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- 논문의 다양한 Supplemental Materials (보조 자료)와 급격한 증가 현상
- Supplemental Materials를 적극적으로 수용하기 위하여 필요한 조치
- Publisher/Editor의 역할
- 참고문헌

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 - Online 학술지 (Electronic Journal)의 특성을 적극적으로 활용한 다양한 내용과 다양한 형식의 자료 제공, 또는 링크 제공
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 - **Supplemental Journal Article Materials**
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Korean J Urol. 2010 Sep;51(9):601-612. English.
Published online 2010 September 16. <http://dx.doi.org/10.4111/kju.2010.51.9.601>
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Development and Validation of the Korean Version of Expanded Prostate Cancer Index Composite: Questionnaire Assessing Health-Related Quality of Life after Prostate Cancer Treatment

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Abstract

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Purpose

Although the quality of life (QoL) of prostate cancer (Pca) patients is a major issue, there is no unified and useful methodology for assessing QoL. The Expanded Prostate Cancer Index Composite (EPIC) is a globally used tool to measure QoL after Pca treatment that comprises urinary, bowel, sexual, and hormonal domains. Acknowledging the need for such a tool applicable to Korean Pca patients, we translated EPIC into Korean and validated the new version.

Materials and Methods

The Korean version of EPIC was devised by translation, back-translation, and reconciliation. Subsequently, we randomly selected 153 patients with localized Pca treated with radical perineal prostatectomy (87, 43.8%), radical retropubic prostatectomy (19, 12.4%), laparoscopic radical prostatectomy (12, 7.8%), robot-assisted laparoscopic radical prostatectomy (36, 23.5%), and high-intensity focused ultrasound ablation of the prostate (19, 12.4%) and asked them to complete EPIC. Reliability was assessed by test-retest correlation and Cronbach's alpha. Validity was assessed by factor analysis, interscale correlation, and correlation with Functional Assessment of Cancer Therapy-Prostate (FACT-P).

Results

Test-retest correlation and Cronbach's alpha were high in each of the domains (0.92, 0.91, 0.76, 0.84 and 0.88, 0.84, 0.92, 0.83, p<0.0001). Interscale correlation among the domains was low (r<0.37), which indicated that EPIC is composed of proper domains. Interscale correlation between the function and bother subscales was high (0.94, 0.81, 0.84 and 0.80, p<0.0001). EPIC domains had low correlation with FACT-P, permitting complementary use.

Conclusions

The Korean version of EPIC was developed by a proper process, as evident by its high reliability and validity. Therefore, it is a reliable, comprehensive, systematic method that evaluates QoL in Korean patients after Pca treatment. Furthermore, it can be adapted as an objective methodology for research globally.

Keywords: Prostatic neoplasms, Quality of life, Reproducibility of results.

INTRODUCTION

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Development and Validation of the Korean Version of EPIC 607

Appendix

< The Expanded Prostate Cancer Index Composite >

본 설문은 진단전환 환자의 삶의 질을 측정하기 위해 만들어졌습니다. 정확한 평가를 위해서는 모든 질문에 솔직하게 답변해주시는 것이 무엇보다 중요합니다.

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다음 문항은 배뇨기능에 대한 내용입니다. 최근 4주간의 상태를 고려하여 답해 주십시오.

1. 지난 4주 동안 얼마나 자주 소변이 새어 나왔습니까?

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하루에 한 번 정도	→ 2
일주일에 한 번 이상	→ 3
일주일에 한 번 정도	→ 4
전혀, 또는 거의 없음	→ 5

3. 지난 4주 동안 소변 볼 때 얼마나 자주 통증이나 따가움을 느꼈습니까?

하루에 한 번 이상	→ 1
하루에 한 번 정도	→ 2
일주일에 한 번 이상	→ 3
일주일에 한 번 정도	→ 4
전혀, 또는 거의 없음	→ 5

4. 다음 중 지난 4주 동안 귀하의 소변 조절 상태를 가장 잘 설명하는 것은 어느 것입니까?

소변 조절이 전혀 안 된다	→ 1
자주 소변이 똑똑 떨어진다	→ 2
가끔 소변이 똑똑 떨어진다	→ 3
소변 조절을 완벽하게 한다	→ 4

Korean J Urol 2010;51:601-612



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Genomic and Epigenomic Landscapes of Adult De Novo Acute Myeloid Leukemia

The Cancer Genome Atlas Research Network
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BACKGROUND

Many mutations that contribute to the pathogenesis of acute myeloid leukemia (AML) are undefined. The relationships between patterns of mutations and epigenetic phenotypes are not yet clear.

[Full Text of Background...](#)

METHODS

We analyzed the genomes of 200 clinically annotated adult cases of de novo AML, using either whole-genome sequencing (50 cases) or whole-exome sequencing (150 cases), along with RNA and microRNA sequencing and DNA-methylation analysis.

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RESULTS

AML genomes have fewer mutations than most other adult cancers, with an average of only 13 mutations found in genes. Of these, an average of 5 are in genes that are recurrently mutated in AML. A total of 23 genes were significantly mutated, and another 237 were mutated in two or more samples. Nearly all samples had at least 1 nonsynonymous mutation in one of nine categories of genes that are almost certainly relevant for pathogenesis, including transcription-factor fusions (18% of cases), the gene encoding nucleophosmin (*NPM1*) (27%), tumor-suppressor genes (16%), DNA-methylation-related genes (44%), signaling genes (59%), chromatin-modifying genes (30%), myeloid transcription-factor genes (22%), cohesin-complex genes (13%), and spliceosome-complex genes (14%).

