattacharya,[1] Philip A. Nunn,[1,2]
Anthony P. D. W. Ford,[1] Margaret A. Vizzard,[5] and Debra A. Cockayne[1,2]





Disfunção Miccional

Am J Physiol Renal Physiol 297: F1101–F1108, 2009.
First published July 8, 2009; doi:10.1152/ajprenal.90749.2008.

Social stress in mice induces voiding dysfunction and bladder wall remodeling

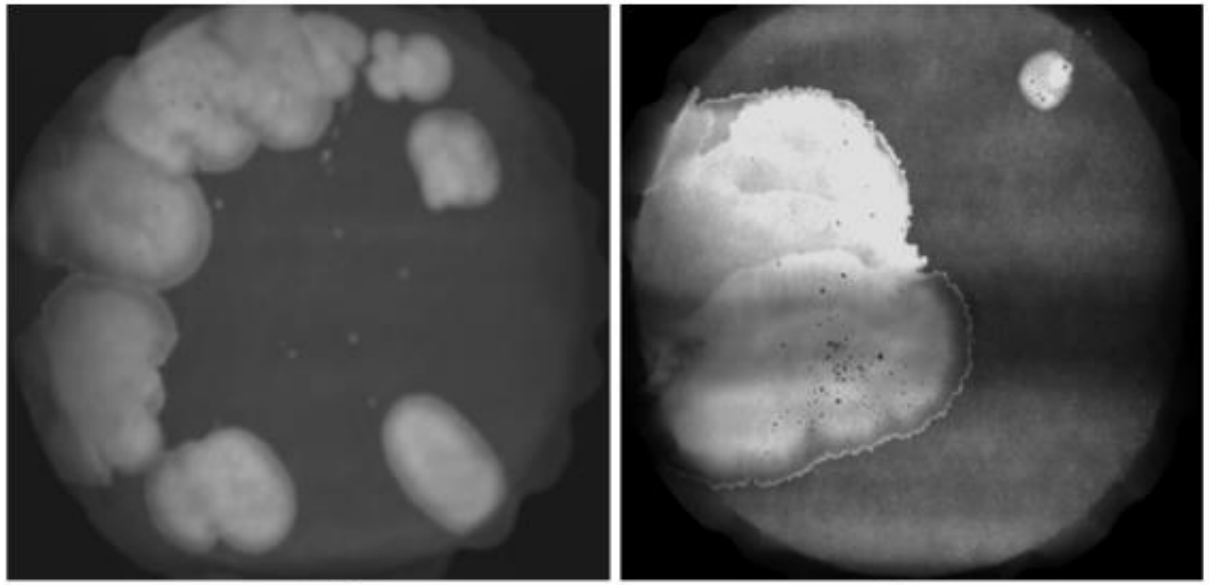
Andy Chang,[1] Stephan Butler,[1] Joanna Sliwoski,[1] Rita Valentino,[2] Douglas Canning,[1] and Stephen Zderic[1]

FVB Male Mice 6 weeks of age
Randomize Litter

Stress Protocol
1 FVB mouse
House with C57 aggressor
1 hour direct exposure
23 hours visual contact
(Screen in place)
Rotate FVB mice among aggressors

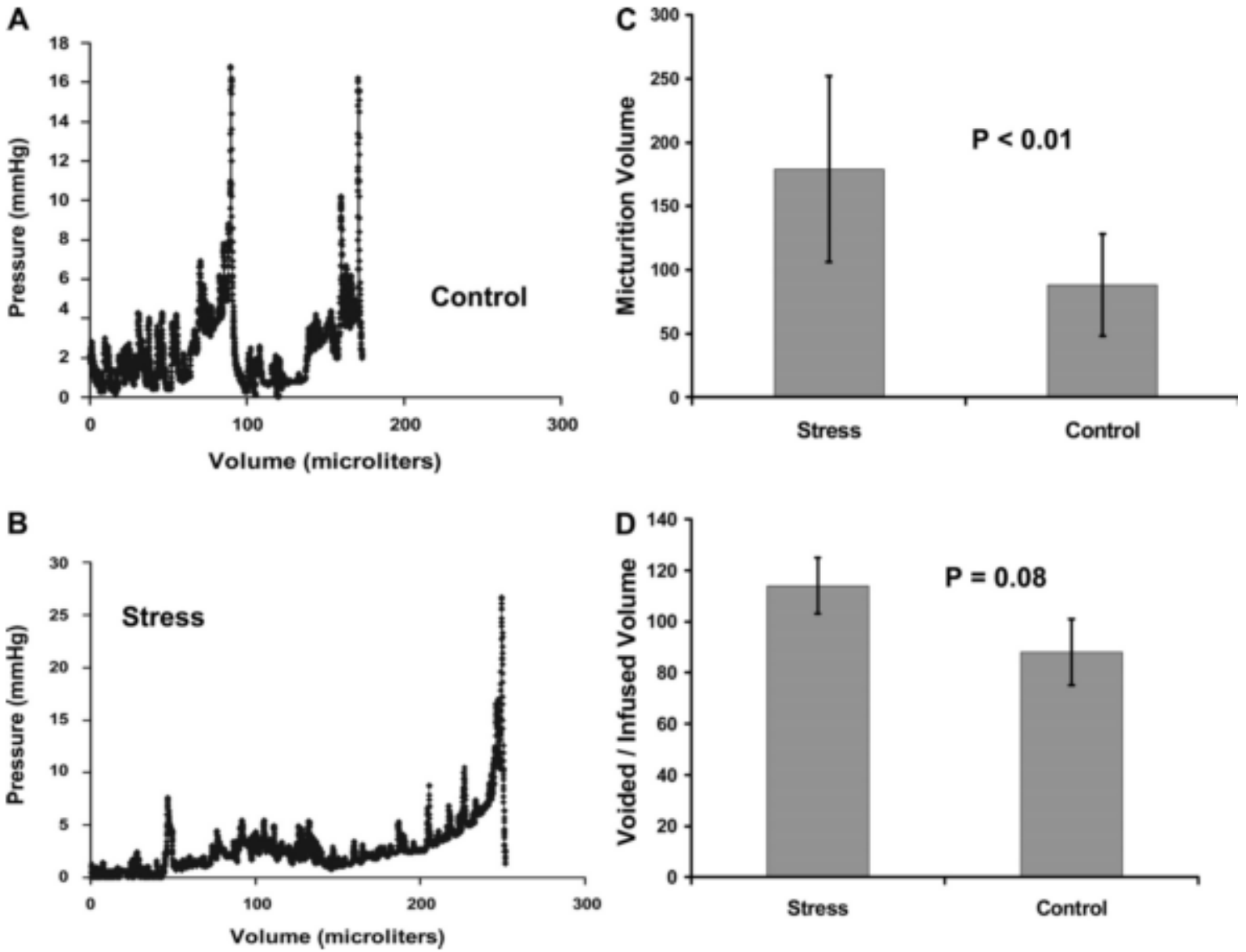
Control Arm
Single cage housing
Move screen into place
Rotate among cages

