

2018

비뇨기계기초의학연구회 요로생식기손상재건연구회 공동심포지엄

| 주최 | 대한비뇨기과학회, 대한비뇨기과학재단

| 주관 | 비뇨기계기초의학연구회, 요로생식기손상재건연구회

| 일시 | 2018년 2월 10일(토) 08:20-13:00

| 장소 | 연세대학교 의과대학 1층 의대강당 및 131호

| 평점 | 대한의사협회 3점



INVITATION

존경하는 대한비뇨기과학회 회원 여러분, 안녕하십니까!

2018년도 대한비뇨기과학회 비뇨기계기초의학연구회와 요로생식기손상재건연구회 공동심포지엄이 2018년 2월 10일에 개최함을 알려드립니다.

이번 심포지엄의 공동세션 부분에서는 Korean Prostate Bank와 이와 관련된 genome study 분야 및 prostate cancer의 tumorigenesis에 관련된 최신 지견을 소개합니다. 또한 요로 손상 환자의 emergency management 및 gender reassignment surgery 치료에 대하여 국내 저명하신 연자를 초청하였습니다.

후반부의 기초의학연구회 세션에서는 종양 분야의 연구를 활발히 하시는 세 분의 연자를 모시고 심도 깊은 강의를 있을 예정입니다. 요로생식기손상재건 세션에서는 요로생식기 손상에 대한 최신 이슈를 소개하는 자리를 마련하였습니다. 비뇨기과 수술 후 발생하는 의인성 손상 및 소아 환자에서 요로손상의 치료에 대해서 전문가들을 초청하였고 위 분야에 대한 허심탄회한 토의를 할 수 있는 자리를 마련하였사오니 여러분의 많은 참여와 관심 부탁드립니다.


그동안 대한비뇨기과학회 비뇨기계기초의학연구회와 요로생식기손상재건연구회 발전에 힘써 주신 학회 회원분들께 감사드리며, 많은 관심과 열정으로 참석하여 주셔서 자리를 빛내주시기를 부탁드립니다.

감사합니다.

2018년 2월

비뇨기계기초의학연구회장 **김준철**

요로생식기손상재건연구회장 **박홍석**



비뇨기계기초의학연구회

| | | |
|-------|-------|---------|
| 회 장 | 김 준 철 | 가톨릭의대 |
| 고 문 | 김 원 재 | 충 북 의 대 |
| 고 문 | 천 준 | 고 려 의 대 |
| 고 문 | 최 영 득 | 연 세 의 대 |
| 고 문 | 이 규 성 | 성균관의대 |
| 총무이사 | 정 병 창 | 성균관의대 |
| 학술이사 | 한 웅 규 | 연 세 의 대 |
| 연구이사 | 류 지 간 | 인 하 의 대 |
| 기획이사 | 전 성 수 | 성균관의대 |
| 교육이사 | 이 지 열 | 가톨릭의대 |
| 협력이사 | 이 상 돈 | 부 산 의 대 |
| 정보이사 | 변 석 수 | 서 울 의 대 |
| 편집이사 | 박 홍 석 | 고 려 의 대 |
| 부 총 무 | 김 계 환 | 가 천 의 대 |

요로생식기손상재건연구회

| | | |
|-------|-------|---------|
| 고 문 | 정 재 용 | 인 제 의 대 |
| 고 문 | 이 종 복 | 국립중앙의료원 |
| 고 문 | 안 현 수 | 아 주 의 대 |
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| 학술이사 | 박 민 구 | 인 제 의 대 |
| 홍보이사 | 오 경 진 | 전 남 의 대 |
| 보험이사 | 성 현 환 | 성균관의대 |
| 연구이사 | 나 웅 | 국립중앙의료원 |
| 윤리이사 | 유 지 형 | 인 제 의 대 |
| 정보이사 | 조 대 연 | 인 제 의 대 |
| 개원이사 | 김 진 홍 | 세인트비뇨기과 |
| 감 사 | 강 택 원 | 전 남 의 대 |

2018

비뇨기계기초의학연구회 - 요로생식기손상재건연구회 공동심포지엄

| 일시 | 2018년 2월 10일(토) 08:20-13:00

| 장소 | 연세대학교 의과대학 1층 의대강당 및 131호

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|---|---|--|
| 08:20-08:50 | Registration | |
| 08:50-08:55 | Welcome & Introduction | 김준철 (비뇨기계기초의학연구회장) 박홍석 (요로생식기손상재건연구회장) |
| 08:55-09:00 | KUA President's Welcome | 천 준 (대한비뇨기과학회장) |
| Session I. GU Trauma & Reconstruction Update | | 좌장: 박홍석 (고려의대) |
| 09:00-09:30 | Emergency management of urogenital trauma patients | 이경원 (인제의대) |
| 09:30-10:00 | Gender reassignment surgery: lessons learned over the last 2 years in a single center | 나 웅 (국립중앙의료원) |
| Session II. Special Lecture | | 좌장: 김준철 (가톨릭의대) |
| 10:00-10:30 | Korea Prostate Bank and Genomic Study | 이지열 (가톨릭의대) |
| 10:30-11:00 | α -Casein Changes Gene Expression Profiles and Promotes Tumorigenesis of Prostate Cancer Cells | 이상돈 (부산의대) |
| 11:00-11:20 | Break | |
| Session III. 해외 연수를 통한 최신 연구 경험 | | 좌장: 한응규 (연세의대) |
| 11:20-11:40 | Regional Hypothermia during RARP: does it really helpful? Experience from UCI | 고영희 (영남의대) |
| 11:40-12:00 | Expression of NlpC protein and Penicillin-Binding Protein 2 (PBP2) in Neisseria Gonorrhoeae | 최현섭 (가톨릭의대) |
| Session IV (기초). Current Status of Urological Research in Korea 좌장: 강석호 (고려의대) | | Session IV. (장소 이동: 131호) Issues of GU Trauma & Reconstruction 좌장: 문홍상 (한양의대) |
| 12:00-12:20 | Expression of HMGB1 in prostate cancer: clinical and biological correlations 박용현 (가톨릭의대) | Management of perforation injuries during and following penile prosthesis surgery 송기현 (강원의대) |
| 12:20-12:40 | 신장암 세포주에서 메트포르민과 에버로리무스의 효과 및 상승효과에 대한 연구 윤영은 (한양의대) | Repair of vesicorectal fistula after radical prostatectomy 정원식 (광주기독병원) |
| 12:40-13:00 | Role of TRPM7 in urological cancer 하윤석 (경북의대) | Urogenital reconstructions for pediatric trauma 김상운 (연세의대) |

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2018

**비뇨기계기초의학연구회
요로생식기손상재건연구회
공동심포지엄**

Session I. GU Trauma & Reconstruction Update

좌장: 박홍석 (고려의대)

Emergency management of urogenital trauma patients

이경원 (인제의대)

Gender reassignment surgery: lessons learned over
the last 2 years in a single center

나 웅 (국립중앙의료원)

Emergency management of urogenital trauma patients

이 경 원

인제의대

Colon Vaginoplasty in Gender Reassignment Surgery (Male to Female) and Congenital Disorders

Woong Na

National Medical Center

Vaginoplasty

- Vaginoplasty is the surgical creation of a functional vagina
- Vaginal reconstruction is of major importance for psychological and sexual wellbeing and quality of life in case of absence of the vagina

Inclinations of MtF GRS

BOTTOM SURGERIS

- Orchiectomies
- Penectomies
- Clitoroplasty
- Labioplasty
- Vulvoplasty
- Vestibuloplasty
- Urethroplasty
- **Vaginoplasty**

AESTHETIC SURGERIES

- Facial feminizing surgeries
- Body contouring
- Breast Augmentations
- Hip Augmentations
- Adam's apple removal
- Voice surgeries

Vaginoplasty techniques

SKIN

- Surgical techniques
 - flaps (penile & scrotal skin)
 - grafting
- Advantages
 - Less invasive operative technique
 - can be performed under epidural anesthesia
- Disadvantages
 - Needs for postoperative vaginal dilations
 - Dry vagina which needs lubricants for sexual intercourse

INTESTINE

- Usages of organ
 - Sigmoid colon
 - Ileum
- Advantages
 - Lubricating vagina
 - Less chance of vaginal narrowing and less need for postoperative vaginal dilations
- Disadvantages
 - More invasive operative technique than the usages of skin, which needs general anesthesia

Skin vagina

SKIN FLAPS

- Advantages
 - Easy to achieve depth & width
 - Less need for vaginal dilations
- Disadvantages
 - Hairy vagina
 - Vaginal prolapse due to flap sliding

SKIN GRAFTS

- Advantages
 - Non-hairy vagina
 - No vaginal protrusion
- Disadvantages
 - Difficult to achieve depth & width
 - Continuous needs of vaginal dilations

Functional & Aesthetic Vagina?

- Non-hairy
- Lubricating
- Good width & depth
- Sensate
- Good symmetry & tissue distributions
- Less scarring

Colon vaginoplasty: Indications

- Transgender women with penile hypoplasia
 - small or circumcised penis with insufficient penile skin
- Transgender women with failed primary vaginoplasty
- Biological women with either acquired or congenital absence of a functional vagina



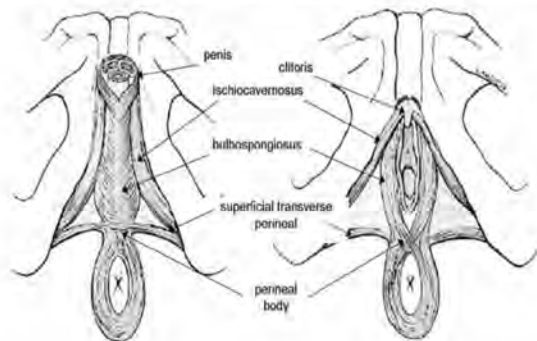
Contraindication

- History of intestinal malignancy
- History of inflammatory bowel disease
- History of extensive abdominal surgery

Relative contra-indication

- Smoking
- Obesity (BMI >30kg/m2)

Homogeneity of Structure



Modern Era Dawn of Sexology



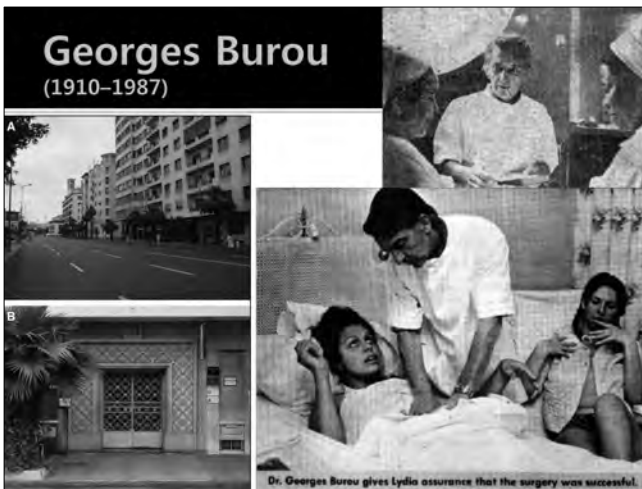
Eugen Steinach (1861-1944)



E. Steinach

- the best known hormone researcher of his day and the first to feminize male rats by means of castration (he also masculinized female rats by implanting testicles)
- Steinach operation=vasectomy





SAVA PEROVIC (1937.2.11.~2010.4.4)

Urethral flap combined with Penile fasciocutaneous flap

Male to female surgery. A new contribution to operative technique. *Plast Reconstr Surg* 1993; 91: 703-12

Construction of a neoditoris in male transsexuals. *Plast Reconstr Surg* 1994; 93: 646-8

Vaginoplasty in male transsexuals using penile skin and a urethral flap. *BJU International* 86: 843-850, November 2000

Sacrospinous ligament fixation for neovaginal prolapse prevention in male-to-female surgery. *Urology* 2007 Oct;70(4):767-71



Lines of incisions are marked



Penis is degloved leaving inner preputial layer with the glans



Penile disassembly starts with complete urethral mobilization



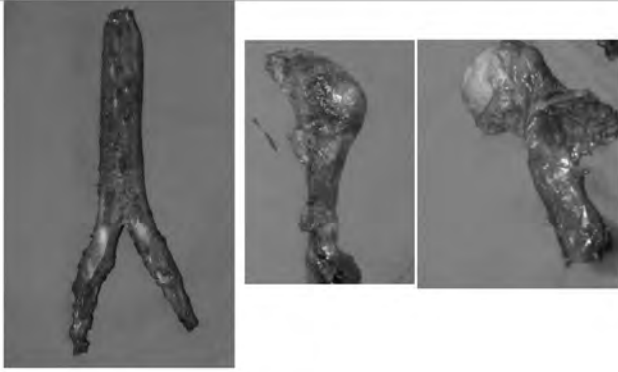
Neurovascular bundle is mobilized using combined sharp and blunt dissection



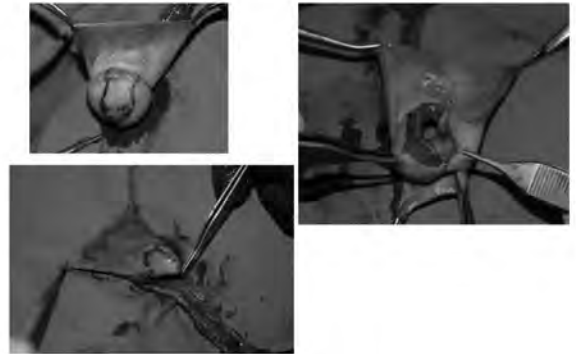
Complete penile disassembly



Corpora and testicles are excised



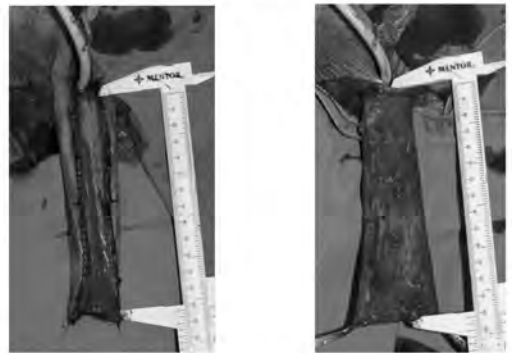
Clitoris is created from reduced glans, preserving preputial vascularization



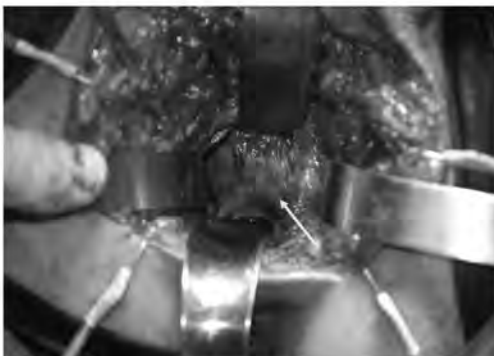
Distal part of urethra is used to bridge the gap between neoclitoris and urethral meatus



Creation of long neovagina using inverted combined urethral and penile skin flap



Creation of deep and wide perineal space between posterior urethra, prostate and seminal vesicles anteriorly and rectum posteriorly



Placement of neovagina into perineum and its fixation to the sacrospinous ligament in order to prevent its protrusion



Appearance at the end of surgery – labia minora are created from inner preaputal layer



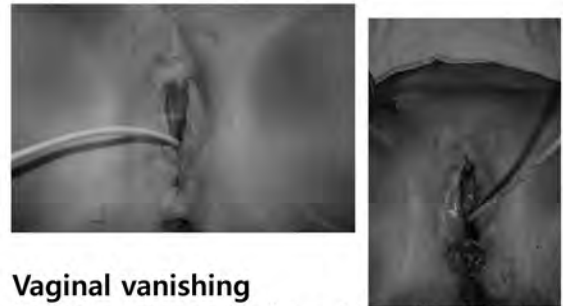
Outcome after 6 months



Outcome 2 years after surgery



COMPLICATIONS



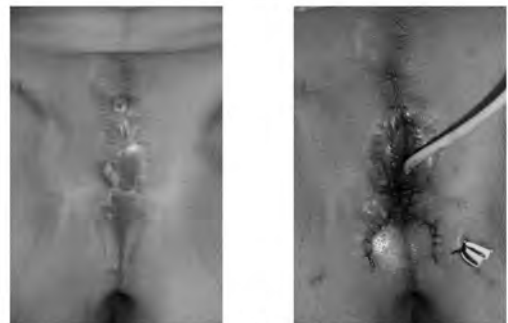
Vaginal vanishing
Treatment – rectosigmoid vaginoplasty