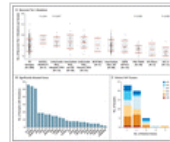
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Acute Myeloid Leukemia (AML).

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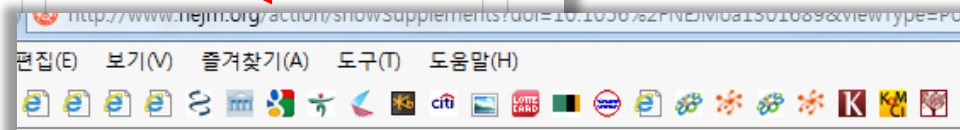


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Eric Lavigne, epidemiologist^{1,2}, Eric J Holowaty, adjunct professor of epidemiology², Paul J Villeneuve, senior research scientist², adjunct professor⁵, Dean A Fergusson, senior scientist and director², Morrison, director², Jacques Brisson, full professor¹

Author Affiliations

Correspondence to: E Lavigne, Unité de recherche en santé de l'Université de Québec (URESP), Centre de recherche du CHU de Québec, Hôpital du Saguenay, 1015, Avenue de la Médecine, Québec, QC, Canada G1S 4L8 elavigne@chq.quebec.ca

Accepted 5 April 2013

Abstract

Objectives To evaluate whether the stage distribution among women having breast cancer differs between those who have received cosmetic breast implants and those with no implants and to evaluate whether breast augmentation before the detection of breast cancer is associated with breast cancer diagnosis survival.

Design Systematic review of observational studies with two meta-analyses.

Data sources Systematic search of the literature published between 1960 and 2012 conducted in Medline, Embase, Global health, CINAHL, IPAB, and Proquest.

Study selection Eligible publications were those that included women having breast cancer and who had had augmentation mammoplasty for cosmetic purposes.

Results The overall odds ratio of the first meta-analysis based on 1.26 (95% confidence interval 0.99 to 1.60; P=0.058; I²=35.6%) of breast cancer at diagnosis comparing women with implants and women without implants who had breast cancer. The second meta-analysis based on 1.12 (95% confidence interval 0.99 to 1.26; P=0.062; I²=0%) of breast cancer at diagnosis comparing women with implants and women without implants who had breast cancer.

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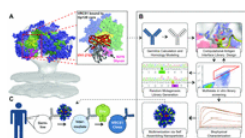
Rational HIV Immunogen Design to Target Specific Germline B Cell Receptors

Joseph Jardine^{1,2,3,4,*}, Jean-Philippe Julien^{2,3,4,*}, S
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 Meaghan Jones^{1,2,4}, Travis Nieuwsma^{2,3,4}, John Mat
 Dennis R. Burton^{1,2,3,7}, Leonidas Stamatatos^{5,8}, Da
 William R. Schief^{1,2,3,4,†}

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†Corresponding author. E-mail: schief@scripps.edu

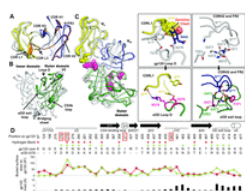
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Originally published in *Science Express* on March 28 2013
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Rational HIV Immunogen Design to Target Specific Germline B Cell Receptors

Joseph Jardine, Jean-Philippe Julien, Sergey Menis, Takayuki Ota, Oleksandr Kalyuzhnyi, Andrew McGuire, D
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Asthma-Predictive Genetic Markers in Gene Expression Profiling of Peripheral Blood Mononuclear Cells

Seung Woo Shin,¹ Tae Jeong Oh,² Se-Min Park,¹ Jong Suk Park,^{1,3} An Soo Jung,^{1,3} Sung Woo Park,^{1,3} Soe Taek Uh,⁴ Sungwan An,^{1,2} and Choon-Sik Park^{1,3,4}

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Seung Woo Shin and Tae Jeong Oh contribute equally as the first author.

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Abstract

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Purpose

We sought to identify asthma-related genes and to examine the potential of these genes to predict asthma, based on expression levels.

Methods

The subjects were 42 asthmatics and 10 normal healthy controls. PBMC RNA was subjected to microarray analysis using a 35K array; t-tests were used to identify genes that were expressed differentially between the two groups. A multiple logistic regression analysis was applied to the differentially expressed genes, and area under the curve (AUC) values from receiver operating characteristic (ROC) curves were obtained.

Results

In total, 170 genes were selected using the following criteria: P<0.001 and <2-fold change. Among these genes, 57 were up-regulated and 113 were down-regulated in asthmatics versus normal controls. A multiple logistic regression analysis was done using more stringent criteria (P<0.001 and 4.5-fold change), and eight genes were selected as candidate asthma biomarkers. Using these genes, 255 models (2⁸-1) were generated. Among them, only 85 showed P<0.05 by multiple logistic regression analysis. Based on the AUCs from ROC curves for the 85 models, we found that the best model consisted of the genes *MEPE*, *MLSTD1*, and *TRIM37*. The model showed 0.928 of the AUC with 98% sensitivity and 80% specificity.

Conclusions

MEPE, *MLSTD1*, and *TRIM37* may be useful biomarkers for asthma.

Keywords: Asthma, gene expression profiling, PBMC, ROC.