Outcomes analysis at 4 weeks



	Control	Stress	
Voids/12 hours	9.8 ± 4	2.9 ± 1.1	P < 0.01
Average Volume	0.06 ± 0.02	0.37 ± 0.1	P < 0.01

Disfunção Miccional



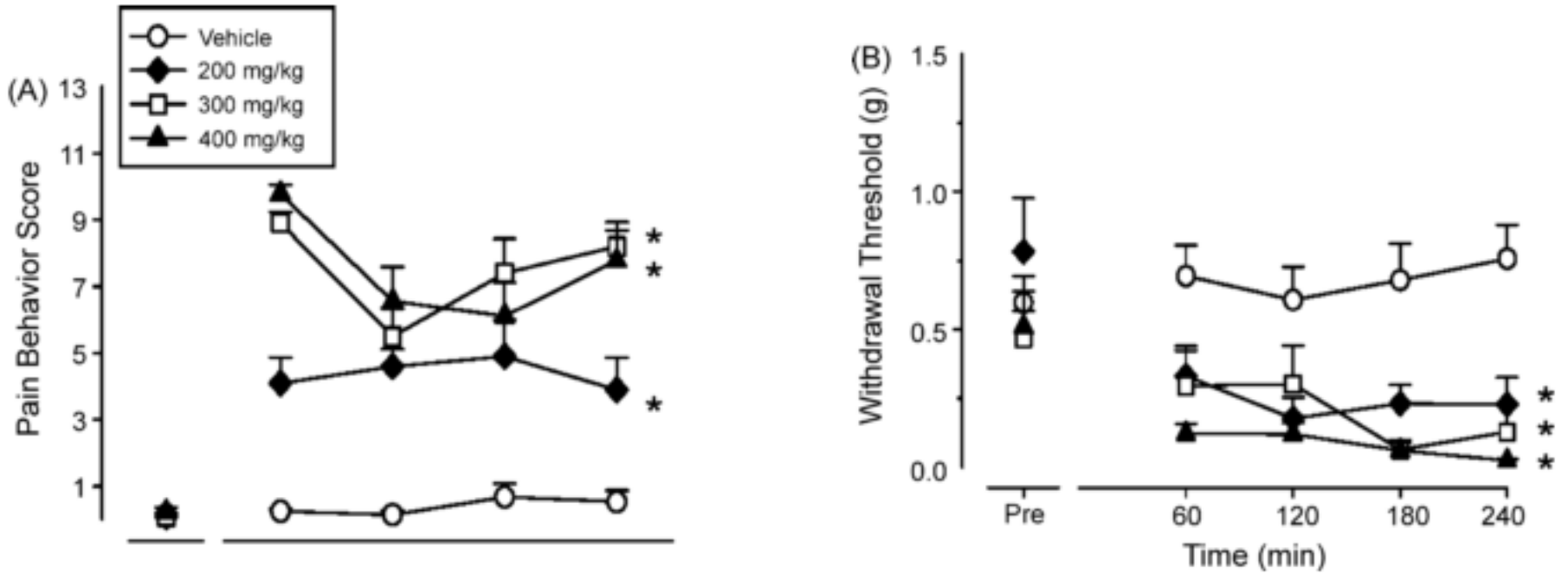
Cistite Intersticial

Pharmacological validation of a model of cystitis pain in the mouse

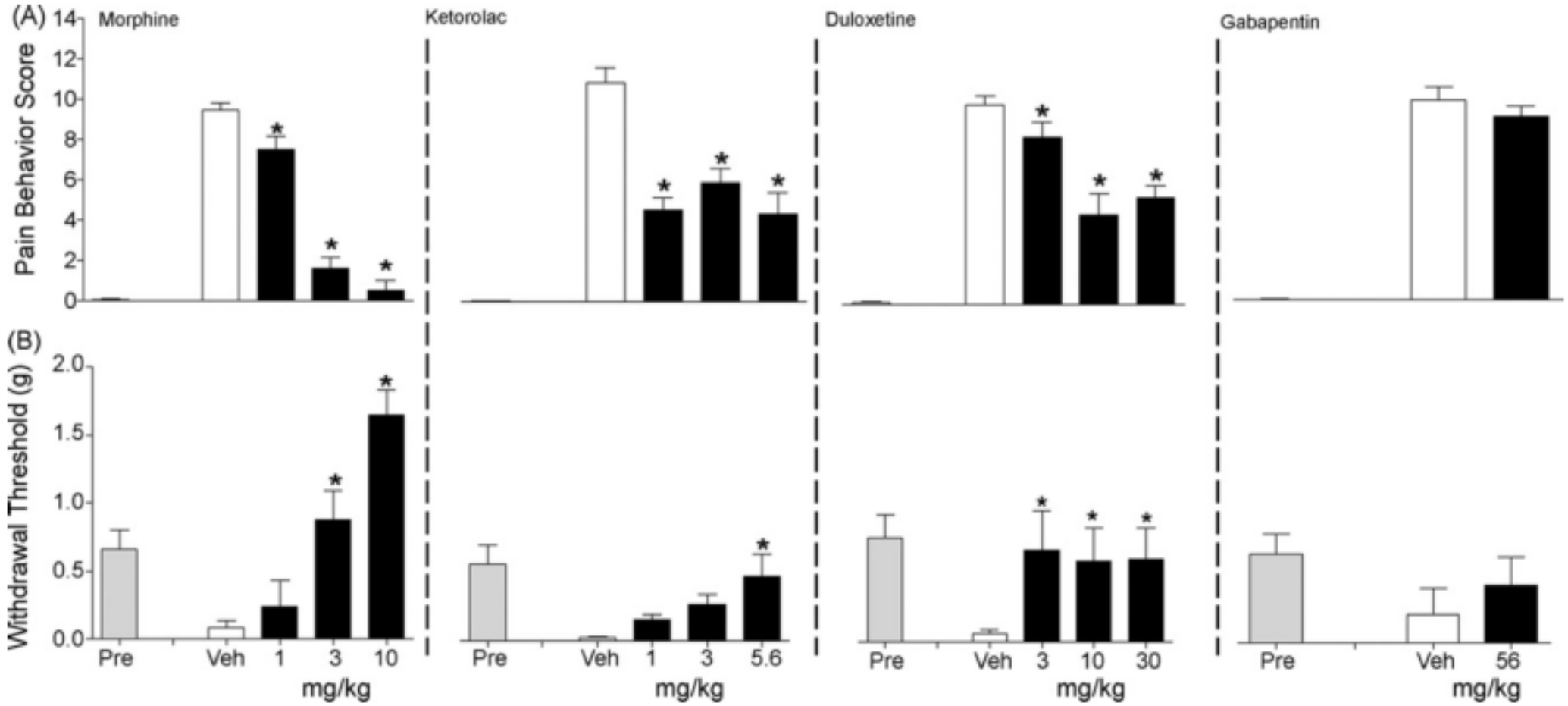
Caitlin Wantuch, Michael Piesla, Liza Leventhal *

Wyeth Research, Neuroscience Discovery Research, CN 8000, Princeton, NJ 08543, United States

Received 9 May 2007; received in revised form 17 May 2007; accepted 20 May 2007



Cistite Intersticial



Disfunção Miccional

JOURNAL OF PHYSIOLOGY AND PHARMACOLOGY 2009, 60, 4, 85-91
www.jpp.krakow.pl