COMPLICATIONS



Large rectovaginal fistula. Absence of proximal vagina

Complete vaginal absence



Treatment – rectosigmoid vaginoplasty

RECTOSIGMOID VAGINOPLASTY

- step-by-step technique -

- **Preoperative evaluation**
 - assessment of the pelvis and perineum
- **Intraoperative assessment**
 - characteristics of the rectosigmoid
 - blood supply
 - its relationship to the other pelvic organs and structures

SIGMOID COLON – SURGICAL ANATOMY: Variations in length and position



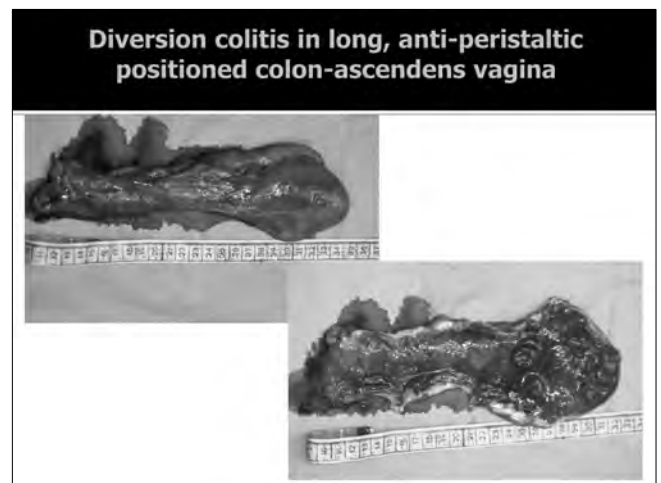
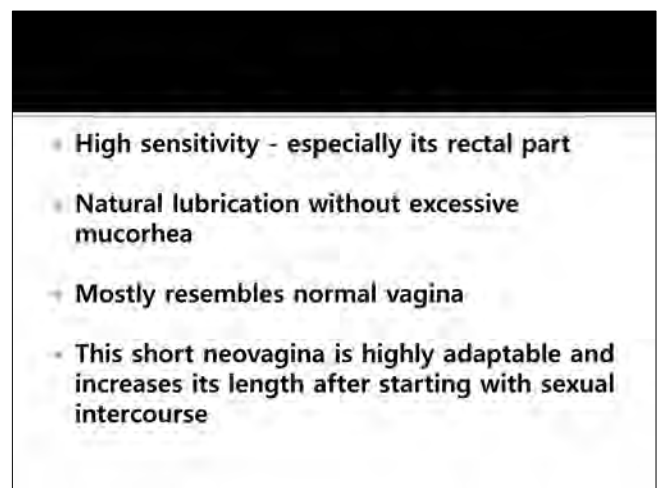
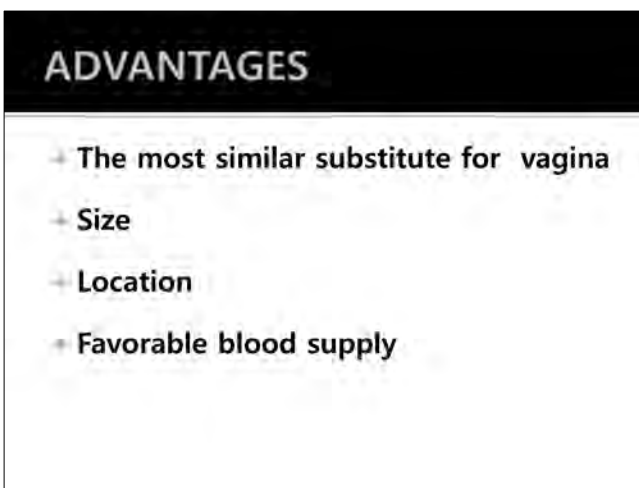
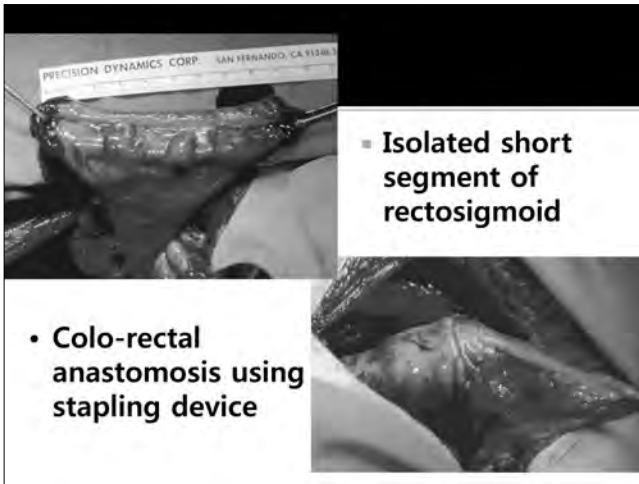
- Division of rectal segment from its mesentery can be done due to its good intramural vascularization
- Bowel segment should be placed in peristaltic position to allow better mucous discharge



- Precise dissection using abdominoperineal approach should be done in order to avoid injury of rectum, bladder and urethra
- Postoperative dilation of neovaginal introitus is recommended during three months after surgery to prevent stenosis

Isolation of bowel segment





Case

수술 동영상

Lapascopic colon vaginoplasty

Conclusions

- Sigmoid vaginoplasty can provide the patient with a self lubricating, esthetically pleasing neovagina of adequate size.
- It has a low complication rate and a low incidence of interoital stenosis with no need for daily vaginal dilatation or vaginal stenting by vaginal molds. Moreover, the reported functional outcome is excellent

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Session II. Special Lecture

좌장: 김준철 (가톨릭의대)

Korea Prostate Bank and Genomic Study

이지열 (가톨릭의대)

α -Casein Changes Gene Expression Profiles and
Promotes Tumorigenesis of Prostate Cancer Cells

이상돈 (부산의대)

Korea Prostate Bank and Genomic Study

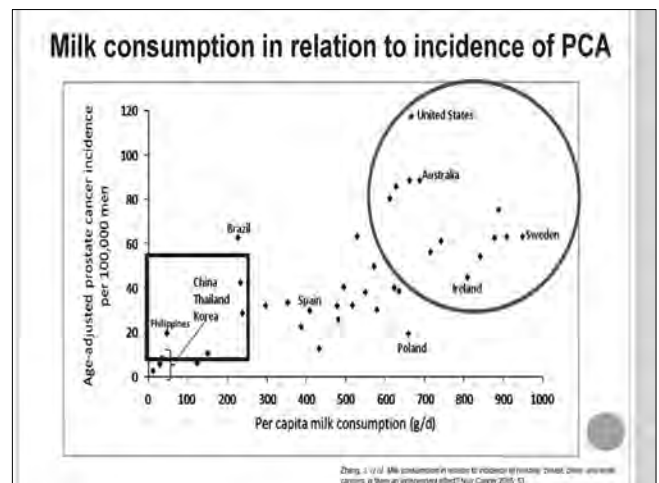
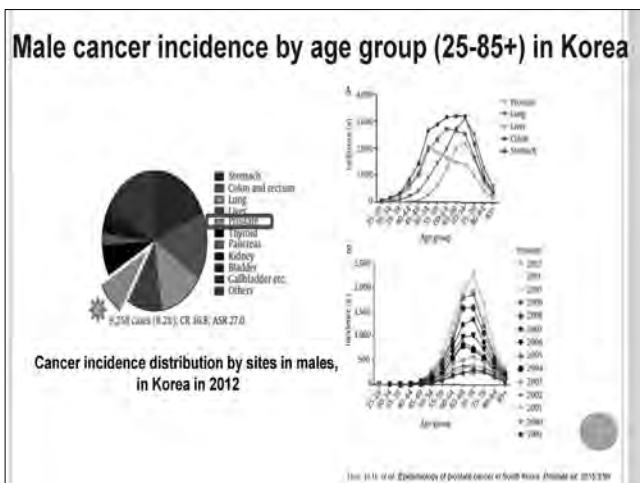
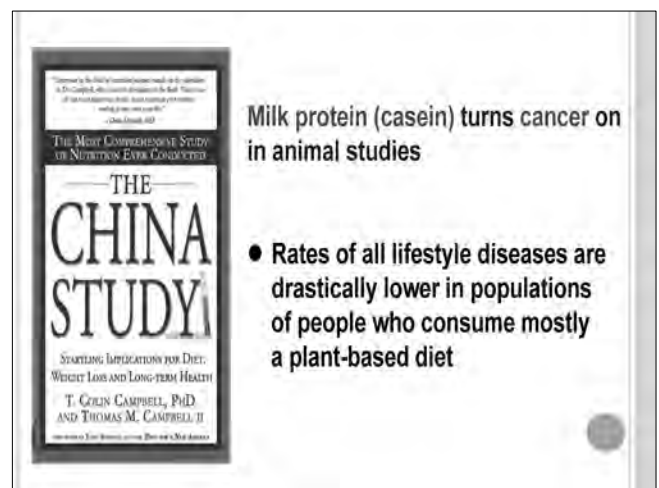
이 지 열

가톨릭의대

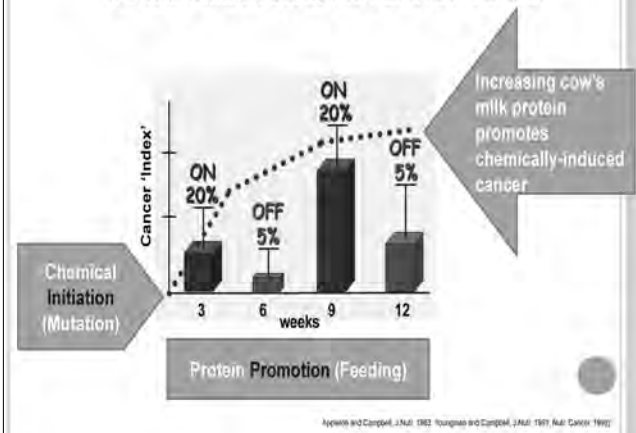
α -Casein Changes Gene Expression Profiles and Promotes Tumorigenesis of Prostate Cancer Cells

Sang Don Lee, M.D., Ph.D.

Pusan National University School of Medicine



| Constituents | Unit | Cow |
|------------------|------|------|
| Water | g | 87.8 |
| Protein | g | 3.2 |
| Fat | g | 3.9 |
| Carbohydrate | g | 4.8 |
| Energy | kcal | 66 |
| Sugars (lactose) | g | 4.8 |
| Cholesterol | mg | 14 |
| Calcium | mg | 120 |



- Milk protein in mammalian milk, highest in cow's milk (80%)
- Animal experiments show a correlation of high casein intake and cancer development



| Milk- and milk protein-induced disturbances of insulin-IGF-1 signalling and development of chronic Western diseases | | | | | |
|---|------------------|---------------------|--|---------------------------|-------------------------------------|
| prenatal | postnatal | adolescence | adulthood | old age | |
| disturbed thymic T-cell maturation | fetal overgrowth | endocyte activation | adipocyte differentiation | atherosclerosis formation | neurodegenerative disease formation |
| allergic atopy autoimmune disease | fetal macrosomia | obesity | atherosclerosis cardiovascular disease, stroke | cancer | neurodegenerative diseases |

[illegible]

A. Breast feeding

Physiological low protein / leucine content of human milk

Leucine → Liver cells → Insulin → IGF-1

Amino acids → Liver cells → Insulin → IGF-1

Physiological milk signaling

Leucine → IGF-1R → PI3K → Akt → mTORC1

Leucine → 4EBP1 → mTORC1

Normal prostate morphogenesis

B. Formula feeding

High protein / leucine content of infant formula

Leucine → Liver cells → Insulin → IGF-1

Amino acids → Liver cells → Insulin → IGF-1

Excessive milk signaling

Leucine → IGF-1R → PI3K → Akt → mTORC1

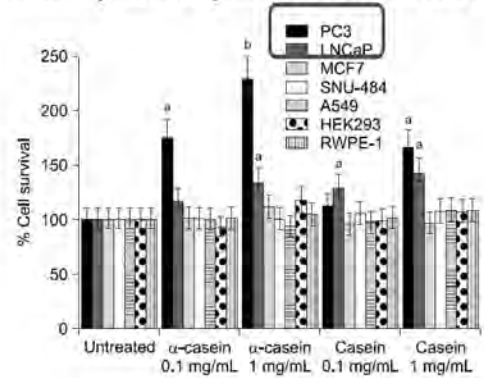
Leucine → 4EBP1 → mTORC1

Aberrant prostate morphogenesis → tumorigenesis

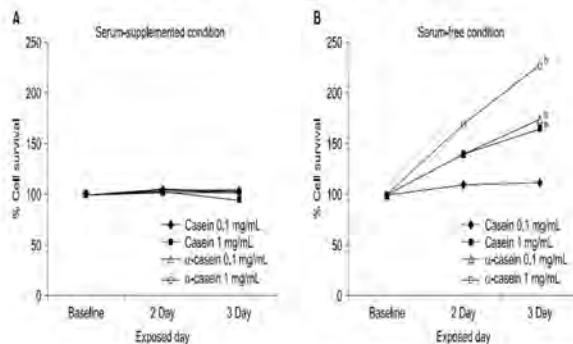
Purpose

- PCA is among the most prevalent malignancies in men.
- High intake of dairy products is associated with an increased risk of PCA.
- However, no study has examined the gene profiles change and molecular mechanism by which casein, milk protein, affects PCA cells.

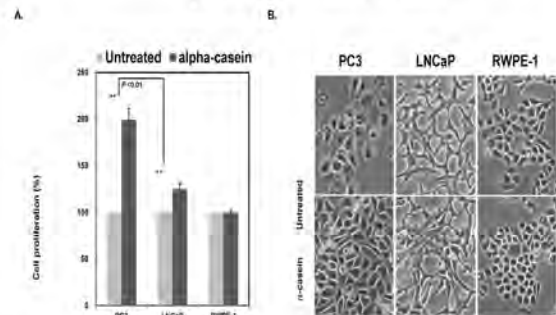
Casein can promote proliferation of PCA cells



Growth induction of casein and α-casein on proliferation of PC-3 cells



α-casein promotes proliferation of prostate cancer cells

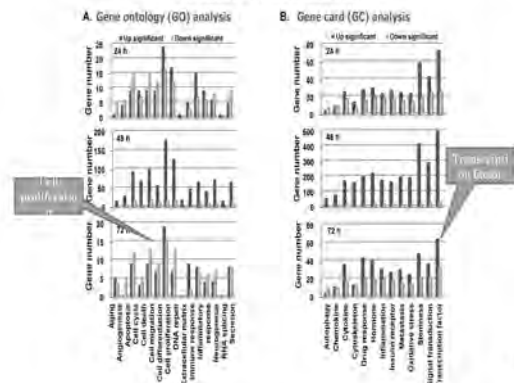


Microarray analysis

Microarray total gene n= 34,127

| | 24 hours | 48 hours | 72 hours | Cutoff criteria p<0.05 |
|-----------------|----------|----------|----------|------------------------|
| Up-regulation | 257 | 1451 | 167 | >2 |
| Down-regulation | 41 | 58 | 58 | <0.5 |

Microarray analysis on gene expression profiling in PC3 cells treated with α-casein