INTRODUCTION

Go to:

Asthma is a common and heterogeneous respiratory disease characterized by intermittent airway obstruction and respiratory symptoms that are related to chronic airway inflammation and remodeling.¹ Pathological features of airway remodeling include goblet cell hyperplasia, subepithelial fibrosis, collagen deposition, mucosal gland hyperplasia, smooth muscle hypertrophy, and changes in the extracellular

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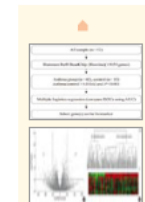
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State-of-the-Art CT Imaging Techniques for Congenital Heart Disease

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CT is increasingly being used for evaluating the cardiovascular structures and airways in the patients with congenital heart disease. Multi-slice CT has traditionally been used for the evaluation of the extracardiac vascular and airway abnormalities because of its inherent high spatial resolution and excellent air-tissue contrast. Recent developments in CT technology primarily by reducing the cardiac motion and the radiation dose usage in congenital heart disease evaluation have helped expand the indications for CT usage. Tracheobronchomalacia associated with congenital heart disease can be evaluated with cine CT. Intravenous contrast injection should be tailored to unequivocally demonstrate cardiovascular abnormalities. Knowledge of the state-of-the-art CT imaging techniques that are used for evaluating congenital heart disease is helpful not only for planning and performing CT examinations, but also for interpreting and presenting the CT image findings that consequently guide the proper medical and surgical management.

Keywords: Computed tomography (CT) techniques, Multi-slice CT, Congenital heart disease.

The recent developments in CT techniques are characterized by faster speed, longer anatomic coverage, a more flexible ECG-synchronized scan and a lower radiation dose, and these advances have noticeably increased the cardiac applications of CT. This increasing role of CT also includes the evaluation of congenital heart disease (1-3). Minimization of the radiation exposure delivered by CT is an important issue particularly for children (4,5). Various dose reduction techniques are currently available for cardiac CT as a result of the efforts to reduce the CT dose (6,7). Thus, cardiac radiologists should be familiar with the CT techniques that are associated with a cardiac protocol and dose reduction. The CT imaging techniques for congenital heart disease are not the same as those for acquired heart disease: they are different according to the imaged anatomic structures, the purposes of the study and the study population evaluated with CT (e.g. children and adults with congenital heart disease). The state-of-the-art CT imaging techniques for acquired heart disease have been extensively appraised and frequently updated, while those for congenital heart disease have not been thoroughly reviewed in the literature. In this article, I review the current CT imaging techniques for congenital heart disease. These include the CT scan techniques, the dose reduction techniques and the methods for intravenous injection of contrast agent. The

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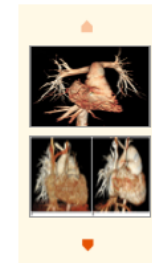
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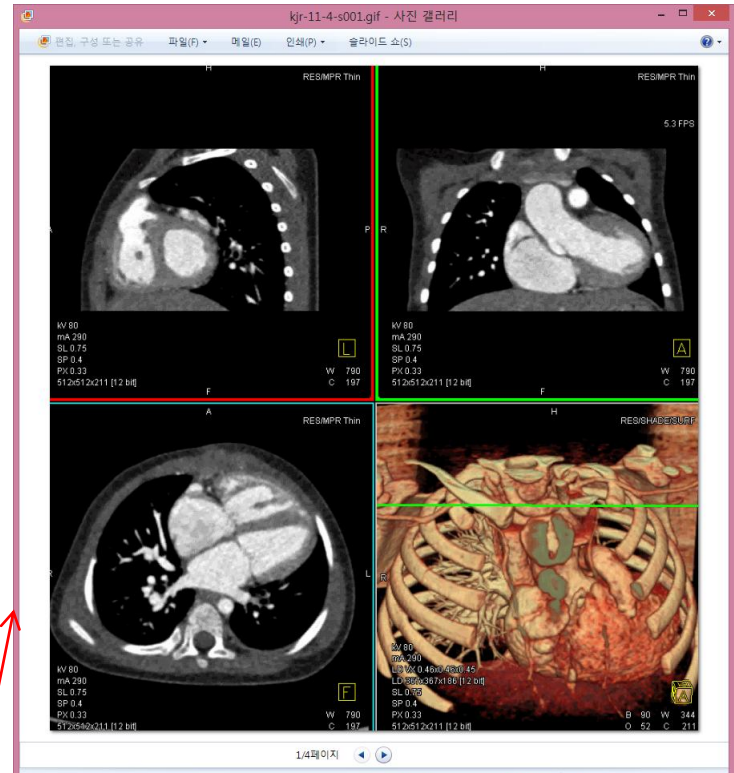
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Policization

Scott H. Kozin, MD

finger. Adrian Flatt, MD (personal communication) has been an inspiration, mentor, and abounding with sage advice. He has extended congenital indications for policization to include a thumb smaller than a small finger and I concur! Reconstruction of a small hypoplastic thumb even with a stable CMC joint will pale in comparison to policization of a "normal" index finger. This decision requires a "heart to heart" conversation with the parents. The parents make the ultimate decision but the established surgeon has substantial influence. I spend substantial time explaining that "function trumps form" and that thumb ablation and index policization will result in enhanced function versus reconstruction of a small scrawny thumb. In addition, people are not very observant and a robust thumb with excellent function has better appearance compared to a small skinny thumb that contributes little to hand function. When in doubt, I recommend the parents discuss this decision with other parents who have made a similar difficult decision. This exchange is facilitated via a list of willing parents and support groups. Of course, cultural influences are important factors to be considered during this decision making process. Parents and society may ultimately negate the concept of thumb ablation and index finger policization. The parents are welcome to keep the "thumb", however, I avoid surgery to reconstruct a type IIB hypoplastic thumb as the results of index finger policization are far superior.⁴)

BRAIN PLASTICITY

Cortical plasticity and motor relearning play a pivotal in functional following policization. There is a large region of the sensorimotor cortex (SMC) homunculus dedicated to the hand. Researchers are trying to understand the changes in SMC following injury, repair, and reconstruction.⁵) Techniques include transcranial magnetic stimulation, electroencephalography, magnetoencephalography, functional magnetic resonance imaging (MRI), structural MRI, and positron emission tomography.⁵⁻⁹) Human cortical plasticity is a complex process that involves the unweaving of previously ineffective connections and sprouting of intact afferents from nearby cortical and/or subcortical territories.