K. JUSZCZAK[1,2], A. ZIOMBER[1], M. WYCZOLKOWSKI[2], P.J. THOR[1]

URODYNAMIC EFFECTS OF THE BLADDER C-FIBER AFFERENT ACTIVITY MODULATION IN CHRONIC MODEL OF OVERACTIVE BLADDER IN RATS

[1]Department of Pathophysiology, Jagiellonian University, Medical College, Cracow, Poland;
[2]Department of Urology, Rydygier Memorial Hospital, Cracow, Poland

Modelos animais de HBP

HBP

The Prostate 58:156 – 163 (2004)

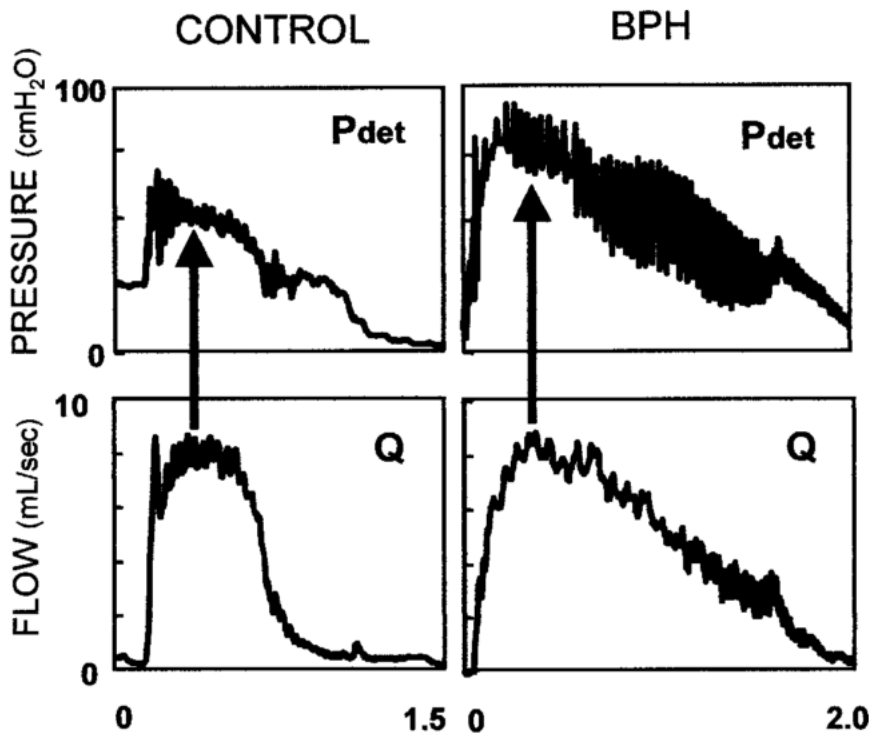
Functional and Anatomical Effects of Hormonally Induced Experimental Prostate Growth: A Urodynamic Model of Benign Prostatic Hyperplasia (BPH) in the Beagle

Takeshi Yokota,[1] K. Honda,[1] Y. Tsuruya,[1] M. Nomiya,[1] Osamu Yamaguchi,[1] K. Gotanda,[1] and Christos E. Constantinou[2*]