List of differentially expressed genes based on microarray analysis

| Genes | Accession No. | Symbol | Log fold change |
|---|---------------|--------|-----------------|
| Cell proliferation | | | |
| transcription factor 7 (cell-specific, HMG-box) | NM_020252 | TGTF | 4.548874 |
| CDP domain-containing protein 1 | NM_020233 | TGFB | 4.681474 |
| transcription factor 7-like 1 (cell-specific, HMG-box) | NM_0114824 | TCF7L2 | 4.83274 |
| polyoma virus-transformed nucleolar protein | NM_020214 | TOPBP1 | 4.217126 |
| protein binding protein 4 (p40) | NM_020213 | TOPBP2 | 4.335221 |
| growth factor 1 (MMP3, metalloproteinase 3, family, member 1) | NM_020213 | YM178 | 4.130311 |
| Ras guanine nucleotide exchange factor 1 (GEF1) | MJ_002321 | ARGG1 | 3.95522 |
| transcription factor 1 (myeloblastic leukaemia, inhibitor) | NM_020213 | ARGG2 | 3.95522 |
| Cytoskeleton protein 1 (Cytoskeleton protein 1) | NM_020211 | CHCH | 3.94479 |
| cytoskeleton growth factor 1 (Cytoskeleton growth factor 1) | NM_020211 | CHCH2 | 3.94479 |
| cytoskeleton growth factor 2 (Cytoskeleton growth factor 2) | NM_020211 | CHCH3 | 3.94479 |
| cytoskeleton growth factor 3 (Cytoskeleton growth factor 3) | NM_020211 | CHCH4 | 3.94479 |
| cytoskeleton growth factor 4 (Cytoskeleton growth factor 4) | NM_020211 | CHCH5 | 3.94479 |
| cytoskeleton growth factor 5 (Cytoskeleton growth factor 5) | NM_020211 | CHCH6 | 3.94479 |
| cytoskeleton growth factor 6 (Cytoskeleton growth factor 6) | NM_020211 | CHCH7 | 3.94479 |
| cytoskeleton growth factor 7 (Cytoskeleton growth factor 7) | NM_020211 | CHCH8 | 3.94479 |
| cytoskeleton growth factor 8 (Cytoskeleton growth factor 8) | NM_020211 | CHCH9 | 3.94479 |
| cytoskeleton growth factor 9 (Cytoskeleton growth factor 9) | NM_020211 | CHCH10 | 3.94479 |
| cytoskeleton growth factor 10 (Cytoskeleton growth factor 10) | NM_020211 | CHCH11 | 3.94479 |
| cytoskeleton growth factor 11 (Cytoskeleton growth factor 11) | NM_020211 | CHCH12 | 3.94479 |
| cytoskeleton growth factor 12 (Cytoskeleton growth factor 12) | NM_020211 | CHCH13 | 3.94479 |
| cytoskeleton growth factor 13 (Cytoskeleton growth factor 13) | NM_020211 | CHCH14 | 3.94479 |
| cytoskeleton growth factor 14 (Cytoskeleton growth factor 14) | NM_020211 | CHCH15 | 3.94479 |
| cytoskeleton growth factor 15 (Cytoskeleton growth factor 15) | NM_020211 | CHCH16 | 3.94479 |
| cytoskeleton growth factor 16 (Cytoskeleton growth factor 16) | NM_020211 | CHCH17 | 3.94479 |
| cytoskeleton growth factor 17 (Cytoskeleton growth factor 17) | NM_020211 | CHCH18 | 3.94479 |
| cytoskeleton growth factor 18 (Cytoskeleton growth factor 18) | NM_020211 | CHCH19 | 3.94479 |
| cytoskeleton growth factor 19 (Cytoskeleton growth factor 19) | NM_020211 | CHCH20 | 3.94479 |
| cytoskeleton growth factor 20 (Cytoskeleton growth factor 20) | NM_020211 | CHCH21 | 3.94479 |
| cytoskeleton growth factor 21 (Cytoskeleton growth factor 21) | NM_020211 | CHCH22 | 3.94479 |
| cytoskeleton growth factor 22 (Cytoskeleton growth factor 22) | NM_020211 | CHCH23 | 3.94479 |
| cytoskeleton growth factor 23 (Cytoskeleton growth factor 23) | NM_020211 | CHCH24 | 3.94479 |
| cytoskeleton growth factor 24 (Cytoskeleton growth factor 24) | NM_020211 | CHCH25 | 3.94479 |
| cytoskeleton growth factor 25 (Cytoskeleton growth factor 25) | NM_020211 | CHCH26 | 3.94479 |
| cytoskeleton growth factor 26 (Cytoskeleton growth factor 26) | NM_020211 | CHCH27 | 3.94479 |
| cytoskeleton growth factor 27 (Cytoskeleton growth factor 27) | NM_020211 | CHCH28 | 3.94479 |
| cytoskeleton growth factor 28 (Cytoskeleton growth factor 28) | NM_020211 | CHCH29 | 3.94479 |
| cytoskeleton growth factor 29 (Cytoskeleton growth factor 29) | NM_020211 | CHCH30 | 3.94479 |
| cytoskeleton growth factor 30 (Cytoskeleton growth factor 30) | NM_020211 | CHCH31 | 3.94479 |
| cytoskeleton growth factor 31 (Cytoskeleton growth factor 31) | NM_020211 | CHCH32 | 3.94479 |
| cytoskeleton growth factor 32 (Cytoskeleton growth factor 32) | NM_020211 | CHCH33 | 3.94479 |
| cytoskeleton growth factor 33 (Cytoskeleton growth factor 33) | NM_020211 | CHCH34 | 3.94479 |
| cytoskeleton growth factor 34 (Cytoskeleton growth factor 34) | NM_020211 | CHCH35 | 3.94479 |
| cytoskeleton growth factor 35 (Cytoskeleton growth factor 35) | NM_020211 | CHCH36 | 3.94479 |
| cytoskeleton growth factor 36 (Cytoskeleton growth factor 36) | NM_020211 | CHCH37 | 3.94479 |
| cytoskeleton growth factor 37 (Cytoskeleton growth factor 37) | NM_020211 | CHCH38 | 3.94479 |
| cytoskeleton growth factor 38 (Cytoskeleton growth factor 38) | NM_020211 | CHCH39 | 3.94479 |
| cytoskeleton growth factor 39 (Cytoskeleton growth factor 39) | NM_020211 | CHCH40 | 3.94479 |
| cytoskeleton growth factor 40 (Cytoskeleton growth factor 40) | NM_020211 | CHCH41 | 3.94479 |
| cytoskeleton growth factor 41 (Cytoskeleton growth factor 41) | NM_020211 | CHCH42 | 3.94479 |
| cytoskeleton growth factor 42 (Cytoskeleton growth factor 42) | NM_020211 | CHCH43 | 3.94479 |
| cytoskeleton growth factor 43 (Cytoskeleton growth factor 43) | NM_020211 | CHCH44 | 3.94479 |
| cytoskeleton growth factor 44 (Cytoskeleton growth factor 44) | NM_020211 | CHCH45 | 3.94479 |
| cytoskeleton growth factor 45 (Cytoskeleton growth factor 45) | NM_020211 | CHCH46 | 3.94479 |
| cytoskeleton growth factor 46 (Cytoskeleton growth factor 46) | NM_020211 | CHCH47 | 3.94479 |
| cytoskeleton growth factor 47 (Cytoskeleton growth factor 47) | NM_020211 | CHCH48 | 3.94479 |
| cytoskeleton growth factor 48 (Cytoskeleton growth factor 48) | NM_020211 | CHCH49 | 3.94479 |
| cytoskeleton growth factor 49 (Cytoskeleton growth factor 49) | NM_020211 | CHCH50 | 3.94479 |
| cytoskeleton growth factor 50 (Cytoskeleton growth factor 50) | NM_020211 | CHCH51 | 3.94479 |
| cytoskeleton growth factor 51 (Cytoskeleton growth factor 51) | NM_020211 | CHCH52 | 3.94479 |
| cytoskeleton growth factor 52 (Cytoskeleton growth factor 52) | NM_020211 | CHCH53 | 3.94479 |
| cytoskeleton growth factor 53 (Cytoskeleton growth factor 53) | NM_020211 | CHCH54 | 3.94479 |
| cytoskeleton growth factor 54 (Cytoskeleton growth factor 54) | NM_020211 | CHCH55 | 3.94479 |
| cytoskeleton growth factor 55 (Cytoskeleton growth factor 55) | NM_020211 | CHCH56 | 3.94479 |
| cytoskeleton growth factor 56 (Cytoskeleton growth factor 56) | NM_020211 | CHCH57 | 3.94479 |

List of differentially expressed genes based on microarray analysis

[illegible]

Top KEGG pathway ranking based on the number of input genes in the pathway

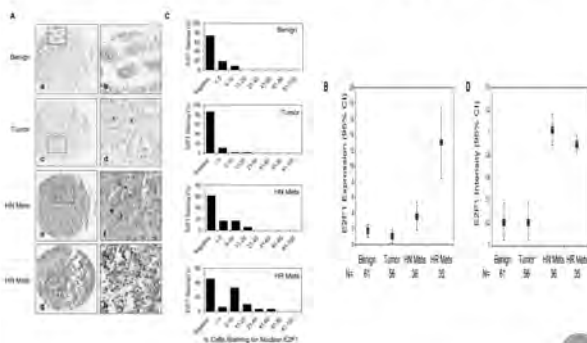
[illegible]

E2F FAMILY

- Transcription factors, 8 characterized family members (E2Fs 1-8)
- **Function**
 - progression through the cell cycle by regulating the transcription of genes that are essential for DNA synthesis and cell cycle progression
- **E2F1**
 - Oncogenes
 - induce quiescent cells to enter the cell cycle
 - override various growth-arrest signals
 - transform primary cells
 - Hyperproliferation & hyperplasia
 - Tumor suppressors by activating apoptotic pathways

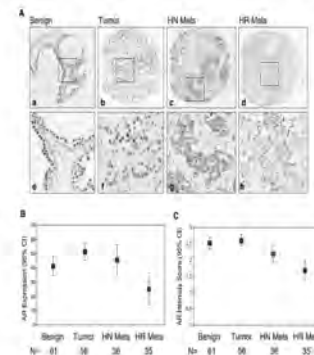
Davis JR, et al: Elevated E2F1 Inhibits Transcription of the Androgen Receptor in Human Hormone-Refractory Prostate Cancer. *Cancer Res* 2006; 66(24)

E2F1 expression during prostate cancer progression.

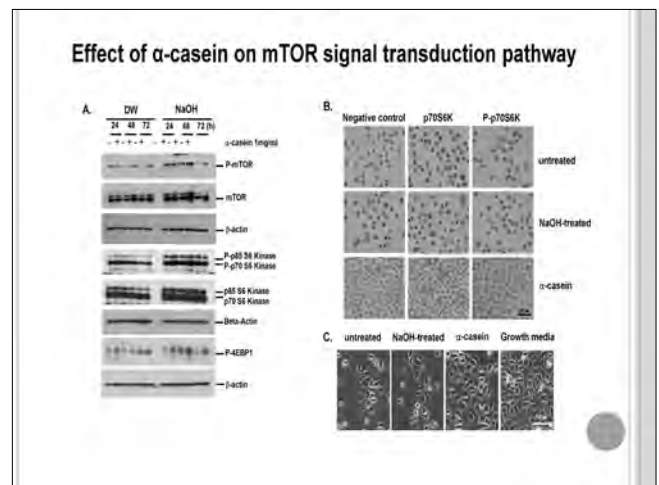
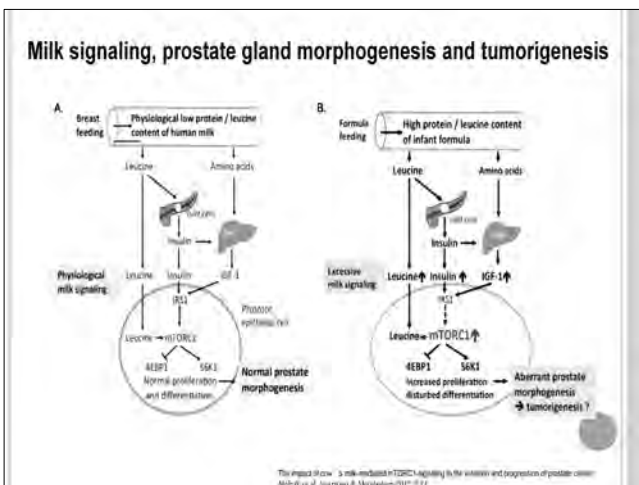
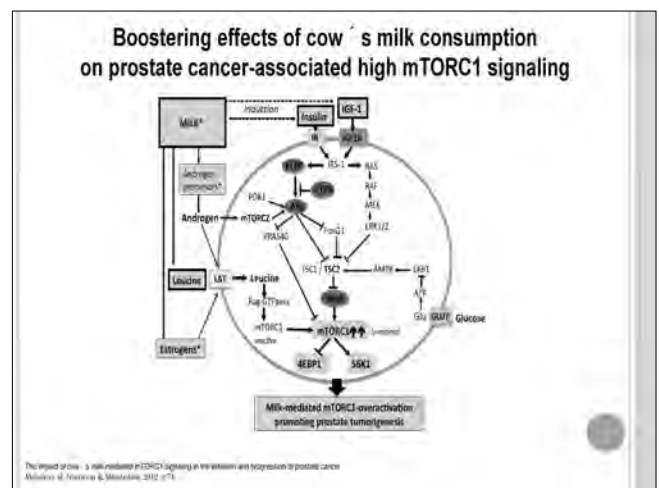
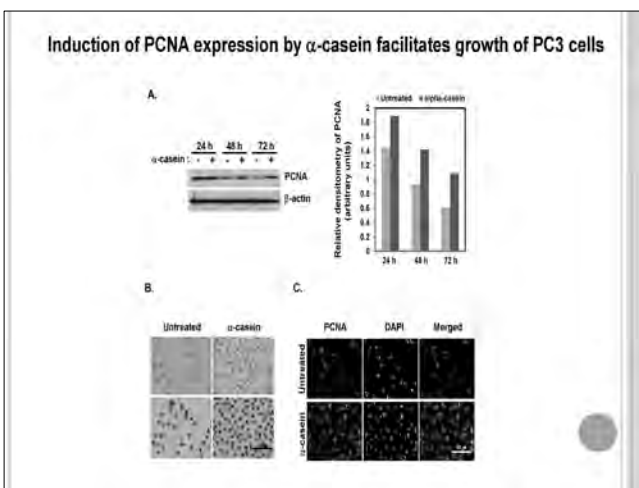
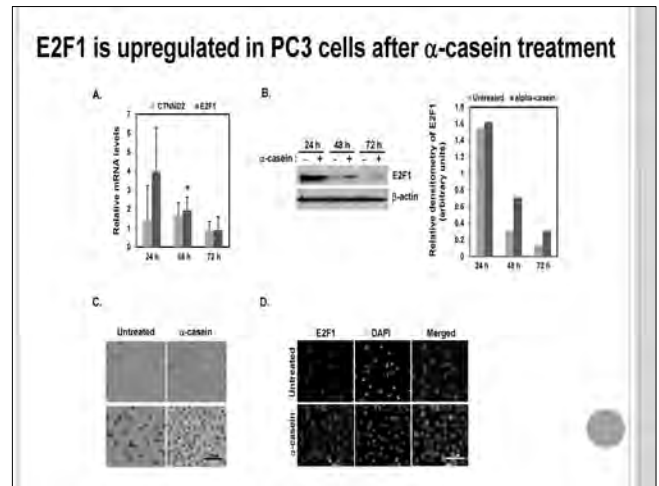
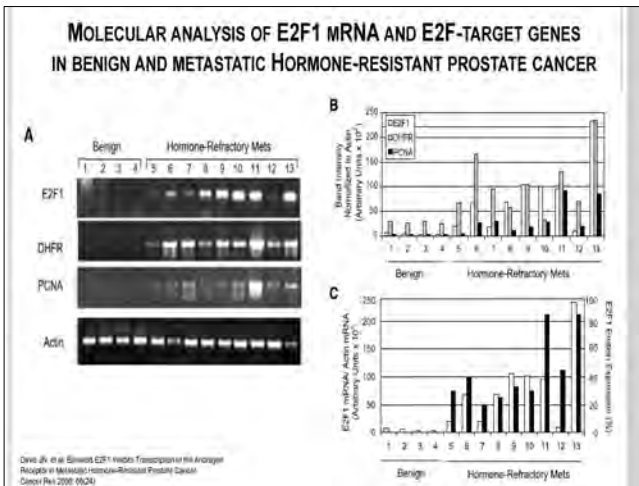


Davis JN, et al. Elevated E2F1 Inhibits Transcription of the Androgen Receptor in Metastatic Hormone-Resistant Prostate Cancer. *Cancer Res* 2006; 66(24)

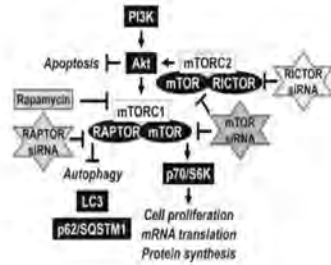
AR expression during prostate cancer progression.



Davis JN, et al. Elevated E2F1 Inhibits Transcription of the Androgen Receptor in Metastatic Hormone-Resistant Prostate Cancer. *Cancer Res* 2008; 68(24).

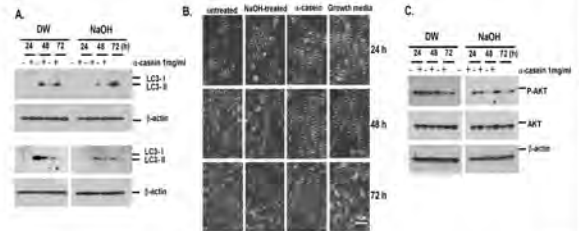


mTOR signaling pathway

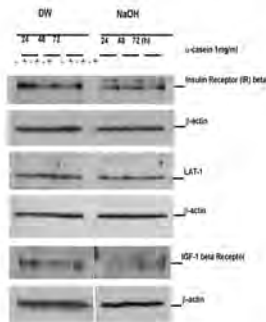


11. Yu et al. Discovered the function of mTORC1/RAPTOR pathway against human hepatocellular carcinoma progression. Autophagy induction promotes proliferation with Akt and Autophagy induction. J. Immunother. 2017;35.