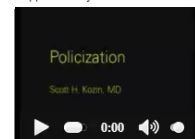
Giroux et al.¹⁰) have demonstrated that after hand transplantation, the original SMC map for hand activation is restored. The transplantation reverses the SMC loss following the initial hand amputation. Similarly, successful toe transfer produces temporal activation within the SMC cortex consistent with cortical plasticity.¹¹) Functional MRI has demonstrated that a patient learning to use their toe transfer lead to an expansion in their motor cortical representation. Practice magnifies the changes within the SMC cortex. As the new motor skill is mastered, there is a subsequent decrease in the amount of cortical representation.^{5,11}) Functional MRI studies have provided evidence that that motor reorganization continues to evolve over time and may be modified by training and experience for a protracted time.¹²) These findings suggest that prolonged therapy and training may be necessary to maximize cortical reorganization and functional outcome.

The effects of policization have yet to be studied with reference to cortical plasticity. The locale and quantity of homunculus thumb representation before and after policization is an intriguing question. Without a doubt, functional changes occur in the SMC cortex as the

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Clin Orthop Surg. 2012 Mar;4(1):19-35. English.
Published online 2012 February 20. <http://dx.doi.org/10.4055/cios.2012.4.1.18>
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Policization: The Concept, Technical Details, and Outcome

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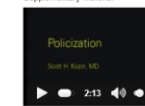
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Science 4 October 2013:
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DOI: 10.1126/science.342.6154.60

NEWS

Who's Afraid of Peer Review?

John Bohannon

A spoof paper concocted by *Science* reveals little or no scrutiny at many open-access journals.

On 4 July, good news arrived in the inbox of Ocorrafoo Cobange, a

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the journal by the end of the year. "I'm really sorry for this," he says. Orhan says that for the past 2 years, he had left the journal's operation entirely to staff led by Ahmed. (Ahmed confirms this.) "I should've been more careful," Orhan says.

Acceptance was the norm, not the exception. The paper was accepted by journals hosted by industry titans Sage and Elsevier. The paper was accepted by journals published by prestigious academic institutions such as Kobe University in Japan. It was accepted by scholarly society journals. It was even accepted by journals for which the paper's topic was utterly inappropriate, such as the *Journal of Experimental & Clinical Assisted Reproduction*.

The rejections tell a story of their own. Some open-access journals that have been criticized for poor quality control provided the most rigorous peer review of all. For example, the flagship journal of the Public Library of Science, *PLOS ONE*, was the only journal that called attention to the paper's potential ethical problems, such as its lack of documentation about the treatment of animals used to generate cells for the experiment. The journal meticulously checked with the fictional authors that this and other prerequisites of a proper scientific study were met before sending it out for review. *PLOS ONE* rejected the paper 2 weeks later on the basis of its scientific quality



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Tangled web. The location of a journal's publisher, editor, and bank account are often continents apart. Explore an interactive version of this map at <http://scim.ag/OA-Sting>.

CREDIT: DAVID QUINN AND DANIEL WIESMANN

Interactive map <http://scim.ag/OA-Sting>



John Bohannon. Who's Afraid of Peer Review? (Science, Oct. 4, 2013)
<http://www.sciencemag.org/content/342/6154/60.full>

Rejection Letter of YMJ's Editor-in-Chief to a fake manuscript submitted by Science

From: "Yonsei Medical Journal"
Date: Monday, 20 May 2013 19:52:00 Eastern Daylight Time
To: "Sharboo Highlee"
Cc:
Subject: Yonsei Medical Journal



Manuscript ID : YMJ13199

Dear Dr. Sharboo Highlee :

I am sorry to inform you that your manuscript "Di-betaeactic acid inhibits the growth of murine polyploid colorectal blastoma cells in vitro" has not been accepted for publication in the Yonsei Medical Journal.

Your manuscript was evaluated by members of our editorial staff, and we think it is more suitable for a specialty journal and therefore it is our editorial decision not to consider your paper further.

We are informing you of this promptly so that you can submit it elsewhere.

Thank you to us for consideration.

Sincerely yours,

In-Hong Choi, M.D., Ph.D.
Editor-in-Chief
Yonsei Medical Journal

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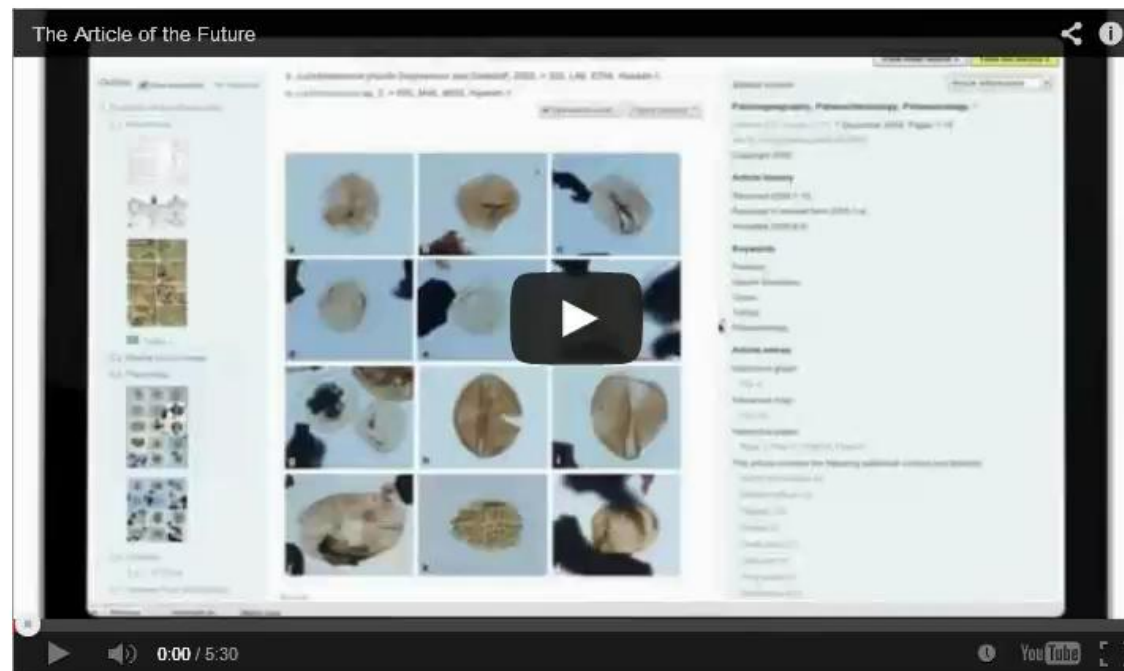
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Learn what we are doing and why by viewing the video below.