MATERIALS AND METHODS. Hormonally induced prostatic enlargement was produced using seven beagles, given DHT 75 mg/day together with E 0.75 mg/day for 28 days via an implantable pump. The functional effects of DHT + E treatment on micturition pressure/flow

TABLE I. Micturition Pressure/Flow Characteristics and Prostate Wet Weight of Controls, DHT + E-Treated, and BPH Groups

	Control (n = 7)	DHT + E (n = 7)	BPH (n = 5)
PdetmaxQmax(cmH_2O)	33.3 ± 10.5	50.8 ± 10.7*	64.4 ± 10.3**
Qmax (ml/sec)	8.6 ± 2.1	6.9 ± 0.9*	8.0 ± 1.9
Prostate Weight (g)	11.9 ± 2.5	31.6 ± 10.0***	29.3 ± 8.9****
Age (years)	3.5 ~ 7.2		5.5 ~ 8.7

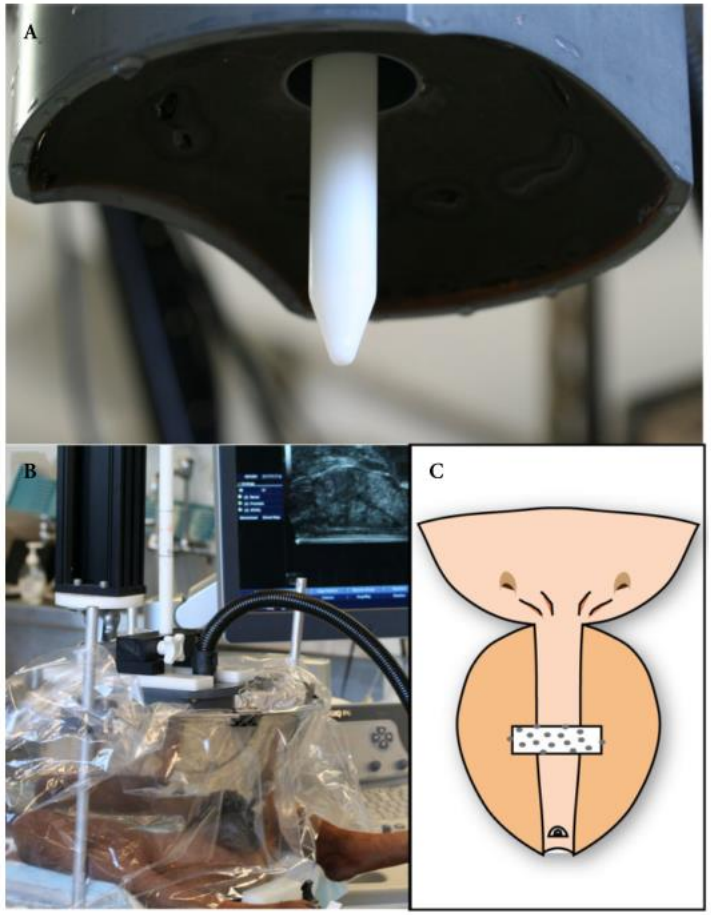


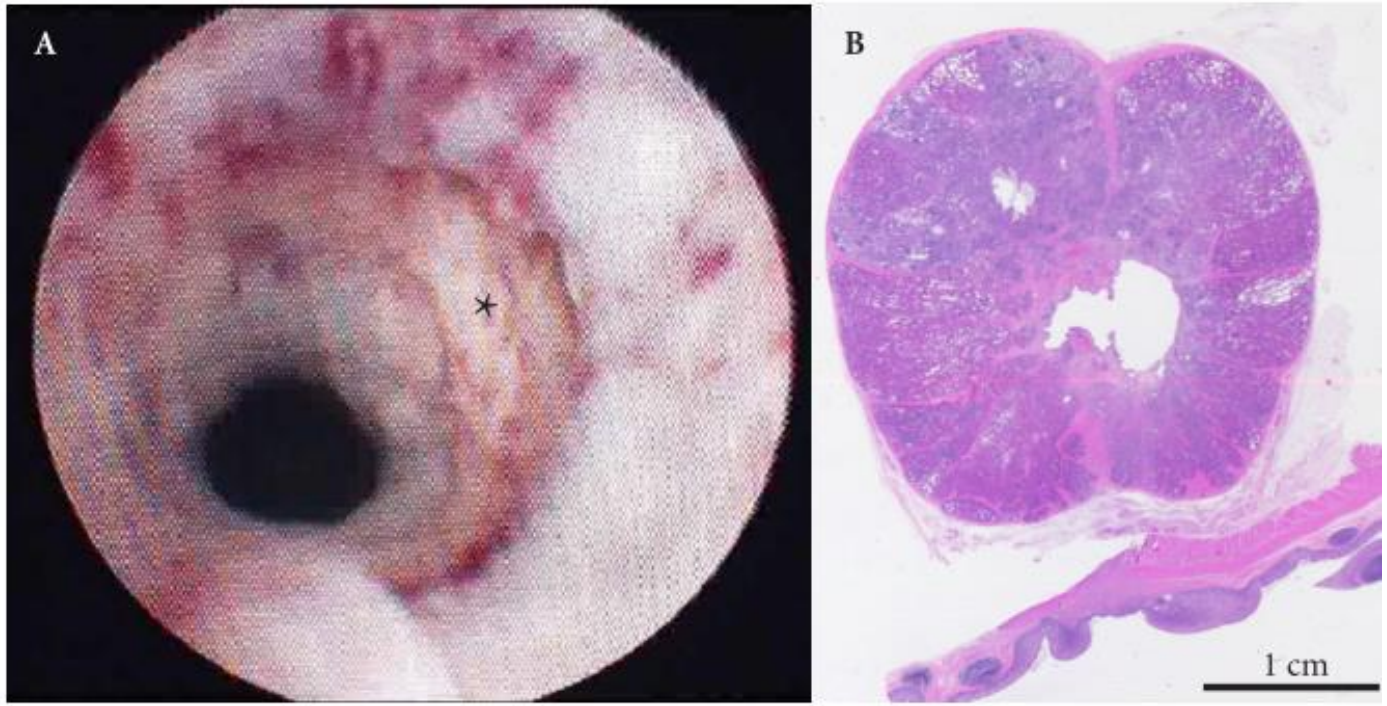
BJU Int. 2014 March ; 113(3): 498–503. doi:10.1111/bju.12333.