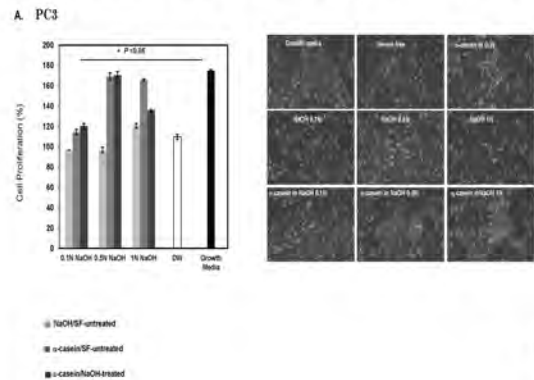
α -casein enhances survival of PC-3 cells by inhibiting starvation-induced autophagy



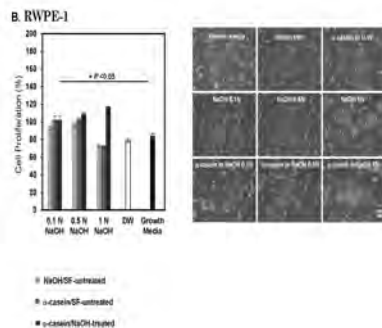
Impact of IGF/Insulin Signaling in PC3 cells by α -casein



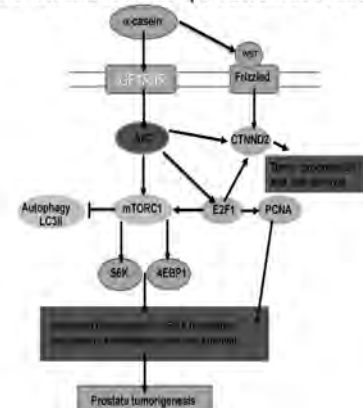
The pH difference changes the growth of prostate cancer cells



The pH difference changes the growth of prostate cells



Proposed mechanism by which α -casein induces PC3 cell growth, proliferation and survival upon serum starvation



Conclusion & Summary

- α -casein altered the expression of a large number of genes related to the control of growth, cell survival, and physiologic behaviors in PC3 cells.
- α -casein also induced the activation of mTORC1, which provides a pro-survival and an anti-autophagy environment for the initiation and progression of proliferation in PC3 cells under nutrient deprived and alkalized conditions.
- These data will be helpful in determining the molecular mechanisms of action of the milk protein, casein, on prostate cancer cells and in development of new preventive or therapeutic strategies for prostate cancer.

정청해 주셔서 감사합니다.



2018

**비뇨기계기초의학연구회
요로생식기손상재건연구회
공동심포지엄**

Session III. 해외 연수를 통한 최신 연구 경험

좌장: 한웅규 (연세의대)

Regional Hypothermia during RARP: does it really helpful?
Experience from UCI

고영휘 (영남의대)

Expression of NlpC protein and Penicillin-Binding Protein 2 (PBP2)
in Neisseria Gonorrhoeae

최현섭 (가톨릭의대)

Hypothermic nerve-sparing radical prostatectomy facilitates earlier recovery of potency

Young Hwii Ko,^{1,2} Starecky Douglas,¹ Linda Huynh,¹ Thomas Ahlering¹

¹Department of Urology, UC Irvine, CA, USA

²Department of Urology, Yeoungnam University, Daegu, Korea

Introduction: Reginal hypothermia (RH) had been suggested based on pilot trial as an attempt to accelerate regains of potency after radical prostatectomy by reducing the consequences of acute trauma and the inflammatory cascade. We investigated its substantial advantage in large number of patients, in comparison with normothermia (NT) counterparts.

Materials and Methods: Among 930 nerve-sparing robotic assisted radical prostatectomies (RARPs) for non-high risk patients with minimal follow-up of 12 months after initial 100 cases, half of the procedure (n=466) was performed under RH, remaining the other half (n=464) in NT. RH was achieved by devising an endorectal cooling balloon system using cold saline (4°). Postoperatively, the regain of potency were monitored using sexual health profile for men (SHIM) score, using definition of recovery over 17.

Results: The mean (±SD) age (61.35±7.35 vs. 60.67±7.37 yrs), prostate volume (54.09±18.20 vs. 51.77±19.30 g), preoperative PSA (5.79±.83 vs. 5.64±2.78 ng/ml), and body mass index (BMI; 27.06±3.44 vs. 26.65±3.37 kg/m²) were similar between RH and NT group. SHIM score was higher in RH group both at 3 (6.87±7.70 vs. 4.91±6.41 p<.001) and 12 months (13.19±8.31 vs. 9.75±8.67 p=.001), despite of their similarity on preoperative score (19.96±6.51 vs. 19.60±6.93, p=.422). In RH group, 17.35% at 3 months (9.7% in NT, p=.002) and 44.4% at 12 months (29.0% in NT, p=.008) regained their potency. For 421 men (44.3%) with relatively young (<65 yrs) and normal preoperative SHIM (> 21), potency rate at 3 and 12 months was 27.0 % and 75.0% in RH group (17.1% and 47.1% in NT, p=.024 and .003, respectively). In this particular subgroup, multiple logistic regression models on potency at 12 months using covariates of age, GS, PSA, pathologic stage, prostate volume, BMI, preoperative SHIM, and learning curve demonstrated RH as a significant predictor (Odds ratio; OR=5.440, p=.013, R²=.198) along with prostate volume (over 50g: OR=.352, p=.010) and pathologic stage (over T3: OR=.382, p=.027). In multiple linear regressions for identical setting, RH was a sole predictor on return of potency at 12 months (Table 1).

Conclusion: Applying RH during RARP improves the recovery of potency after surgery in a patient with minimum a year follow-up.

Appendix

Table 1. Summary of univariate and multivariate Linear regression on SHIM at 12 month after surgery

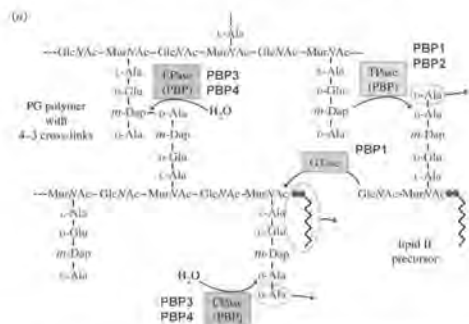
| | Univariate | | | | Multivariate | | | |
|-----------------------------|------------|--------------|--------|---------|--------------|--------------|--------|---------|
| | B | 95% CI for B | | p-value | B | 95% CI for B | | p-value |
| | | Lower | Upper | | | Lower | Upper | |
| GS (>8) | -.811 | -3.709 | 2.088 | .581 | -1.447 | -4.346 | 1.453 | .326 |
| PSA (>20ng/ml) | -4.488 | -11.078 | 2.103 | .181 | -3.969 | -10.578 | 2.640 | .237 |
| Volume (>50g) | -1.903 | -4.683 | .877 | .178 | -2.326 | -5.120 | .467 | .102 |
| pStage (>T3) | -2.625 | -5.840 | .590 | .109 | -3.140 | -6.408 | .128 | .060 |
| BMI (>30kg/m ²) | .013 | -3.112 | 17.424 | <.001 | -.084 | -3.286 | 3.118 | .959 |
| Learning curve | 1.131 | -.732 | 2.994 | <.001 | -1.019 | -3.773 | 1.736 | .466 |
| RH vs. NT | 4.153 | 1.096 | 7.210 | .008 | 5.871 | 1.336 | 10.406 | .012 |

Expression of NlpCprotein and Penicillin-Binding Protein 2 (PBP2) in *Neisseria Gonorrhoeae*

Hyun-Sop Choe

The Catholic University of Korea St. Vincent's Hospital

Activities of PBPs during Peptidoglycan Synthesis/Remodeling



Egan et al. (2015) Activities and regulation of peptidoglycan synthases. Philos Trans R Soc Lond B Biol Sci 370(1679)

Antibiotic Resistance in *Neisseria gonorrhoeae* is a long-standing problem

- *N. gonorrhoeae* has become resistant to nearly every antibiotic used to treat infections
- Ceftriaxone remains the most effective antibiotic in clinical use, but its continued effectiveness is in doubt due to the emergence of resistant strains
- Resistance is due to acquisition of altered *penA* genes encoding Penicillin-Binding Protein 2 (PBP²), the lethal target of ceftriaxone
- PBP2 is an essential peptidoglycan transpeptidase during cell division

Alterations of PBPs

- Mutations in PBPs cause a decrease in the rates of inactivation by β -lactam antibiotics
- Observed in *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Neisseria gonorrhoeae*
- Altered PBPs have evolved by recombination with DNA from commensal (non-pathogenic) species
- This leads to many amino acid changes, only some of which decrease inactivation by the antibiotic

Penicillin- and Ceftriaxone-Resistant *Neisseria gonorrhoeae*

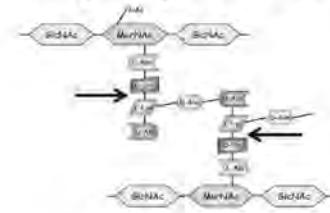
- *Neisseria* becomes resistant to penicillin in two ways:
 - Plasmid-mediated production of a β -lactamase
 - Chromosomal mutations in endogenous genes
- Chromosomal resistance genes can be transferred from a resistant strain to a sensitive strain by homologous recombination
- Genes are transferred in a specific order
- The mutations in PBP 2 determine whether the strain is penicillin- or ceftriaxone-resistant

Experimental Subject

Ceftriaxone resistant *N. Gonorrhoeae*
with PBP2

↑
penA41 gene from strain H041

NlpC protein



Endopeptidase
= Cell wall hydrolase

protein family NlpC/p60 codes for endopeptidases with peptidoglycan hydrolyzing activity, helping in cell wall reorganization, development and cell division

HA tagging in Western Blot

HA tag = a part of haemagglutinin

target protein ~+HA (tagging)

Sequence
: 5' TAC CCA TAC GAT GTT CCA GAT TAC GCT 3'
or 5' TAT CCA TAT GAT GTT CCA GAT TAT GCT 3'

= Amino acid
: YPYDVPDYA

We can insert HA sequence into genome, in specific site.
(Transformation)
And we can detect HA protein expression by Western Blot.

Transformation of HA tag

Genome of *Neisseria Gonorrhoeae*, FA19 strain



Add HA sequencing Tag

5' TAC CCA TAC GAT GTT CCA GAT TAC GCT 3'



FA19 *nlpC*-HA_{comp}

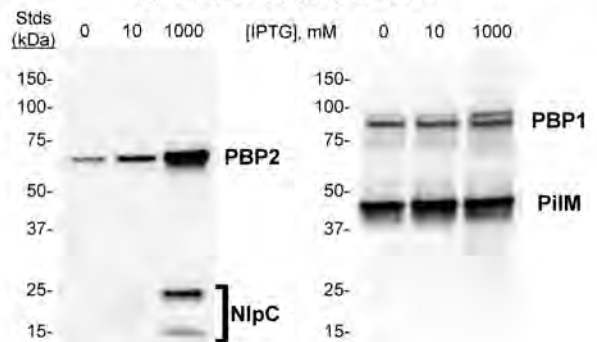
FA19 *nlpC*::kan^R *nlpC*-HA_{comp}

FA19 *nlpC*-HA_{comp} *penA41*-HA

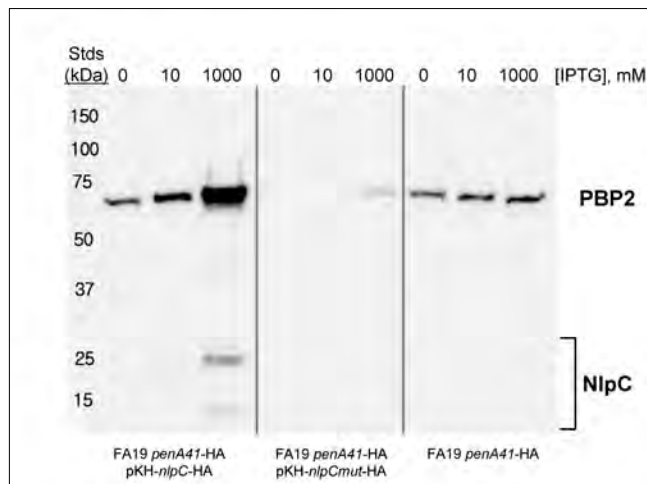
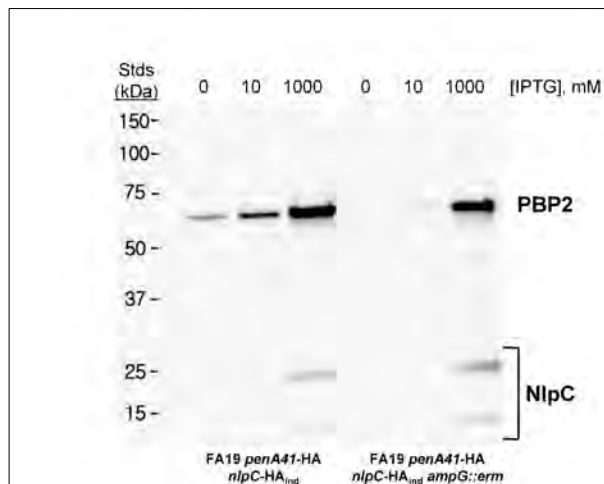
FA19 *nlpC*::kan^R *nlpC*-HA_{comp} *penA41*-HA

FA19 *nlpC*-HA_{comp} *penA41*-HA *ampG*::erm^R

Overproduction of NlpC induces expression of PBP2 but not PBP1



FA19 *penA41*-HA *nlpC*-HA_{comp}



Conclusion

- As increasing of NlpC expression, increasing of PBP2 expression occurred.
- There should be some important role of NlpC to PBP2 expression (Ceftriaxone resistance) (genetic level or protein level)
- Further evaluation should be done
which level of effect ?
direct ? or indirect ? (secreted protein particle)
- If we could make NlpC inhibitor or modulator, the compound may be a candidate of new antibiotic drug which overcome PBP-related beta-lactam resistance.

2018

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공동심포지엄

Session IV (기초). Current Status of Urological Research in Korea

좌장: 강석호 (고려의대)

Expression of HMGB1 in prostate cancer: clinical and biological correlations 박용현 (가톨릭의대)

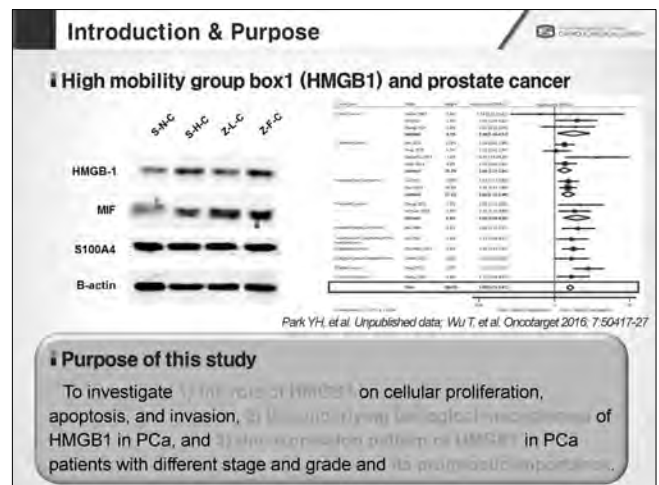
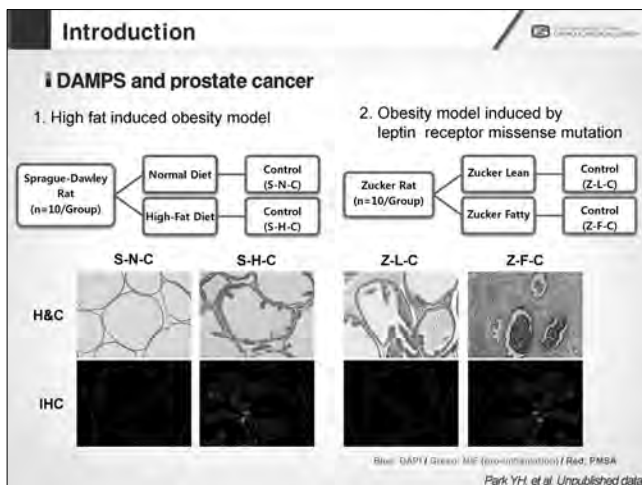
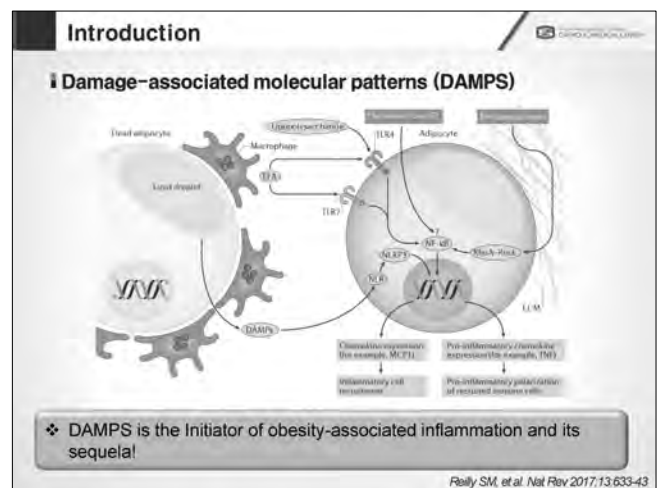
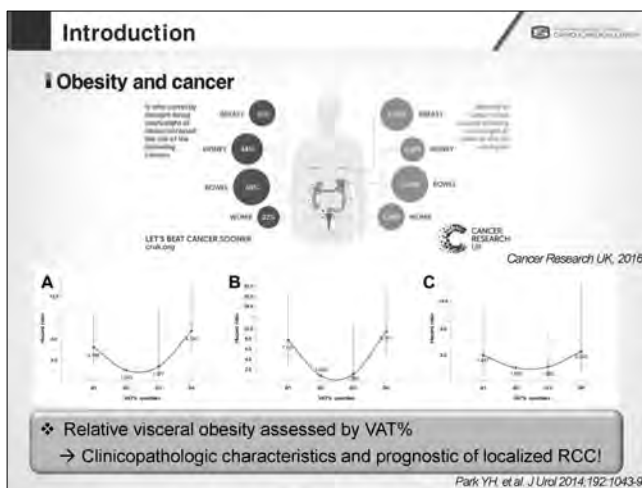
신장암 세포주에서 메트포르민과 에버로리무스의 효과 및 상승효과에 대한 연구 윤영은 (한양의대)