Last year, we introduced you to the Article of the Future project along with prototypes in 7 scientific areas. To achieve this evolution of the traditional research article, a three-pane article view has been proposed, which separates navigation (left pane) and value-added enhancements (right pane) from the core article (middle pane). Find out more in our [About section](#).

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Introduction
Results

Three Assays to Track Kinetochore Attachment and Organization



Kinetochore Distribution Is Bilobed and Symmetric for Spindles Longer Than One Micrometer

The Bilobed Distribution of Kinetochores Results from a Tight Regulation of SPB-CEN Distance, Regardless of the Type of Attachment



Biorientation Is Established Gradually up to Anaphase Onset



Synthetic Attachments in *ipf1-321* Mutant

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CEN Distances



stu2-277 Mutant Cells Fail to Establish Bipolar Attachments yet Exhibit a Bilobed Kinetochore Distribution



cin8Δ Mutant Cells Exhibit a Weaker Bilobed Distribution of Kinetochores due to Less-Regulated SPB-CEN Distance

Cell

Cell

Volume 154, Issue 5, 29 August 2013, Pages 1127–1139

Article

S. cerevisiae Chromosomes Biorient via Gradual Resolution of Syntelic between S Phase and Anaphase

Eugenio Marco^{1,2,4,6}, Jonas F. Dorn^{3,4}, Pei-hsin Hsu¹, Khuloud Jaqaman^{2,6}, Peter K. Sorger², Gaudenz

Danuser¹

¹Department of Cell Biology, Harvard Medical School, Boston, MA 02115, USA

²Department of Systems Biology, Harvard Medical School, Boston, MA 02115, USA

³Institute for Research in Immunology and Cancer, University of Montreal, Montreal QC H3C 3J7, Canada

Research Highlights

Really Are Like People

August 2013, Pages 959-961

Highlights

- *S. cerevisiae* chromosomes biorient in a stochastic process until anaphase onset
- Microtubule length control discriminates bioriented from syntelic attachments
- Bilobed kinetochore distribution is not synonymous with biorientation

Summary

Following DNA replication, eukaryotic cells must biorient all sister chromatids prior to cohesion cleavage at anaphase. In animal cells, sister chromatids gradually biorient during prometaphase, but current models of mitosis in *S. cerevisiae* assume that biorientation is established shortly after S phase. This assumption is based on the observation of a bilobed distribution of yeast kinetochores early in mitosis and suggests fundamental differences between yeast mitosis and mitosis in animal cells. By applying super-resolution imaging methods, we show that yeast and animal cells share the key property of gradual and stochastic chromosome biorientation. The characteristic bilobed distribution of yeast kinetochores, hitherto considered synonymous for biorientation, arises from kinetochores in mixed attachment states to microtubules. In animal cells, kinetochores biorient by resolution of syntelic attachments. Our results offer a mechanistic model for chromosome biorientation in *S. cerevisiae* that augments the relevance of mechanistic information in animal mitosis.

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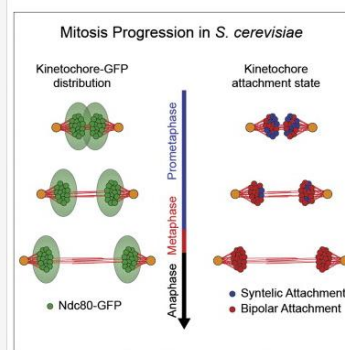