HBP

Prostate Histotripsy: Evaluation of Prostatic Urethral Treatment Parameters in a Canine Model

George R. Schade, MD[1], Nicholas R. Styn, MD[1], Kimberly A. Ives, DVM[2], Timothy L. Hall, PhD[2], and William W. Roberts, MD[1,2]





Modelos animais de litíase urinária

Oxalato Cálcio

0022-5347/04/1713-1301/0
THE JOURNAL OF UROLOGY®

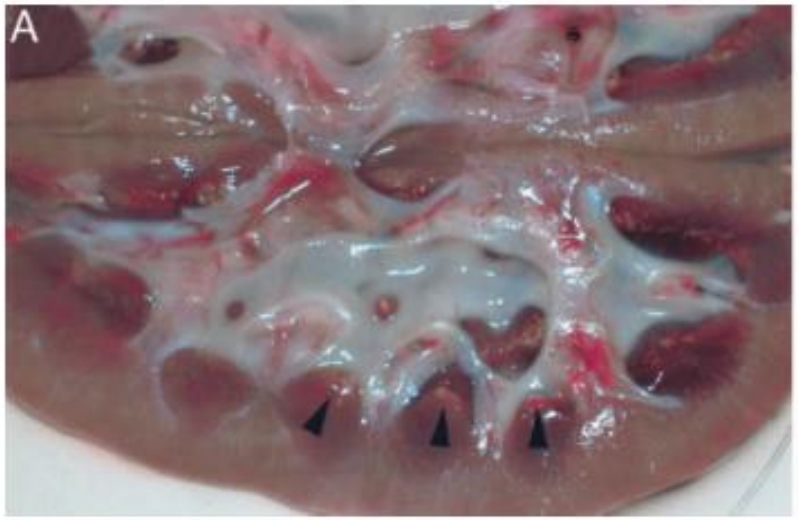
Vol. 171, 1301–1303, March 2004
Printed in U.S.A.
DOI: 10.1097/01.ju.0000110101.41653.bb

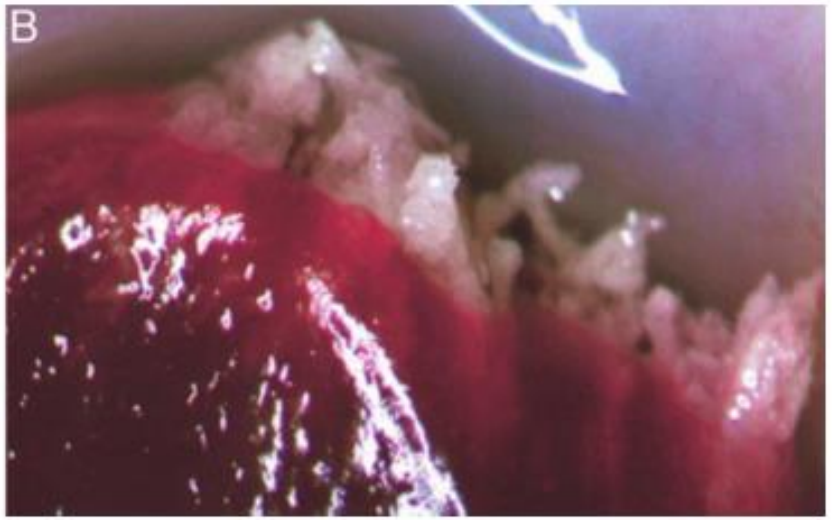
A PORCINE MODEL OF CALCIUM OXALATE KIDNEY STONE DISEASE

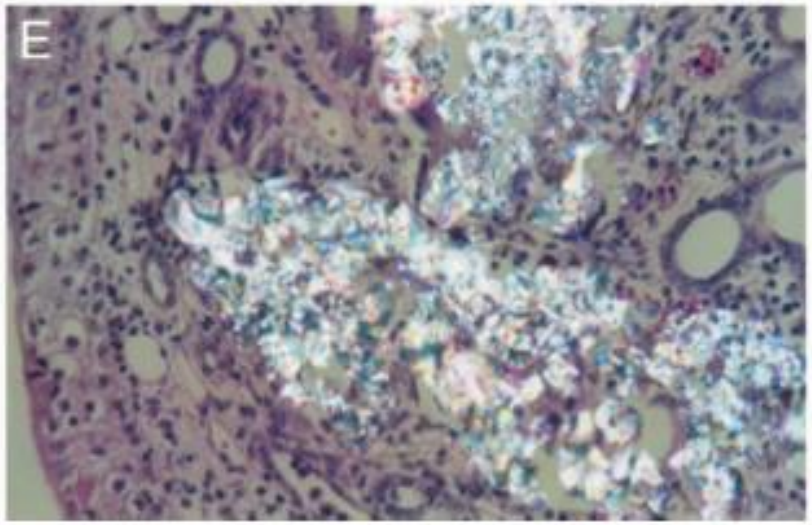
NEIL S. MANDEL,* JAMES D. HENDERSON, JR., LINDA Y. HUNG, DAVID F. WILLE AND JOHN H. WIESSNER

From the Departments of Medicine and Surgery, Medical College of Wisconsin and Department of Veterans Affairs, Zablocki Veterans Affairs Medical Center, Milwaukee, Wisconsin

resemble those of man. In this study we determined if feeding pigs trans-4-hydroxy-L-proline (HP) increased urine oxalate levels and if it would serve as a model for human hyperoxaluria and stone disease.