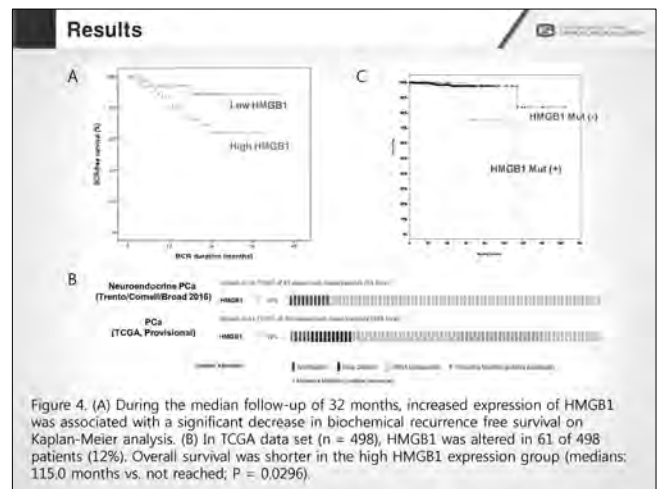
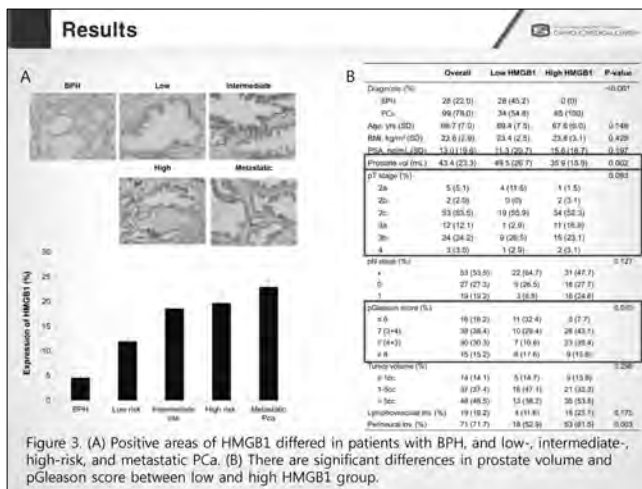
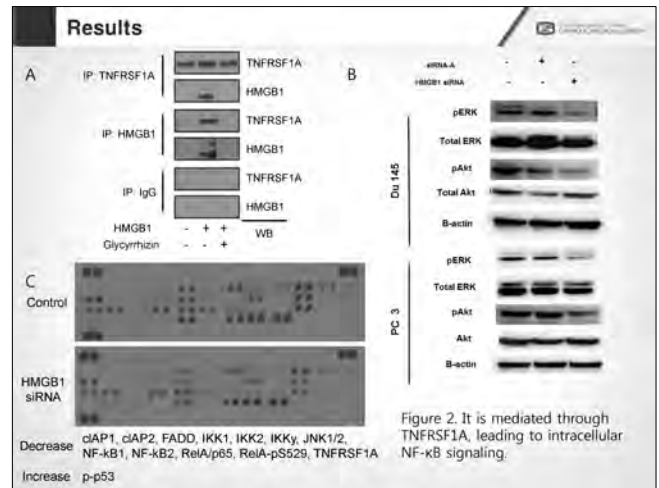
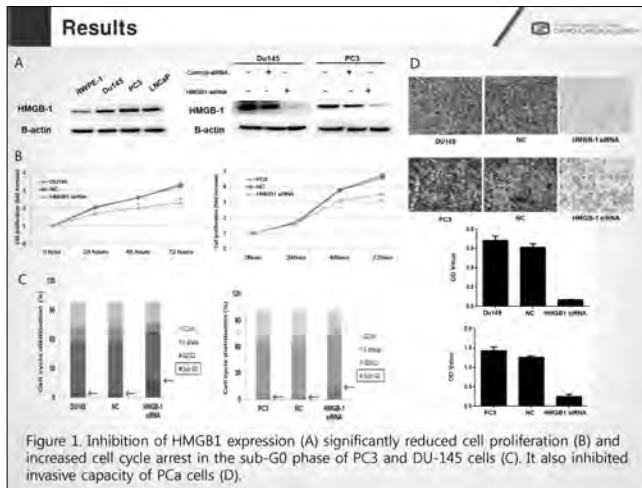
Role of TRPM7 in urological cancer 하윤석 (경북의대)

Expression of HMGB1 in Prostate Cancer: Clinical and Biological Correlations

YH Park, AR Jung, KE Kim, MY Kim, JY Lee

The Catholic University of Korea





Conclusions

- Our findings demonstrate an important role of HMGB1 and novel relationship between HMGB1 and TNFRSF1A in PCa.
- Therapy targeting HMGB-associated pathways may represent a novel therapeutic avenue for PCa.



The Synergic Effect of Metformin and Everolimus in Renal Cell Carcinoma

Young Eun Yoon

Department of Urology, Hanyang University College of Medicine, Seoul, Korea

We investigated the antitumor effect of metformin combined with everolimus on renal cell carcinoma cell lines.

The water-soluble tetrazolium salt (WST) cell viability assay and colony formation assays was performed to investigate the effects of metformin, everolimus and their combination on normal kidney epithelial cells (HK-2, LLC-PK1) and RCC (Caki1, Caki2) cell growth. Signaling molecules involved in mTOR signaling was analyzed by immunoblot analysis of various proteins including mTOR, AMPK, 4EBP1, p70S6K.

WST cell viability assay showed that both metformin and everolimus reduced cell viability of normal kidney cells and renal cancer cells in a dose-dependent manner. And metformin combined with everolimus had a synergistic inhibitory effect in a dose-dependent manner. In Caki-2 cell, metformin combined with everolimus effectively inhibits colony formation. Metformin and everolimus inhibited mTOR down signaling molecules, AMPK, 4EBP1, p70S6K in Caki-2 cell. And these results were more maximized when metformin was combined with everolimus.

These results indicated the synergic antitumor effects between metformin and everolimus, which may be a prospective therapy strategy to achieve potent antitumor effects on renal cell carcinoma.

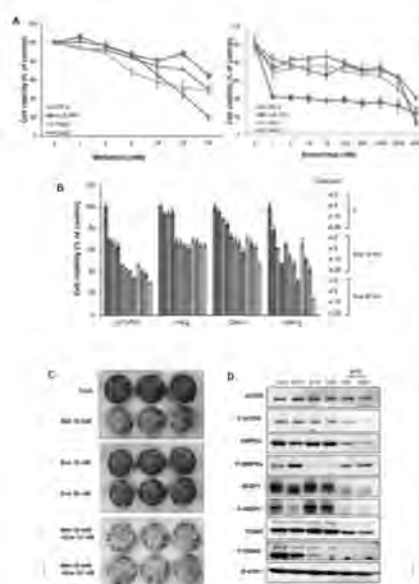


Fig.1. (A) Metformin and everolimus inhibits normal kidney epithelial cells (HK-2, LLC-PK1) and RCC (Caki1, Caki2) growth. Cells were treated with metformin (0, 1, 2, 5, 10, 20, and 50 mM) and everolimus (0, 1, 5, 10, 50, 100, 500, 1000, 2000, and 4000 mM) for 72 hours and cell viability assay was performed. After 72h, WST was added to each well and incubated for 4 hours at 37°C. The absorbance at 450nm, 650nm was measured. (B) Metformin combined with everolimus synergistically inhibits normal kidney epithelial cells (HK-2, LLC-PK1) and RCC (Caki1, Caki2) growth. Cells were treated with metformin (0, 1, 2, 5, 10, and 20 mM) and everolimus (0, 10, and 50 mM) for 72 hours and cell viability assay was performed. After 72h, WST was added to each well and incubated for 4 hours at 37°C. The absorbance at 450nm, 650nm was measured. (C) Metformin and everolimus inhibits colony formation of Caki-2 cells. Metformin combined with everolimus synergistically inhibits colony formation of Caki-2 cell. Cells were seeded in 6-well plates in triplicate at a density of 200 cells/well with 10% FBS. After 24 hours, cultures were replaced with fresh medium containing 5% FBS as control, or the same medium containing different concentrations of metformin, everolimus and their combination for 14 days at 37°C. The formed colonies were stained with a solution maintaining 0.5% crystal violet and 25% methanol, followed by washing with water to remove excess dye. (D) Metformin and everolimus inhibits mTOR signaling in Caki-2 cells. Caki-2 cells were treated with 10 mM metformin and 10nM, 50nM everolimus for 72 hours and cell lysates were resolved by SDS-PAGE. Immunoblot analysis was carried out using antibodies against mTOR, phospho-mTOR, AMPK, phospho-AMPK (Thr172), 4E-BP1, phospho-4E-BP1 (Thr37/46), 70S6K, phospho-70S6K and β-actin.

Role of TRPM7 in Urological Cancer

Yun-Sok Ha

Department of Urology KyungpookNational University

Projects

- The role and mechanism of TRPM7 in prostate cancer cell migration and invasion; involvement of AKT, Src and MAPK pathways: 한국아스트라제네카(주)_2014
- 신장암 세포의 migration 과 invasion에서의 TRPM7 유전자의 역할 및 기전: AKT, Src, MAPK 신호 전달 체계: 경북대학교병원_2015
- 방광암에서 TRPM7 유전자의 발현: 종양 성장과 전이에 대한 기전 규명 및 예후 인자로서의 가치 탐구: 연구재단 신진_2016

The role and mechanism of an endogenous Mg^{2+}/Ca^{2+} channel TRPM7 in prostate cancer cell migration and invasion

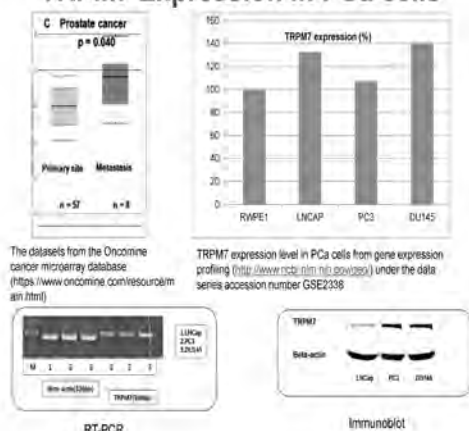
Department of Urology, Kyungpook National University
Yun-Sok Ha, Yeon-Yong Kim, So-Young Chun, Jae-Wook Chung,
Seock-Hwan Choi, Jun-Nyung Lee, Bum-Soo Kim, Hyun-Tae Kim,
Tae-Hwan Kim, Tae-Gyun Kwon

TRPM7 (transient receptor potential melastatin 7 channel):

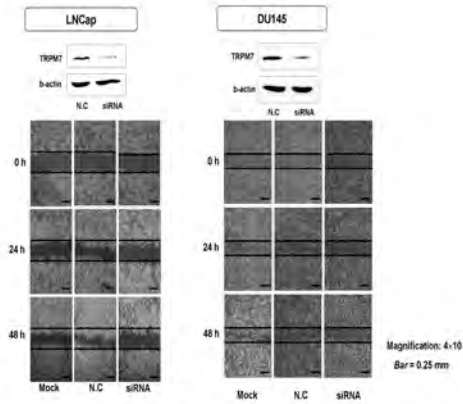
- ✓ TRPM7 is a novel magnesium-nucleotide-regulated meta current channel that is regulated by serum Mg^{2+} concentration.
- ✓ Changes in Mg^{2+} concentration and Ca^{2+}/Mg^{2+} have been shown to play a critical role in cell proliferation.
- ✓ Recent studies have shown that TRPM7 is expressed in prostate cancer (PCa) cells and is involved in the proliferation of PCa cells.
- ✓ However, signaling pathways link to TRPM7 to modulate PCa cell migration and invasion is largely unknown.
- ✓ The objective of this study was to determine whether TRPM7 regulate PCa cells migration and invasion through linkage with one or more signal transduction pathways.



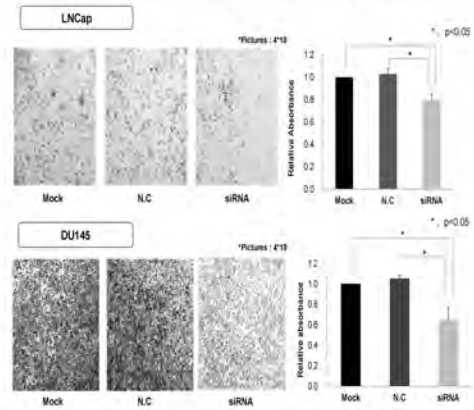
TRPM7 Expression in PCa cells



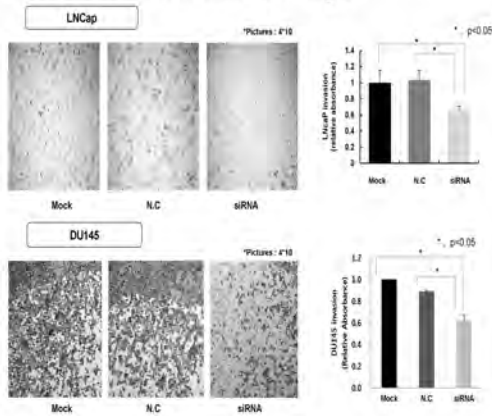
Downregulation and wound healing assays of TRPM7 in PCa cells



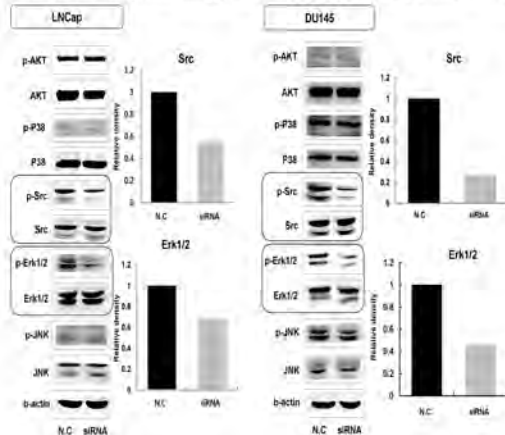
Migration assays with transparent PET membrane



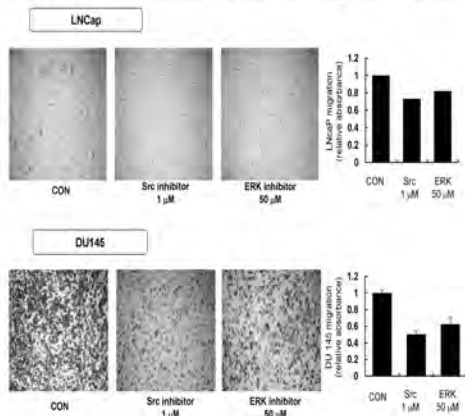
Transwell invasion assays



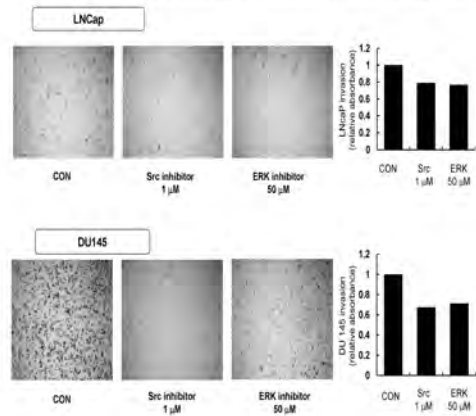
TRPM7 downregulation suppresses activation of Src and ERK 1/2



Effect of Src and ERK1/2 inhibitors on inactivation of migration in PCa cells.