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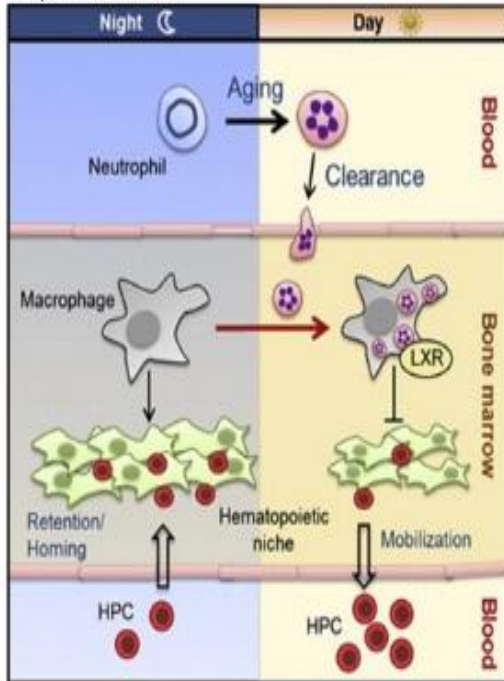
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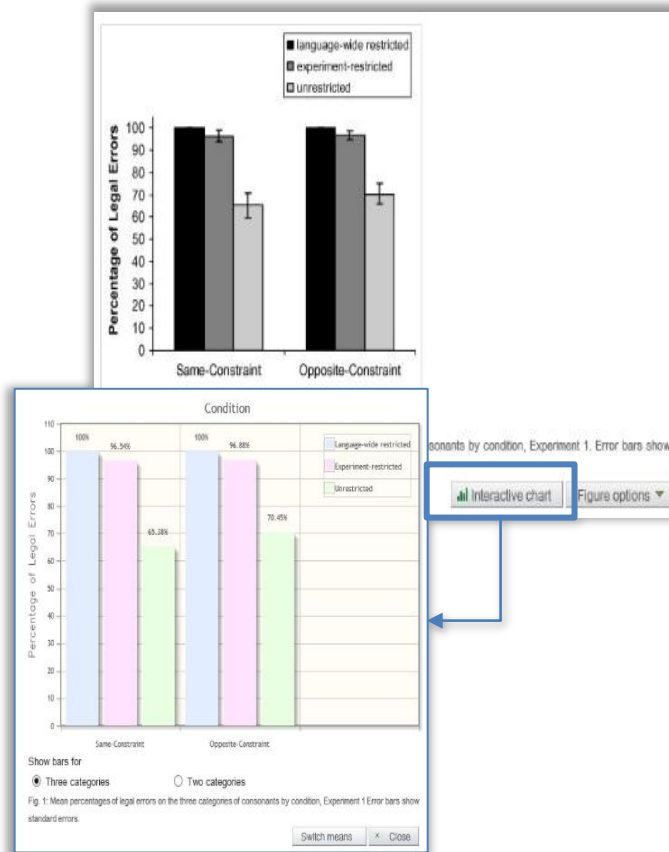
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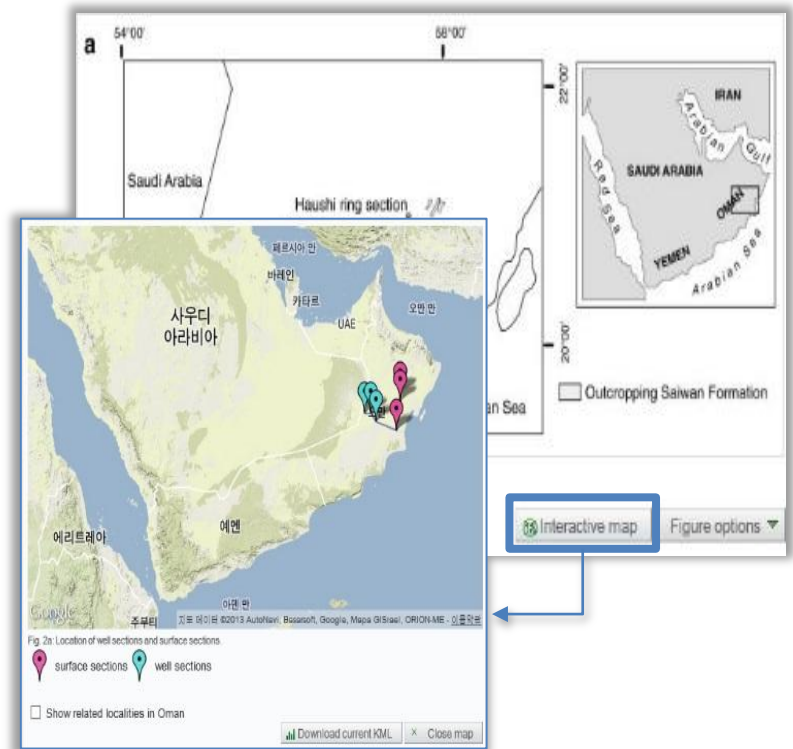
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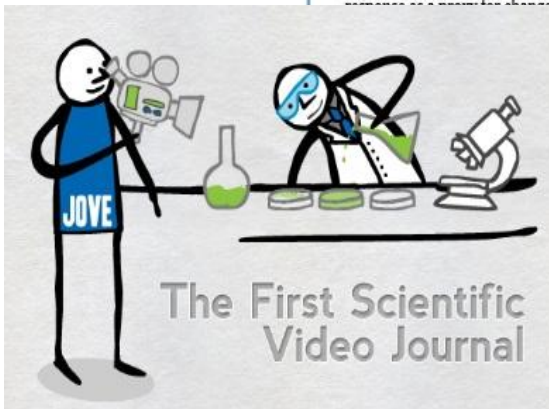
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Series GSE45694

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CAS Registry Number

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Chemical Name

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Cephalosporins, such as ceftazidime, disrupt the synthesis of the peptidoglycan layer of bacterial cell walls.