Oxalato Cálcio

0022-5347/10/1843-1189/0
THE JOURNAL OF UROLOGY®

Vol. 184, 1189-1196, September 2010
Printed in U.S.A.
DOI:10.1016/j.juro.2010.04.065

Experimental Induction of Calcium Oxalate Nephrolithiasis in Mice

Saeed R. Khan and Patricia A. Glenton

From the Department of Pathology, Immunology and Laboratory Medicine, College of Medicine, University of Florida, Gainesville, Florida

Materials and Methods: We administered ethylene glycol, glyoxylate or hydroxyl proline via diet in male and female normocalciuric B6 mice, and in hypercalciuric sodium phosphate co-transporter type 2 a −/− mice for 4 weeks. We collected

Oxalato Cálcio

http://www.kidney-international.org original article

see commentary on page 327

Ethylene glycol induces calcium oxalate crystal deposition in Malpighian tubules: a *Drosophila* model for nephrolithiasis/urolithiasis

Yung-Hsiang Chen[1,4], Hsin-Ping Liu[1,4], Huey-Yi Chen[1,2], Fuu-Jen Tsai[1,2], Chiao-Hui Chang[1], Yuan-Ju Lee[3], Wei-Yong Lin[1] and Wen-Chi Chen[1,2]

[1]*Graduate Institute of Integrated Medicine, Graduate Institute of Acupuncture Science, College of Chinese Medicine, China Medical University, Taichung, Taiwan;* [2]*Department of Urology, Department of Obstetrics and Gynecology, Department of Pediatrics, China Medical University Hospital, Taichung, Taiwan and* [3]*Department of Urology, National Taiwan University Hospital, Taipei, Taiwan*

Several animal species are used to study calcium oxalate urolithiasis; however, an ideal model has yet to be identified. We used *Drosophila* as a model organism and fed the flies lithogenic agents such as ethylene glycol, hydroxyl-L-proline, and sodium oxalate. At different times, the Malpighian tubules, the kidney equivalent of insects, were dissected and a polarized light microscope used to highlight the birefringent crystals. Scanning electron microscopy and energy-dispersive X-ray spectroscopy confirmed that the crystal composition was predominately calcium oxalate.

NESU SUTR

Oxalato Cálcio

Drosophila melanogaster as an Emerging Translational Model of Human Nephrolithiasis

Joe Miller,*,† Thomas Chi, Pankaj Kapahi, Arnold J. Kahn, Man Su Kim, Taku Hirata, Michael F. Romero, Julian A. T. Dow and Marshall L. Stoller‡

From the University of California-San Francisco (JM, TC, MLS), San Francisco and Buck Institute for Research on Aging (PK, AJK, MSK), Novato, California, Mayo Clinic College of Medicine (TH, MFR), Rochester, Minnesota, and University of Glasgow (JATD), Glasgow, United Kingdom

0022-5347/13/1905-1648/0
THE JOURNAL OF UROLOGY®

http://dx.doi.org/10.1016/j.juro.2013.03.010
Vol. 190, 1648-1656, November 2013
Printed in U.S.A.

Results: The genetic composition, anatomical structure and physiological function of Drosophila malpighian tubules are remarkably similar to those of the human nephron. The direct effects of dietary manipulation, environmental alteration and genetic variation on stone formation can be observed and quantified in a matter of days. Several Drosophila models of human nephrolithiasis have been developed, including genetically linked and environmentally induced stones. A model of calcium oxalate stone formation is among the most recent fly models of human nephrolithiasis.

NESU SUTR

Cistinúria

OPEN ACCESS Freely available online

PLOS ONE

An Animal Model of Type A Cystinuria Due to Spontaneous Mutation in 129S2/SvPasCrl Mice

Marine Livrozet[1,2], Sophie Vandermeersch[1,2], Laurent Mesnard[3], Elizabeth Thioulouse[4], Jean Jaubert[5,6], Jean-Jacques Boffa[1,2,7], Jean-Philippe Haymann[1,2,8], Laurent Baud[1,2,8], Dominique Bazin[9], Michel Daudon[1,2,8], Emmanuel Letavernier[1,2,8]*

1 Sorbonne Universités, UPMC Univ Paris 06, UMR S 702, Paris, France, **2** INSERM, UMR S 702, Paris, France, **3** Department of Physiology and Biophysics, Cornell University, Ithaca, New York, United States of America, **4** Biochimie, AP-HP, Hôpital Trousseau, Paris, France, **5** Institut Pasteur, Mouse Functional Genetics Unit, Paris, France, **6** CNRS URA 2578, Paris, France, **7** Néphrologie, AP-HP, Hôpital Tenon, Paris, France, **8** Explorations Fonctionnelles Multidisciplinaires, AP-HP, Hôpital Tenon, Paris, France, **9** CNRS-LCMCP- Sorbonne Universités UPMC Univ Paris 06, Collège de France, Paris, France

Cystinuria is an autosomal recessive disease caused by the mutation of either *SLC3A1* gene encoding for rBAT (type A cystinuria) or *SLC7A9* gene encoding for $b^{0,+}$AT (type B cystinuria). Here, we evidenced in a commonly used congenic 129S2/SvPasCrl mouse substrain a dramatically high frequency of kidney stones that were similar to those of patients with cystinuria. Most of 129S2/SvPasCrl exhibited pathognomonic cystine crystals in urine and an aminoaciduria profile similar to that of patients with cystinuria. In addition, we observed a heterogeneous inflammatory infiltrate and cystine tubular casts

NESU SUTR

Litotrícia Extracorpórea

0022-5347/14/1924-1257/0
THE JOURNAL OF UROLOGY®

http://dx.doi.org/10.1016/j.juro.2014.03.035
Vol. 192, 1257-1265, October 2014
Printed in U.S.A.