Effect of Src and ERK1/2 inhibitors on inactivation of invasion in PCa cells.

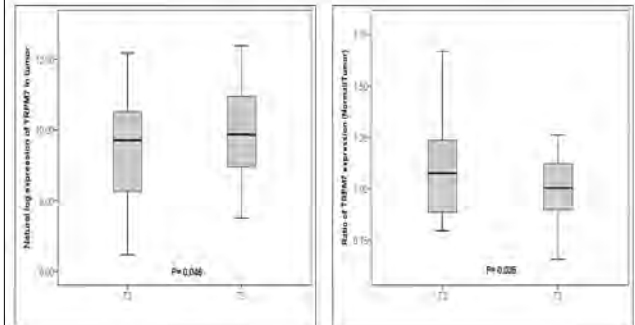


Clinical significances

- N= 95
- Tumor tissues and corresponding adjacent normal tissues
- QPCR analyses
- Baseline characteristics

| | |
|---|--------------|
| Mean Age (yr) ± SD | 65.43 ± 6.20 |
| Median PSA (ng/ml) ± SD | 8.90 ± 17.83 |
| Body mass index (kg/m ²) ± SD | 24.49 ± 2.77 |
| Pathologic stage (n, %) | |
| pT2 | 41 (43.2) |
| pT3a | 35 (36.8) |
| pT3b | 19 (20.0) |
| Gleason score (n, %) | |
| 6-7 | 66 (69.5) |
| 8-10 | 29 (30.5) |

TRPM7 expression



Conclusions

- The findings of our study suggest that that silencing of TRPM7 in Pca cells results in a significant inactivation of Src and ERK1/2 and prevent migration and invasion of the human Pca cell lines LNCaP and DU145.
- Thus, targeting TRPM7 including Src and ERK1/2 may be a potential candidate for the development of chemotherapeutic treatments for PCa.
- TRPM7 expression was upregulated in PCa patients with stage T3 compared with PCa patients with localized stage T2 disease.
- TRPM7 could be used as a prognostic marker for Pca.

Downregulation of TRPM7 Prevents Migration and Invasion of Renal Cell Carcinoma Cells via Inactivation of the Src and Akt pathway

Yun-Sok Ha, Na Hee Yu, Yoon-Yong Kim, So Young Chun, You Jin Lee, Jae-Wook Chung, Seock Hwan Choi, Jun Nyung Lee, Bum Soo Kim, Hyun Tae Kim, Tae-Hwan Kim, Eun Sang Yoo and Tae Gyun Kwon
Department of Urology, School of Medicine, Kyungpook National University, Daegu, Korea

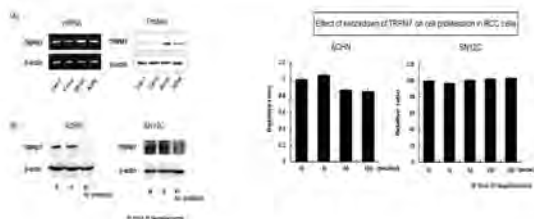
Introduction and objective

- ♦ The transient receptor potential melastatin member 7 (TRPM7) is highly related to distinct human malignancies, but its role in renal cell carcinoma (RCC) has not been investigated.
- ♦ The objective of this study was to determine whether TRPM7 regulate RCC cells migration and invasion through linkage with one or more signal transduction pathways.

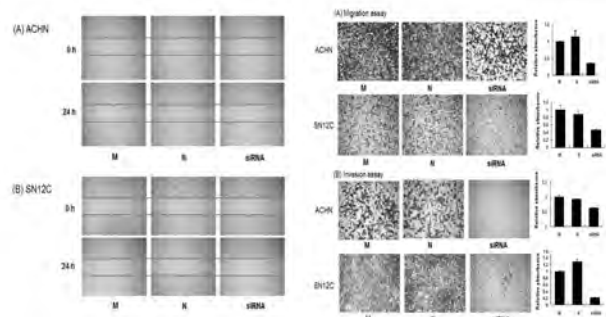
Methods

- ♦ The human RCC cell lines ACHN and SN12C were selected for this study.
- ♦ Western blot analysis and small interfering RNA (siRNA)-based knockdown were used in order to investigate the possible molecular mechanisms.
- ♦ Wound healing migration assay and transwell invasion were conducted to evaluate the effect of TRPM7 knockdown on RCC cells.

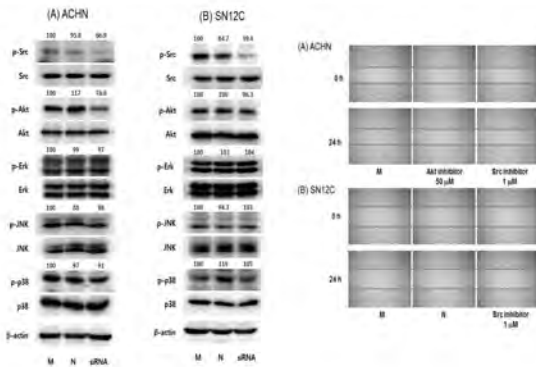
Result (1)



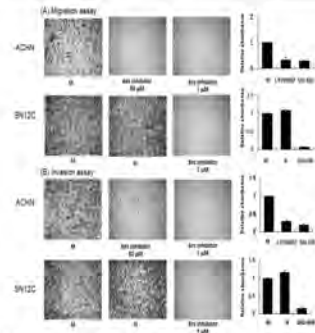
Result (2)



Result (3)



Result (4)



Conclusion

Our findings that TRPM7 modulates migration and invasion of ACHN and SN12C RCC cells through the Src and Akt pathway suggest that depressing this signaling pathway or/and the TRPM7 channel protein may be beneficial in treating RCC patients.

연구목표 선정

방광암에서 TRPM7 유전자의 발현, 종양 성장과 전이에 대한 기전 규명 및 예후 인자로서의 가치 탐색

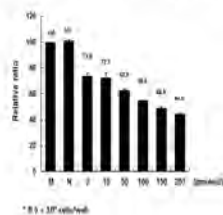
1차년도 계획 및 목표

| 구분 | 년도 | 연구개발과목 | 연구개발내용 | 연구범위 | 평가확인점 |
|------|------|-------------------------|---|--|--|
| 1차년도 | 2016 | 방광암세포에서 TRPM7 발현의 역할 규명 | 방광암세포에서 TRPM7 발현의 역할 규명 | 방광암 세포주에서 mRNA 및 단백질을 발현 확인 후 과발현 cell line, 과발현 cell line screening | 과발현 cell line 2종 이상 선정 여부 |
| | | | Knockdown에 따른 방광암세포에서 TRPM7 억제에 따른 세포 증식 및 전이 억제에 대한 연구 | Gene silencing 후 MTT assay, FACS analysis, wound healing assay 및 invasion assay 시행 | 억제된 유전자 발현 억제 확인과 이에 따른 세포 성장 억제와 전이 억제 여부 |
| | | | 방광암세포에서 TRPM7 억제에 따른 세포 증식 및 전이 억제에 대한 연구 | TRPM7 siRNA 처리 유무에 따라 apoptosis, Akt, Src, MAPK 신호전달체 등에 관여하는 단백질 발현을 | proliferation 및 metastasis에 관여하는 단백질 발현 여부 |
| | | | 방광암세포에서 TRPM7 억제에 따른 세포 증식 및 전이 억제에 대한 연구 | 방광암세포에서 TRPM7 억제에 따른 세포 증식 및 전이 억제에 대한 연구 | 방광암세포에서 TRPM7 억제에 따른 세포 증식 및 전이 억제에 대한 연구 |

1) 방광암세포에서 TRPM7 발현 양상 확인

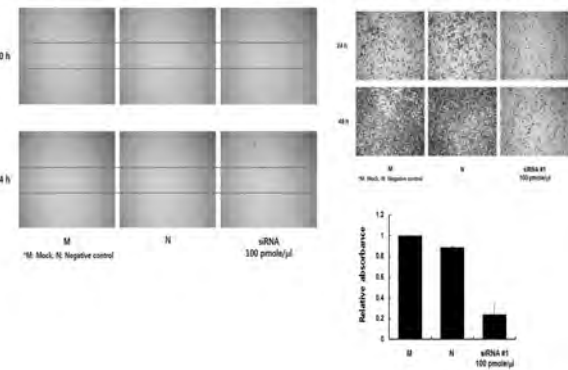


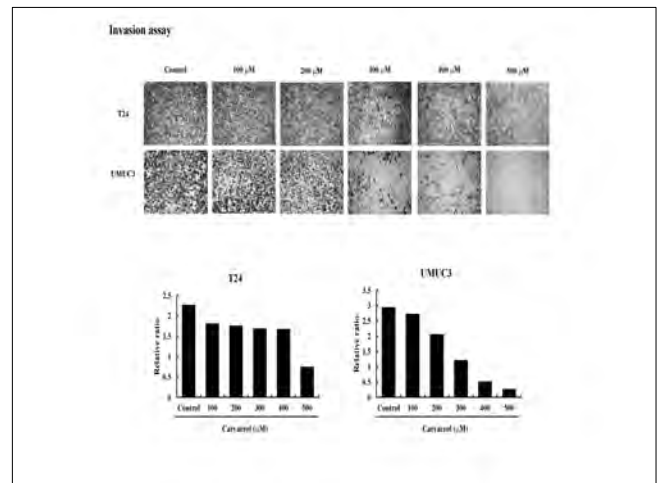
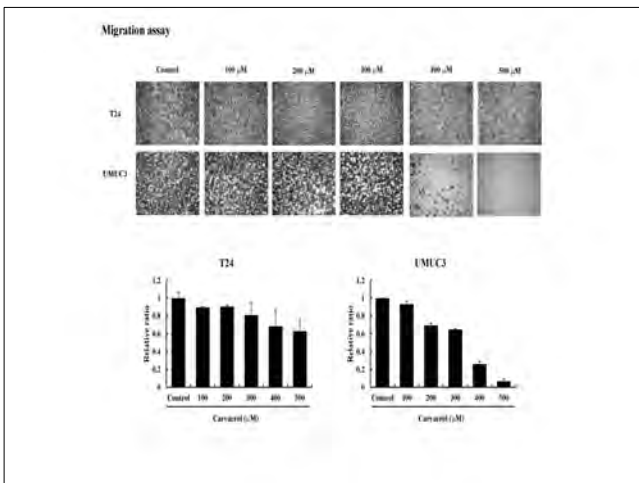
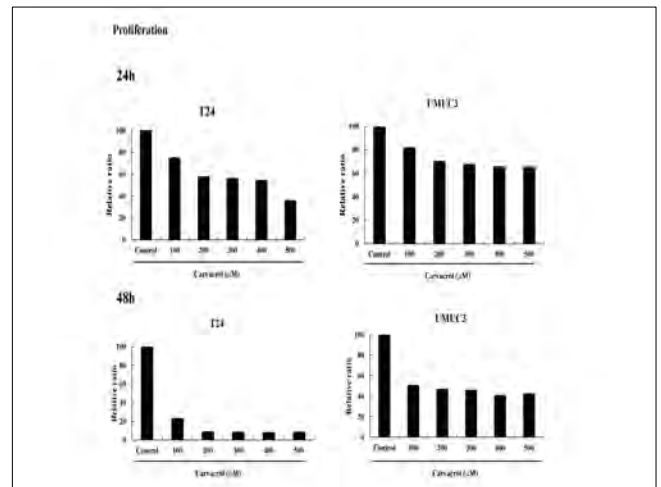
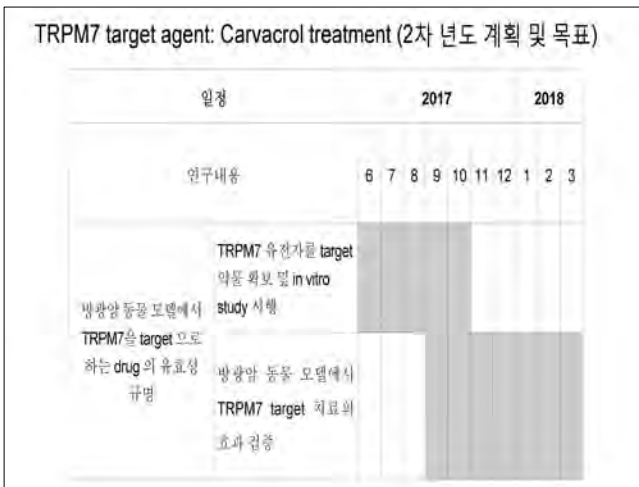
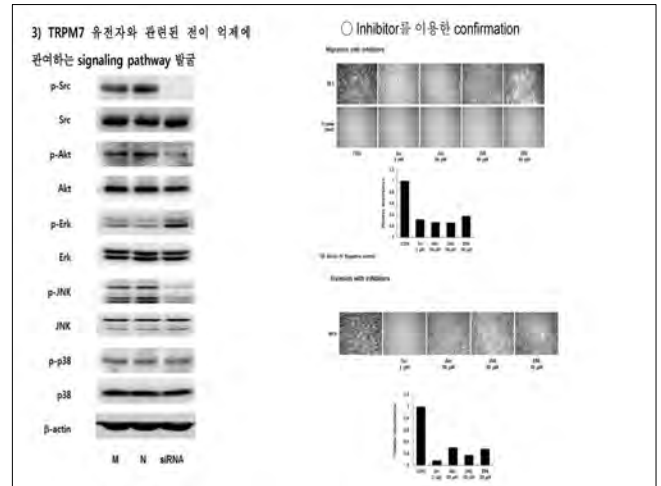
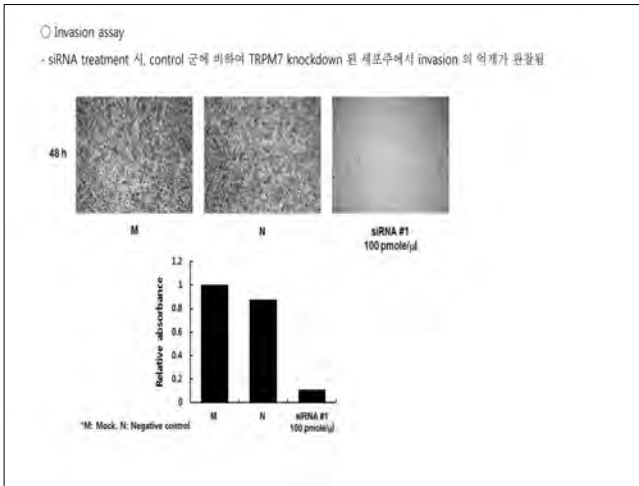
2) 방광암세포에서 TRPM7 억제에 따른 세포 증식 및 전이 억제에 대한 연구



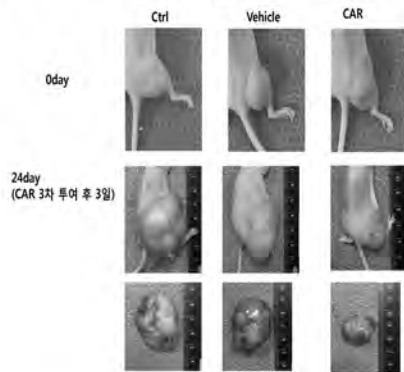
○ Migration assay

- siRNA treatment 시, control 군에 비하여 TRPM7 knockdown 된 세포주에서 migration의 억제에 관찰됨

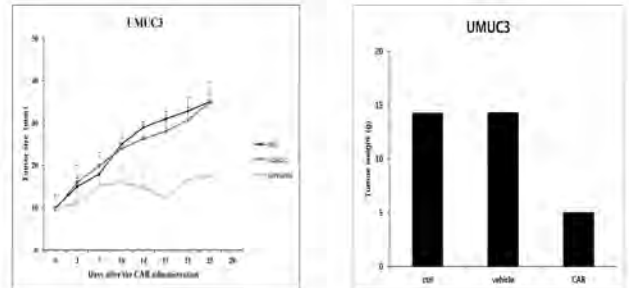




In vivo animal study (tumor shape UMUC3)



In vivo animal study



Thank you
for
listening!

A simple line drawing of a person with a round head, smiling, and holding a cup. The character is standing next to the text 'Thank you for listening!'.