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3.2. Proteomic characterisation of proteins biotinylated with thiol cleavable sulfo-NHS-SS-biotin

Table 1





Table 2

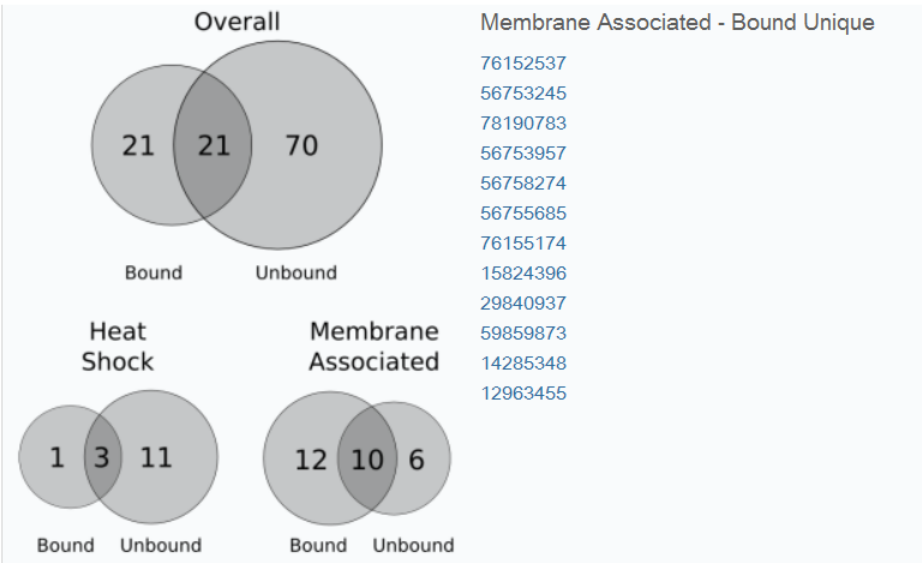
3.3. Proteomic characterisation of tegument proteins that did not incorporate biotin

3.4. Contamination and decoy database searching

4. Discussion




Acknowledgments



- Membrane Associated - Bound Unique
- 76152537
 - 56753245
 - 78190783
 - 56753957
 - 56758274
 - 56755685
 - 76155174
 - 15824396
 - 29840937
 - 59859873
 - 14285348
 - 12963455

Fig. 4: Overview of protein identifications from NCBI nr Mascot database searches. (A) The proportion of total protein identifications belonging to the assigned subcellular locations for biotinylated (bound) and non-biotinylated (unbound) fractions. (B) Venn diagrams showing protein identifications for the biotinylated (bound) and non-biotinylated (unbound) fractions. Overall 23 protein identifications were made in both the bound and unbound fractions. Heat shock proteins were particularly abundant in the unbound fraction, however only four were identified in the bound fraction, one of which was


Sidebar content: Proteins (54)



elongation factor 1-a [Schistosoma japonicum]

348 aa protein

Complete database entry (NCBI)



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Subcellular Location

Cytosol/Nuclear

TABLE 4. File types commonly observed among the 100 SDRs sampled, particularly for export purposes.

File type category	File type/extension
Archives	.zip, .tar, .tar.gz, stuffit (binhex)
Statistical analysis	R, SPSS, SAS, STATA
GIS	many SDRs indicated using GIS related files including raster formats like .bil, ESRI map file formats like .e00, and vector formats like .shp
Extensible markup	.xml, .sgl, .eml (ecological metadata language), VOTable (Virtual Observatory Table)
Flat file	.txt, .ascii, .csv
Image	.tiff, .jpg, .gif, .pic, .fits and .png
Movie/multimedia	.wav, .swf, .mpg, .mov, .mp3, .mp4, .avi, quicktime and anis (Flash animations applet)
Word processor	.pdf, .ps, .doc
Spreadsheet	.xls
Presentation	.ppt
Proprietary or specific tools: Geosciences	Open Geospatial Consortium's Web Map Service (WMS) map and legend images, Web Feature Service (WFS) vector source data in GML format, Web Coverage Service (WCS) raster source data in GeoTIFF format NetCDF (common data format, http://www.unidata.ucar.edu/software/netcdf/docs/faq.html) and .grib (gridded binary)
(Medicine) bioinformatics	GO, FASTA, Contig
Web page	.html

다양한 Supplemental materials 파일 형식

Marcial LH and Hemminger BM. Scientific data repositories on the Web: An initial survey. *JASIST*, 61(2010): 2029–2048.

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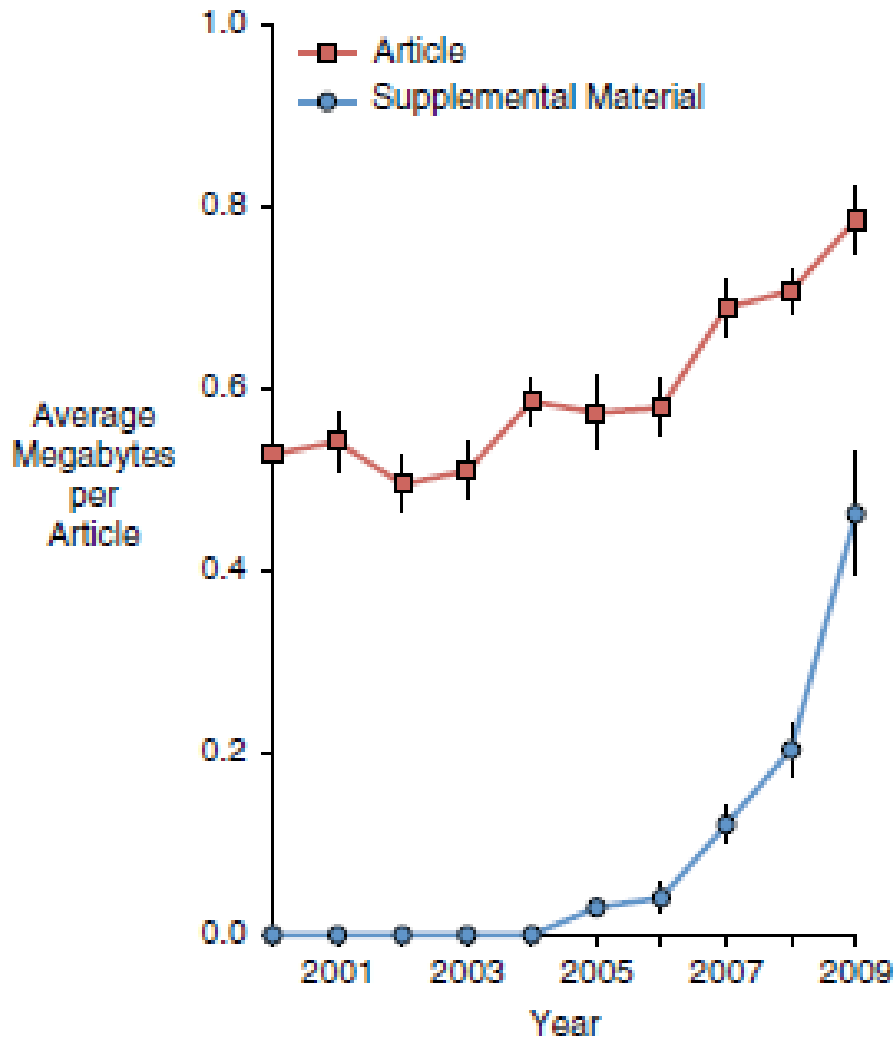