Shock Wave Lithotripsy Targeting of the Kidney and Pancreas Does Not Increase the Severity of Metabolic Syndrome in a Porcine Model

Rajash K. Handa,* Andrew P. Evan, Bret A. Connors, Cynthia D. Johnson, Ziyue Liu, Mouhamad Alloosh, Michael Sturek, Carmella Evans-Molina, Jessica A. Mandeville, Ehud Gnessin and James E. Lingeman†

Departments of Anatomy and Cell Biology (RKH, APE, BAC, CDJ), Cellular and Integrative Physiology (MA, MS), Biostatistics (ZL) and Medicine and Herman B. Wells Center for Pediatric Research (CE-M), Indiana University School of Medicine and Kidney Stone Institute of Indiana University Health Methodist Hospital (JAM, EG, JEL), Indianapolis, Indiana

Conclusions: The metabolic syndrome status of pigs treated with shock wave lithotripsy was unchanged 2 months after kidney treatment with 2,000 high amplitude shock waves or overtreatment with 4,000 high amplitude shock waves. These findings do not support a single shock wave lithotripsy treatment of the kidney as a risk factor for the onset of diabetes mellitus.

NESU SUTR

Lesão Renal Aguda

Clinica Chimica Acta 430 (2014) 96–103

Contents lists available at ScienceDirect

Clinica Chimica Acta

journal homepage: www.elsevier.com/locate/clinchim

Kidney stone distribution caused by melamine and cyanuric acid in rats

Yng-Tay Chen [a,b], Bang-Ping Jiann [c], Chieh-Hao Wu [d], Jhaol-Huei Wu [d], Shih-Chieh Chang [e], Maw-Sheng Chien [d], Shih-Ling Hsuan [d], Yi-Lo Lin [d], Ter-Hsin Chen [d], Fuu-Jen Tsai [a,b], Jiunn-Wang Liao [d,*]

[a] Human Genetic Center, China Medical University Hospital, Taichung, Taiwan
[b] Department of Biomedical Informatics, Asia University, Taichung, Taiwan
[c] Department of Medical Education and Research, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan
[d] Graduate Institute of Veterinary Pathobiology, National Chung Hsing University, Taichung, Taiwan
[e] Department of Veterinary Medicine, National Chung Hsing University, Taichung, Taiwan

Background: Melamine (M), which is composed of multi-amine, has been used as a food additive to falsely increase protein contents. Furthermore, cyanuric acid (CA) is a derivative of melamine. It is known that these mixtures can cause renal toxicity.

Hidronefrose

J Huazhong Univ Sci Technol [Med Sci] 34(4):575-581,2014
DOI 10.1007/s11596-014-1318-9

Renovascular Morphological Changes in a Rabbit Model of Hydronephrosis*

Wan-qiang LI (李万强)[1], Zi-qiang DONG (董自强)[2], Xiao-bing ZHOU (周小兵)[3], Bing LONG (龙 兵)[2], Lu-sheng ZHANG (张路生)[2], Jian YANG (杨 简)[4], Xiao-guang ZHOU (周晓光)[1], Ren-ping ZHENG (郑壬平)[1], Jie ZHANG (张 杰)[1#]
[1]*Department of Urology, Renmin Hospital of Wuhan University, Wuhan 430060, China*
[2]*Department of Urology,* [4]*Department of Cardiology, the First College of Clinical Medical Science, China Three Gorges University/Yichang Central People's Hospital, Yichang 443003, China*
[3]*The Central Laboratory of Human Morphology, University of South China, Hengyang 421001, China*

occur in the renal vasculature in hydronephrosis and the possible mechanisms involved. A model of complete unilateral ureteral obstruction (CUUO) was used. Experimental animals were divided into five

bar artery and afferent arterioles, respectively. In conclusion, renal arterial trees and glomeruli were dramatically altered following CUUO and the changes may be partially ascribed to vascular remodeling.

Modelos animais de transplantação renal

Ureterostomia – Técnica Cirúrgica

MODIFIED TECHNIQUE OF URETEROURETEROSTOMY IN RAT KIDNEY TRANSPLANTATION

ALEXANDER PIETSCH, Dr. Med., PHILIPP C. NETT, Dr. Med., HANS W. SOLLINGER, M.D., Ph.D., and DEBRA A. HULLETT, Ph.D.*

Microsurgery. 2004;24(4):345-9

Transplantation Proceedings, 37, 189–191 (2005)

Ureterostomia – Técnica Cirúrgica

International Braz J Urol Vol. 32 (6): 713-720, November - December, 2006

Technique of Kidney Transplantation in Mice with Anti-Reflux Urinary Reconstruction

Paulo N. Martins

Department of Surgery, Division of Transplant Surgery, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA

Outros modelos animais

Uretra - Hipospádias

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Available online at www.sciencedirect.com
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Environmental Research 94 (2004) 267–275

Environmental Research

http://www.elsevier.com/locate/envres

Induction of hypospadias in a murine model by maternal exposure to synthetic estrogens ☆

Kun Suk Kim, Carlos R. Torres Jr., Selcuk Yucel, Kamakshi Raimondo, Gerald R. Cunha, and Laurence S. Baskin*

UCSF Children's Medical Center, Departments of Urology, Anatomy and Pediatrics, University of California, San Francisco, CA 94143, USA

Received 17 January 2003; received in revised form 11 April 2003; accepted 18 April 2003

We tested the hypothesis that maternal exposure to synthetic estrogen can cause hypospadias in male offspring and defined the morphological changes in the disrupted urethral seam. Timed pregnant C57/6 mice were exposed to synthetic estrogens. The genital

NESU SUTR

Uretra - Uretroplastia

Reconstruction of Penile Urethra With the 3-Dimensional Porous Bladder Acellular Matrix in a Rabbit Model

Jian-Wen Huang, Min-Kai Xie, Yuanyuan Zhang, Gai-Jie Wei, Xiang Li, Hong-Bin Li, Ji-Hong Wang, Wei-Dong Zhu, Chao Li, Yue-Min Xu, and Lu-Jie Song

UROLOGY 84 (6), 2014

In 30 male rabbits, a ventral urethral mucosal defect (1.5 × 0.8 cm) was created. Substitution urethroplasty was performed with 5% peracetic acid (PAA)-treated BAM (3-D porous BAM; 15 rabbits, PAA-treated BAM group) and non–PAA-treated BAM (15 rabbits; non–PAA-treated BAM group) in an onlay fashion. At 1, 2, and 3 months after surgery (5 rabbits at each time point) in the 2 groups, retrograde urethrogram and histologic analysis were performed to evaluate the outcomes of urethroplasty.