2018

**비뇨기계기초의학연구회
요로생식기손상재건연구회
공동심포지엄**

Session IV. Issues of GU Trauma & Reconstruction

좌장: 문홍상 (한양의대)

Management of perforation injuries during and following
penile prosthesis surgery

송기현 (강원의대)

Repair of vesicorectal fistula after radical prostatectomy

정원식 (광주기독병원)

Urogenital reconstructions for pediatric trauma

김상운 (연세의대)

Management of Perforation Injuries During and Following Penile Prosthesis Surgery

송 기 현

강원의대

인공음경보형물 삽입 술 중이나 술 후에 발생할 수 있는 보형물 실린더의 천공(perforation)은 드물지만 생긴다면 환자에게는 매우 심각한 합병증이다. 이는 술 중 확장(dilation)을 과하게 하거나 실린더 삽입 공간인 해면체에 비해 실린더가 큰 경우 등에서 음경백막의 손상에 의해 흔하게 일어날 수 있다고 알려져 있다. 특히 과거 microangiopathy, 방사선 치료, 해면체 섬유화가 있었던 환자에서 잘 일어난다. 이런 합병증이 일어나게 되면 술 후 성적이 떨어지고 환자의 만족도가 매우 떨어지게 된다. 따라서 인공음경보형물 수술을 하는 술자는 이런 합병증의 발생을 잘 인지하고, 대처하는 술식에 익숙해져야 한다.

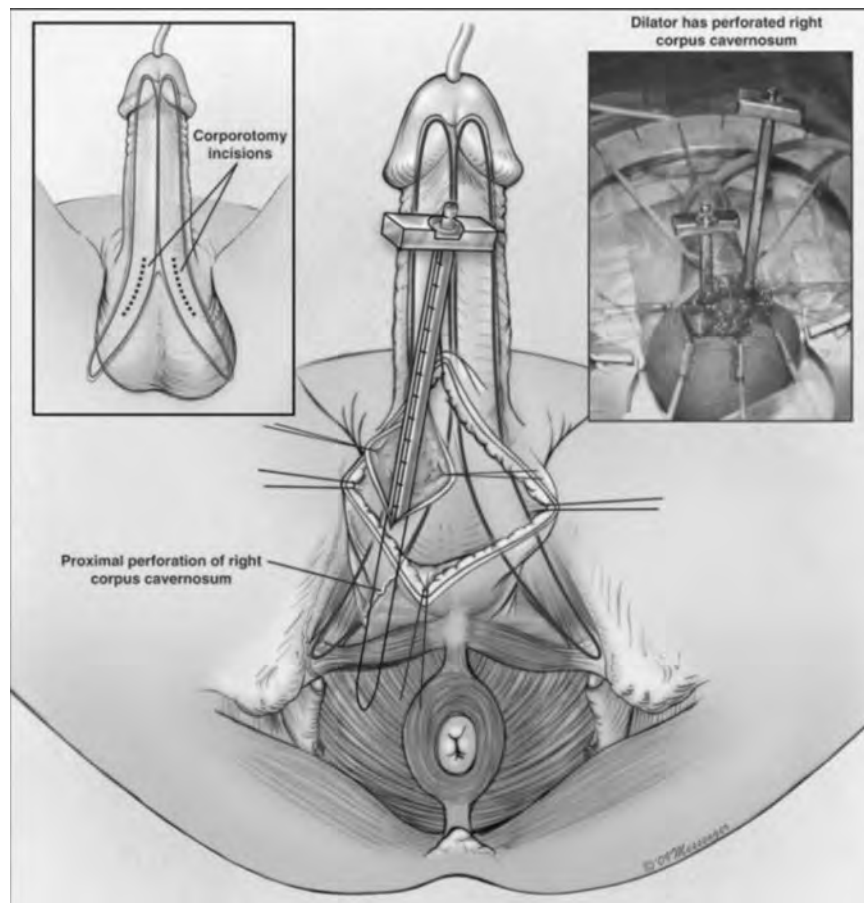
Management of Lateral Extrusion



Hsu와 Brock등에 의해 해부학적으로 음경백막의 원위부(distal), 배부(ventral) 쪽이 다른 부분에 비해 얇아서 보형물이 돌출되는 부분도 주로 이 부분이 될 가능성 높다고 알려져 있다. 특히 큰 실린더나 직경이 작은 dilator를 가지고 과도한 원위부 확장은 위험인자로 잘 알려져 있다. 실린더의 돌출이나 미란(erosion)은 1.2-8.0%까지 현재 보고 되고 있으며, 이는 발생했을 경우 실린더 전부를 제거해야 할 확률이 높아 의사나 환자입장에서는 재앙에 가까운 합병증이다. 또한 제거 후 섬유화와 scarring이 심하게 진행되므로 재삽입술을 하기에는 술자 입장에서는 매우 부담스러운 상황이 된다. 이런 이유로 술자는 미란이 일어나기 전에 외측돌출을 잘 관리하는 법을 아는 것이 매우 중요하다.

Smith 등에 의해 1998년에 천공부위에 이식절편(polytetrafluorethylene distal windsock graft)을 덧대는 방법이 소개된 이후 여러 술자에 의해 여러 이식절편을 이용하는 술식이 소개 되었으나 높은 감염율에 의해 결과가 좋지 못했다. 이후 Mulcahy가 새로운 외측 corporotomy incision을 하여 pseudocapsule layer 만들어 새로운 해면체 공간을 만드는 distal corporoplasty를 소개하였다. 이 방법은 이식절편을 이용하는 술식보다 감염률이 낮고 수술시간은 짧은 편이며 재발율도 낮은 것으로 보고되고 있다. 이후 Shindel 등이 transglanular 접근법을 소개하고 있으나 좁은 술 공간과 귀두부위 출혈이 단점으로 알려져 있다.

Management of Crural Perforation Injuries



Proximal crural bodies를 확장하는 중에 천공이 일어나는 경우가 있다. 천공을 인지하지 못하고 실린더를 삽입하는 경우 penile midshaft에서 실린더가 만져지게 된다. 이런 천공이 일어나는 것을 막기 위해서는 될 수 있으면 확장시 9mm보다 직경이 작은 dilator는 피하는 것이 좋다고 한다. 천공이 일어난 것을 알게 된다면 환자 position을 lithotomy로 바꾸고 회음부 절개로 접근하여야 한다. Primary repair 보다는 windsock graft를 덧대어서 repair 하는 것이 좋다. 하지만 여러 논문에서 이식절편을 덧대는 경우 감염의 확률이 높아지는 단점이 있다고 보고하고 있다. Wilson 등은 nonabsorbable 00 suture를 사용하여 hammock 처럼 작용하게 하여 graft를 덧대지 않고 하는 방법을 고안하였다. 이런 경우 술 후 최소 6주간 천공이 되어 repair한 음경백막 부분의 fibrous scar가 안정화 될 때까지 성교를 금하는 것이 좋다고 알려져 있다.

Management of Distal Urethral Perforation Injuries



원위부 요도 천공은 대부분 확장중 일어나며 요도를 뚫고 나오는 경우 대부분 fossa navicularis 에서 일어난다고 알려져 있다. 특히 Peyronies 병이 있는 경우 더 흔하다. 확장중 요도구에 혈이 보이는 경우나 세척 중 요도구에서 세척액이 나오는 경우 의심해보아야 한다. 이런 경우 대부분의 술자들은 요도천공이 된 부분은 치유가 잘 되지 않을뿐더러, 감염의 가능성이 매우 높아지기 때문에 실린더를 제거하고 수술을 중단하는 경우가 많다. 혹은 천공이 없는 곳에 우선 실린더는 삽입후, 수술을 마치고 몇 달 후 다시 천공이 있었던 곳에 실린더를 삽입하기도 한다. 만약 요도 천공부위가 충분히 봉합이 가능한 원위부라면, 이중 봉합을 하고 실린더를 삽입을 시도하는 경우도 있을 수 있다. 매우 드물게 하는 경우이지만, 인위적으로 요도하열을 만들어 urinary flow가 천공이 일어난 요도에 가지 않게 하는 방법도 있다. 하지만 대부분의 술자들은 two layer closure후 충분히 요도가 치유되는 몇 달 후 다시 수술을 시도하고 있다.

술 중 다른 부위 천공에 비해 요도천공이 일어났을 때 즉시 해결하기 어려운 경우가 많다. Graft repair의 높은 감염률 때문에 현재까지는 Proximal crural 천공은 Wilson's suture sling maneuver가 보편적이며, distal tip의 lateral extrusion의 경우에는 Mulcahy's method가 좋은 성적을 보고하고 있다.

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Repair of Vesicorectal Fistula after Radical Prostatectomy

정 원 식

광주기독병원 비뇨기과

Introduction

- Periprostatic anatomy
 - ; dorsal vein complex (Reiner and Walsh, 1979)
 - ; neurovascular bundle (Walsh and Donker, 1982)
 - ; striated urethral sphincter (Oelrich, 1980)
- significant reduction in operative morbidity
- The anatomic, nerve-sparing **open radical prostatectomy(ORP)** maintained a central role in the management of localized prostate cancer for more than 2 decades.



Introduction

- Less invasive approach to radical prostatectomy
 - ; **Laparoscopic radical prostatectomy(LRP)**
 - ; Schuessler and colleagues, 1997
 - no clear advantages over ORP, because of excessively long operative duration (8 to 11hr)
 - ; Abbou et al, 2000
 - ; Guillonnet and Vallancien, 2000
 - new frontier for LRP
 - reproducible, teachable, standardized
- **Robot assisted radical prostatectomy(RARP)**
 - the da Vinci Surgical System
 - into the US in 2000, Korea in 2005
 - become the dominant surgical approach



Figure 10-1. Intraoperative view of the robot-assisted laparoscopic prostatectomy (A) and laparoscopic radical prostatectomy (B).



Figure 10-2. Creation of working space for robot-assisted laparoscopic prostatectomy. (A) Intraoperative view of the robot-assisted laparoscopic prostatectomy using a robot-assisted surgical system. (B) Intraoperative view of the robot-assisted laparoscopic prostatectomy using a robot-assisted surgical system. (Copyright © 2005, by McGraw-Hill, Inc.)

Complications

- **Complications related to Patient positioning**
 - lower extremity neuropathies due to steep Trendelenburg positioning, hyperextension of the hip & prolonged operation (Koc et al, 2012).
 - posterior ischemic optic neuropathy (Weber et al, 2007)
- **Vascular and Bowel Injury**
 - during placement of abdominal trocars.
 - injury along the path of the instruments.
- **Open conversion**
 - usually during a surgeon's early experience with LRP or RARP
 - rare(<2%) in the cited literature
- **Thromboembolic complications**
 - routine use of pneumatic compression devices (The 2008 AUA)
 - routine use of prophylactic anticoagulants are **not** recommended

Complications

- **Rectal Injury**
 - 0.7% to 2.4%
 - Intraoperative recognition & repair of the injury is crucial.
 - Multilayered primary closure /c or /s interposition of omentum between the rectum and anastomosis.
 - may need open conversion and intestinal diversion.
 - can result in a rectourethral/rectovesical fistula
 - Air bubble test
- **Anastomotic complications**
 - failure to achieve a watertight closure of the anastomosis
 - can result in urinary extravasation & accumulation of urine
 - may require percutaneous drainage or prolonged urethral cath.
 - bladder neck contracture (<2%, Msezane et al, 2008; Webb et al, 2009)

Complications

▪ Bleeding and Transfusion

- tamponade effect of the pneumoperitoneum in LRP & RARP.

▪ Equipment Malfunction

- prepare extra-instruments
- patients need to be counseled about unrecoverable equipment malfunction.

Rectovesical fistula

▪ Major complication of Radical prostatectomy

- Abnormal opening between the rectum and the bladder or the urethra

- Clinical sx.: Fecaluria, pneumaturia, and drainage of urine per anus

- Diagnosis: Retrograde urethrocytography, urethrocytostomy, recto- or coloscopy, enhanced computed tomography(urography)

- Urinary or fecal diversion, Intervention, conservative treatment.

- Transvesical, perineal, transrectal, transsphincteric, transanorectal approaches can be done.

Hiroshi Kitamura and Taiji Tsukamoto. Prostate cancer, 2011

Case review

History

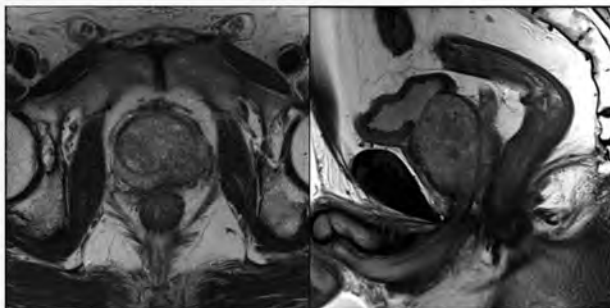
- 74/Male
- C/C: Elevated PSA
- P/H: hypertension (-), DM (-), pul Tbc (-)
appendectomy (20YA)
- P/I: health examination, incidental finding of elevated PSA level.

Examinations & Stage work-up

- U/A: WBC 0-1/HPF, RBC: 0-1/HPF
- PSA: 19.95 ng/ml
- TRUS Bx - 12 cores bx were done. 58.75 gm (34 gm)
Bx) Prostate cancer, Gleason's score 4+3=7,
Left lobe: 6/6 cores, Rt lobe: 1/6 core positive
- Pelvic MRI - r/o T3aN0M0
- WBBS - no bony metastasis

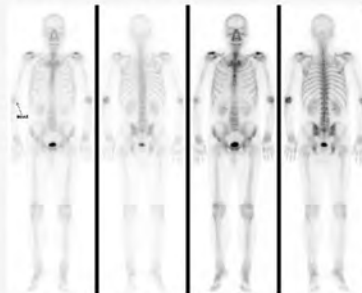
Stage work-up

Prostate MRI & WBBS



Stage work-up

Prostate MRI & WBBS



Case review

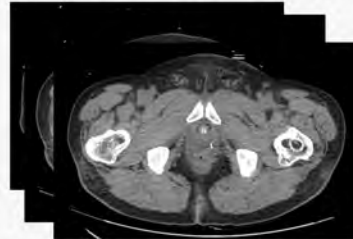
Operation day

- Laparoscopic radical prostatectomy was done.
- Op time 6hr 15min
- EBL: 150cc
- Rectal injury primary closure was done.



Case review

- POD#4
- NPO state, watery diarrhea 발생 (3/day)
- APCT) pericystic fat infiltration, small amount fluid collection in op bed



Case review

POD#5

- GE consultation) recto-sigmoidoscopy & endoscopic clipping was done.



Case review

POD#8

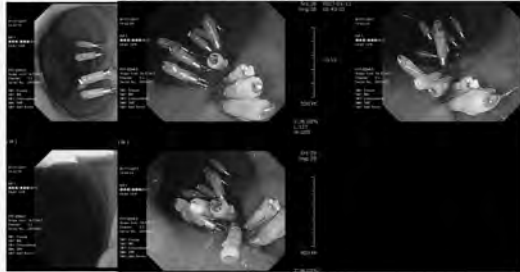
- cystography(150cc filling), no leakage.



Case review

■ POD#23

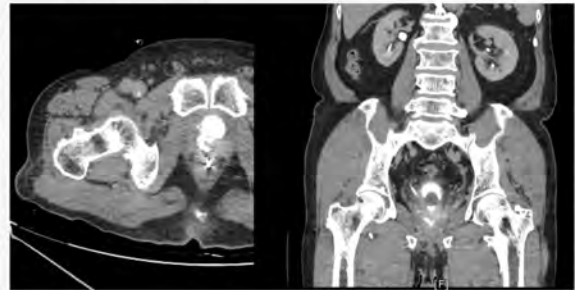
- OPD f/u 당시 urine leakage(+), admission & GE consultation
- sigmoidoscopy & reclipping was done.



Case review

■ POD#37

- APCT /c CE (urography)



Case review

■ POD#43

- urine leakage(+) for several day & KCH GS consultation
- Primary closure of rectum & Laparoscopic loop ileostomy was done.
- Op Finding) Rectum의 6시 방향에 anal verge에서 3cm 상방에 fistula에 rectal opening과 함께 urine discharge가 관찰됨. vicryl2-0를 이용하여 rectum쪽 opening을 closure 하였다.