Disfunção Eréctil

The Effect of PnTx2-6 Protein From *Phoneutria nigriventer* Spider Toxin on Improvement of Erectile Dysfunction in a Rat Model of Cavernous Nerve Injury

Ae Ryang Jung, Yong Sun Choi, Shuyu Piao, Yong Hyun Park, Kshitiz Raj Shrestha, Seung Hwan Jeon, Sung-Hoo Hong, Sae Woong Kim, Tae-Kon Hwang, Ki Hean Kim, and Ji Youl Lee

UROLOGY 84 (3), 2014

major pelvic ganglion. The cavernous nerve was identified and then compressed with a hemostat clamp for 30 seconds. After

Disfunção Eréctil

Efficacy of Pioglitazone on Erectile Function Recovery in a Rat Model of Cavernous Nerve Injury

Louis A. Aliperti, George F. Lasker, Sharika S. Hagan, Joshua A. Hellstrom, Ahmet Gokce, Landon W. Trost, Philip J. Kadowitz, Suresh C. Sikka, and Wayne J. G. Hellstrom

UROLOGY 84 (5), 2014

the cavernosal nerves were identified. BCNI was performed by applying three 15-s applications of a 3-in forceps to the cavernosal nerves at a location 5-mm distal to the major pelvic

Hipertensão Arterial

Am J Physiol Renal Physiol 301: F615–F621, 2011.
First published June 1, 2011; doi:10.1152/ajprenal.00158.2011.

Renovascular hypertension using a modified two-kidney, one-clip approach in mice is not dependent on the α1 or α2 Na-K-ATPase ouabain-binding site

John N. Lorenz,[1] Valerie M. Lasko,[1] Michelle L. Nieman,[1] Thomas Damhoff,[1] Vikram Prasad,[2] William H. Beierwaltes,[3] and Jerry B. Lingrel[2]

Departments of [1]Molecular and Cellular Physiology and [2]Molecular Genetics, Biochemistry, and Microbiology, University of Cincinnati College of Medicine, Cincinnati, Ohio; and [3]Department of Internal Medicine, Hypertension and Vascular Research Division, Henry Ford Hospital, Detroit, Michigan

2K1C model. The Goldblatt model of 2K1C renovascular hypertension has been successfully reported in mice using the standard approach of clipping the renal artery with a silver clip, usually a

Hipertensão Arterial

Hypertension. 2009 January ; 53(1): 49–56. doi:10.1161/HYPERTENSIONAHA.108.121822.

DELETION OF iNOS PROVIDES CARDIOPROTECTION IN MICE WITH 2-KIDNEY, 1-CLIP HYPERTENSION

Ying Sun[1,3], **Oscar A. Carretero**[1], **Jiang Xu**[1], **Nour-Eddine Rhaleb**[1], **James J. Yang**[2], **Patrick J. Pagano**[1], and **Xiao-Ping Yang**[1]

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3 *Department of Pathology, North China Coal Medical College, Tangsan, China*

One week after adapting to their new environment, mice were anesthetized and the left kidney exposed through a flank incision. After separating the renal artery and vein, a silver clip with an internal diameter of 127 μm was placed around the renal artery. With sham operation, mice

Dor Testicular

Behavioral and Urological Evaluation of a Testicular Pain Model

Katsuro Yoshioka, Masayuki Tanahashi, and Wataru Uchida

UROLOGY 75 (4), 2010

In male Wistar rats, acetic acid was injected into the testes, and behaviors and bladder functions with conscious cystometry were examined. The effects of indomethacin and capsaicin pretreatment on both behaviors and bladder functional changes induced by acetic acid injection were examined. The weight of the testes and bladder after the testicular injection were measured.

NESU SUTR

Doença Renal Poliquística

Urolithiasis (2014) 42:301–307
DOI 10.1007/s00240-014-0664-1

ORIGINAL PAPER

Determination of urinary lithogenic parameters in murine models orthologous to autosomal dominant polycystic kidney disease

Renato Ribeiro Nogueira Ferraz · Jonathan Mackowiak Fonseca · Gregory George Germino · Luiz Fernando Onuchic · Ita Pfeferman Heilberg

The generation of the cystic model was based on a *Pkd1* floxed allele ($Pkd1^{cond}$) with lox P sites inserted in introns 1 and 4 and a neomycin cassette flanked by FRT sites inserted in intron 1 [17]. By breeding with nestin-Cre transgenic animals, we have produced $Pkd1^{cond/cond}$:$Nestin^{cre}$ and $Pkd1^{cond/cond}$ animals with the C57BL/6 genetic background. The presence of $Pkd1^{cond}$ alleles and the nestin-Cre

Conclusões

Conclusões

- Mamíferos – estudo de funções humanas complexas, como p.e. o ciclo miccional
- Hiperplasia da Próstata – só ocorre no Homem e no cão!!!
- Técnica cirúrgica – porco, rato, gato, cão
- Xenoenxertos – futuro da transplantação?
- *Drosophila* – modelo pouco complexo para o estudo de litíase

Apresentação disponível em:

Obrigado pela atenção

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