Case review

■ POD#89

- urine leakage(+)로 ER visit, colon study was done.
- suprapubic cystostomy was done (17/03/20)



Case review

■ POD#119 (17/04/18)

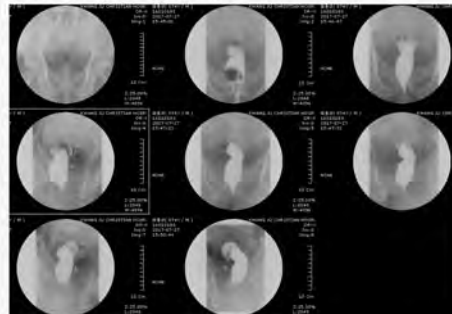
- pre-op cystography
- 전남대병원 GS 의뢰. (high fistular op)
- Dentate line 4cm prox.로 bladder neck 과 연결된 5mm sized fistular opening
- Fistular tract closure 후 mucosal flap 이용해 primary suture



Case review

■ POD#209

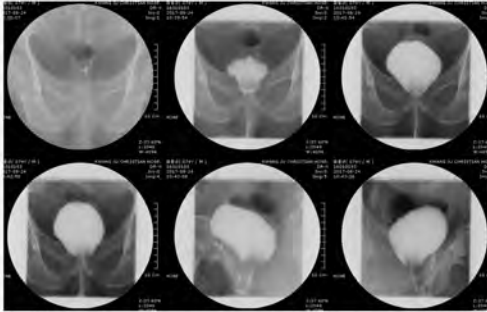
- colon study) no visible fistula



Case review

■ POD#237

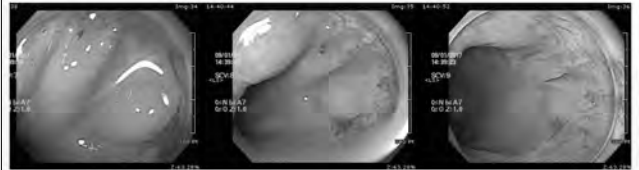
- cystography: no leakage



Case review

■ POD#245

- sigmoidoscopy
- Rectum: AV 직상방에 3mm크기의 fistula opening이 관찰되며 closure 여부는 분명하지 않음.

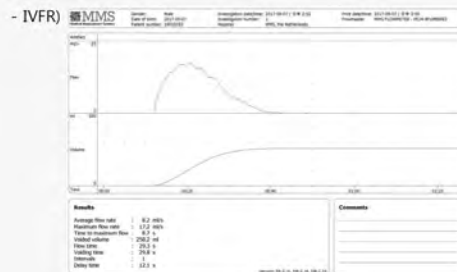


Case review

■ POD#251

- KCH GS admission. Ileostomy take down was done.

■ POD#258



Case review #2

History

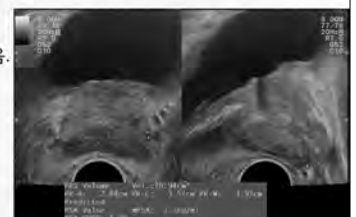
- 46/Male
- C/C: dysuria, tenesmus
- P/H: hypertension (-), DM (-), pul Tbc (-) operation(-)
장거리 운전업
- P/I: 3개월 전 발생, 지속되는 상기 증상으로 내원.

Case review #2

- U/A: WBC 0-1/HPF, RBC: 5-9/HPF
- C/S: no growth
- Lab: W.N.L.
- PSA: 17.21ng/ml, free PSA 1.63 (f/P ratio 0.09)
- A) r/o Acute prostatitis
- P) antibiotic therapy #2weeks.

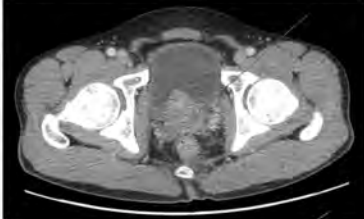
Case review #2

- U/A: WBC 0-1/HPF, RBC: 5-9/HPF
- C/S: no growth
- Lab: W.N.L.
- PSA 17.21ng/ml
- A) r/o Acute prostatitis
- P) antibiotic therapy #2weeks.
- 2주 f/u 당시 증상 개선은 없었음.
- RUA) W0-1, R10-19
- PVR) 18cc
- PSA 15.84ng/ml
- TRUS 20.94gm



Case review #2

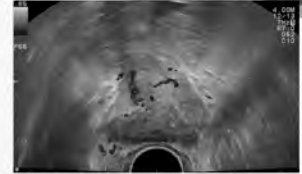
- 1개월 후 fever, voiding difficulty (RU 370cc) 증상으로 내원.
- PSA 12.28ng/ml
- APCT) prostate low density lesion, r/o prostate abscess.



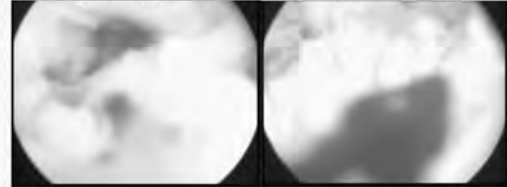
- HD#2) suprapubic cystostomy was done.

Case review #2

- HD#14 perineal discomfort 지속
- PSA 10.49ng/ml
- TRUS) no definite abscess pocket

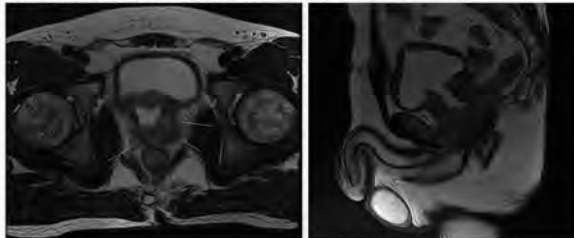


- HD#28 cystoscopy) necrotic material in prostatic urethra



Case review #2

- HD#30 TURP (for unroofing)
- Op finding) prostate Lt.lobe~apex area에 necrotic tissue cavitation
- Bx) Prostate cancer, Gleason's score 4+5=9
- Pelvic MRI) prostate capsular invasion, both side. T3aN0
- WBBS) no bony metastasis



Case review #2

- 1개월 후 Laparoscopic radical prostatectomy 시행함.
- 2point rectal injury(2cm, 0.5cm size) 발생하여 primary closure 시행함.
- POD#2 foley catheter로 fecal material drainage.

Case review #2

- POD#4 GS co-op 시행.
- Laparoscopic loop ileostomy & rectum primary closure
- bilat. Open ended ureteral cath insertion (by using rigid ureteroscopy)



Case review #2

- POD#22, urethro-cystography - no leakage
- POD#29, sigmoidoscopy



Urogenital Reconstructions for Pediatric Trauma

Sang Woon Kim

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Overview

- Renal trauma
- Ureteral trauma
- Bladder trauma
- Urethral trauma
- External genitalia trauma



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Overview

- Renal trauma
- Ureteral trauma
- Bladder trauma
- Urethral trauma
- Urethral reconstruction in children



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Case 1. M/ 11yrs

Urethral trauma

- Blunt trauma (그네 bar 가 등으로 떨어짐), pelvic bone fracture
- Bladder neck & urethral injury
- s/p suprapubic cystostomy
- s/p Anastomotic urethroplasty (6months after accident)
- Self voiding fail
- Recto-urethral fistula
- 8FR Foley catheter insertion status



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Case 1. M/ 11yrs

Urethral trauma



Rectourethral fistula



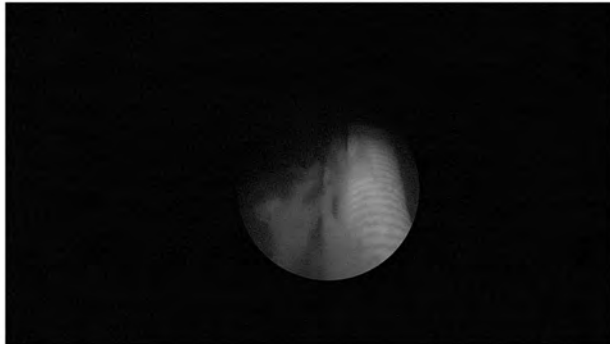
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Case 1. M/ 11yrs

Urethral trauma



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Case 1. M/ 11yrs

Urethral trauma

- Rectourethral fistula repair (perineal approach)
- **Urethroplasty**
 - Redo anastomotic urethroplasty (abdominal vs perineal)
 - Buccal mucosal graft
 - Rectal mucosa flap

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Anatomy of male urethra

Urethral trauma

Posterior urethra
Prostatic + membranous

Anterior urethra
Bulbar + penile



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Classification of urethral injury

Urethral trauma

- Anterior urethral injury
 - Mostly blunt mechanism ('straddle injuries or kick in perineum)
 - Bulbar most common site
- Posterior urethral injury
 - 72% related with pelvic fracture
 - Classified into partial vs complete rupture

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Classification of urethral injury

Urethral trauma

Table 1 - Classification of blunt anterior and posterior urethra with management according to injury grade

| Grade | Description | Appearance | Management |
|-------|--|--|--|
| I | Stretch injury | Elongation of the urethra without extravasation on urethrography | No treatment required |
| II | Contusion | Blind or the urethral prostatic, no extravasation on urethrography | Grades II and III can be managed conservatively with suprapubic cystostomy or urethral catheterization |
| III | Partial disruption | Extravasation of contrast at injury site with contrast contained in the prostatic urethra or bladder | Suprapubic cystostomy can be used for repair or primary reconstructive management in selected patients i.e. delayed repair |
| IV | Complete disruption | Extravasation of contrast at injury site without extravasation of prostatic urethra or anterior urethra or bladder | Primary repair |
| V | Complete or partial disruption of posterior urethra with associated tear of the bladder neck, ureter or vagina | Extravasation of contrast at urethral injury site; presence of blood in the vaginal cavity in women | Extravasation of contrast at bladder neck, ureter, vagina; cystostomy; i.e. must be treated with urethral repair |

EAU guidelines on urethral trauma, 2010

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Cause of urethral injury in children

Urethral trauma

- Traffic accident 53%
- Blunt trauma 20%
- Falls from height 16%
- Iatrogenic 7%
- Stab wound 2%
- Gun fire 2%



- Traffic accident
- Blunt trauma
- Falls
- Iatrogenic
- Stab wound
- Gun fire

M Uysal, 2008, ESPU

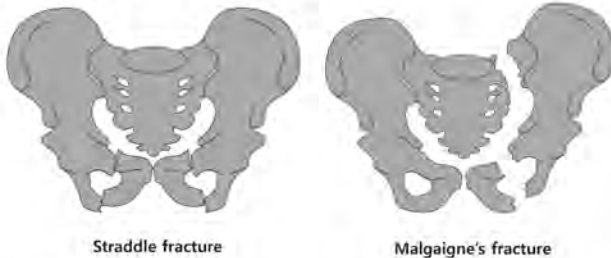
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Considerations for pediatric urethral injury

Urethral trauma

- Straddle pelvic fracture
- Malgaigne's fracture
- Sacroiliac joint fracture



Straddle fracture

Malgaigne's fracture

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Considerations for pediatric urethral injury

Urethral trauma

- Delicate tissues of an immature pelvis
- Relative intra-abdominal position of bladder
- Undeveloped prostate
- Difficulties in repair surgery
 - Restricted surgical access to reach a high lying proximal urethral
 - Long distraction defects
 - Simultaneous bladder neck and membranous urethral lesions
 - Small urethral caliber

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Considerations for pediatric urethral injury

Urethral trauma

- Diagnostic evaluation : retrograde urethrography
- Primary realignment vs delayed repair?

| Recommendations | GR |
|--|----|
| Assess the urethra by retrograde urethrogram in case of suspected urethral trauma. | A |
| Perform a rectal examination to determine the position of the prostate. | B |
| Manage bulbous urethral injuries conservatively with a transurethral catheter. | B |
| Manage posterior urethral disruption by either: | C |
| • primary reconstruction | |
| • primary drainage with a suprapubic catheter alone and delayed repair | |
| • primary re-alignment with a transurethral catheter. | |

2016, ESPU guidelines

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Considerations for pediatric urethral injury

Urethral trauma

The effectiveness of early primary realignment in children with posterior urethral injury

- 20 children with posterior urethral injuries
- 12 primary realignment vs 8 delayed repair
- 3 urethral stricture (37.5%) in delayed repair group
- Less urethral stricture was developed in primary alignment group ($p<0.05$)

E Blakan, 2005, Int J Urol

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Considerations for pediatric urethral injury

Urethral trauma

Delayed surgical repair of posttraumatic posterior urethral distraction defects in children and adolescents: Long-term results

| | SC | Primary alignment |
|-----------------------------------|--------------|-------------------|
| No pts (%) | 35 (71) | 14 (29) |
| Median age (yrs) | 9 (2.4-14.2) | 7.4 (4.1-15.7) |
| At injury (range) | 9.6 (3.5-15) | 8.1 (5.3-17.5) |
| At reconstruction (range) | 3 (2-5) | 4 (2-6) |
| Approach | | |
| Perineal (pts) | 23 | 5 |
| Combined/partial (pubectomy (pts) | 12 | 9 |
| Reconstruction (pts) | 4 | 1 |
| Incontinence (pts) | 5 | 4 |
| Erectile dysfunction (pts) | 2 | 1 |

M Pdesta, 2015, J ped urol

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Erectile dysfunction

Urethral trauma

Postpubertal Genitourinary Function Following Posterior Urethral Disruptions in Children

- 24 children with posterior urethral injuries
- Injury proximal to the prostatomembranous region demonstrated poor outcome
- Impotence 75% vs 31%
- Incontinence 25% vs 0%
- Stricture 75% vs 12%

T.B. Boone, 1992, J urol

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Failed anastomotic urethroplasty

Urethral trauma

ANASTOMOTIC URETHROPLASTY FOR FAILED PREVIOUSLY TREATED MEMBRANOUS URETHRAL RUPTURE

- 13 children who underwent previous es
- 12 primary realignment vs 8 delayed repair
- 3 urethral stricture (37.5%) in delayed repair group
- Less urethral stricture was developed in primary alignment group ($p<0.05$)

OZ Shenfeld, 2004, Urology

Case 1. M/ 11yrs

Urethral trauma

- Rectourethral fistula repair (perineal approach)
- **Urethroplasty**
- Redo anastomotic urethroplasty (Trans-pubic vs perineal)
- Buccal mucosal graft
- Rectal mucosa flap

Case 1. M/ 11yrs

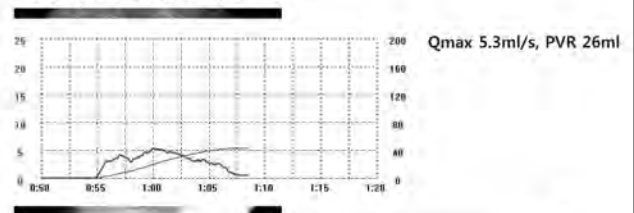
Urethral trauma



Case 1. M/ 11yrs

Urethral trauma

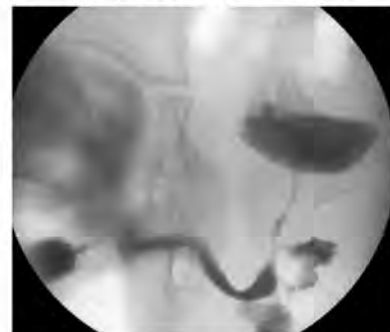
- Perineal approach
- Urethral tract dilation up to 20Fr
- 16Fr Foley catheter insertion
- POD #14 catheter removal



Case 1. M/ 11yrs

Urethral trauma

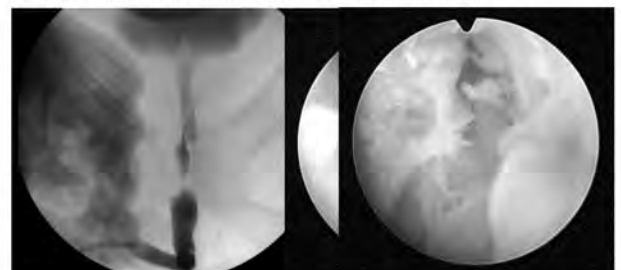
- POD #15 cystoscope & catheter insertion



Case 1. M/ 11yrs

Urethral trauma

- POD #30 catheter removal
- Urethral dilation under GEA x2 (2 weeks & 6month later)



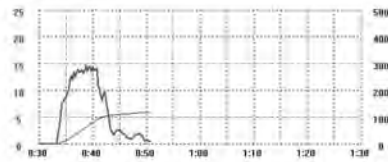
Case 1. M/ 11yrs

Urethral trauma

▪ Postoperative 1 year F/U

Voided Volume: 119.5 ml
 Max Flow Rate: 14.7 ml/seconds
 Voiding Time: 14.5 seconds
 Time To Max Flow: 5.5 seconds
 Average Flow Rate: 8.2 ml/seconds
 Flow Time: 14.3 seconds
 Delay Time: 33.3 seconds

[CubeFlow - Volume/Rate Graph]



Thank you for your attention

2018
비뇨기계기초의학연구회 - 요로생식기손상재건연구회
공동심포지엄

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| 발행일 | 2018년 2월 10일 |
| 발행처 | 비뇨기계기초의학연구회 요로생식기손상재건연구회 |
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