Figure 1. Average size of a *Journal of Neuroscience* article and supplemental material in megabytes. Values are trimmed means (5th–95th percentile) to exclude a handful of unaccountably large articles and supplemental files. Supplemental movies are excluded to facilitate comparisons because a megabyte of a movie is arguably easier to evaluate than a megabyte of text, figures, or tables. Data include only articles published in January of each year. Error bars are standard errors of the trimmed means.

Journal of Neuroscience Announcement
Regarding Supplemental Material. *J*
Neurosci 30(32):10599–10600. August 11,
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Journal List > Korean J Urol > v.54(5); May 2013
Original Article
Korean J Urol 2013 May;54(5):327-332. English.
Published online 2013 May 14.
Laparoscopic Single-Site Surgery With the Second-Generation Single Port Instrument Delivery Extended Reach Surgical System in a Porcine Model
Soo Dong Kim, Jaime Landman, and Gwang Taek Sung
Department of Urology, Dong-A Medical Center, Busan, Korea.
*Department of Urology, University of California Irvine Medical Center, Irvine, CA, USA.
Corresponding Author: Gwang Taek Sung, Department of Urology, Dong-A Medical Center, 26 Daesangongwon-ro, Seo-gu, Busan 602-715, Korea.
Received February 25, 2013; Accepted April 18, 2013.
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Materials and Methods
Results
Conclusions
Keywords: Laparoscopy, Robotics, Urologic surgical procedures.

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FIG. 2 Basic operative setup of the Single Port Instrument Delivery Extended Reach (SPIDER) surgical system. The surgical system is inserted through the right lower quadrant of the swine and faces the target area. The SPIDER platform is locked in position by using the docking ball. The swine is in the left lateral position.

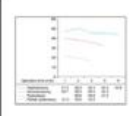


FIG. 3 Operative time depending on the surgery. 1,3,5: right side; 2,4: left side.

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1. Gettman MT, Lotan Y, Napper CA, Cadeddu JA. Transvaginal laparoscopic nephrectomy: development and feasibility in the porcine model. Urology 2002;59:446-450.

SPIDER system. In these authors showed, true triangulation and simple retraction are achieved without added operative time or the need to tolerate uncomfortable techniques that may lead to frustration of the surgeons. In addition, low morbidity, faster recovery, and improved cosmesis are other appealing advantages of the SPIDER system. We have also demonstrated in this study that various urological procedures can be performed effectively in a reasonable operative time with minimal complications by use of the SPIDER surgical system.

In terms of technical aspects, many of the mechanical advantages of the surgical system were apparent: triangulation to obtain a critical operative view, ergonomic handling of the instrument tips, and operation through a true single port. The reduced length of the articulating IDTs and the vertebral design provide the width of two flexible instrument tips in an optimal position with increased forces at the distal instrument tips, thereby facilitating an optimal working environment. Prior laparoscopic experience of the surgeon represented an important variable in the operative procedures. The operating surgeon had only 20 to 30 minutes of device introduction and manipulation and proceeded to perform the surgical procedures on the basis of the protocol. Surgeons with advanced laparoscopic skills

and critical work. The drawbacks of a second-generation SPIDER surgical system require further improvement in design and modification to optimize its clinical application in urology.

CONCLUSIONS

In this initial pilot evaluation, we have demonstrated that the second-generation SPIDER surgical system offered intuitive instrument maneuverability, restored triangulation without external instrument clashing, and provided critical intraoperative views. However, retraction was challenging because of the lack of strength and lack of precise manipulation of the tip when the instruments were fully deployed. Future refinements of the technology and prospective studies are needed to further optimize the application of this surgical system in urology.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

SUPPLEMENTARY MATERIALS

An accompanying video can be found in the 'Urology in Motion' section of the journal homepage (www.kjurology.org).

Korean J Urol 2013;54:327-332

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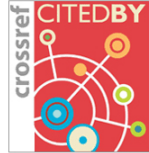
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Laparoendoscopic Single-Site Surgery Using the Second-Generation SPIDER Surgical System in Porcine Model
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Screening of Dihydropyrimidine Dehydrogenase Genetic Variants by Direct Sequencing in Different Ethnic Groups

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Abstract

Dihydropyrimidine dehydrogenase (DPYD) is an enzyme that regulates the rate-limiting step in pyrimidine metabolism, especially catabolism of fluorouracil, a chemotherapeutic agent for cancer. In order to determine the genetic distribution of DPYD, we directly sequenced 288 subjects from five ethnic groups (96 Koreans, 48 Japanese, 48 Han Chinese, 48 African Americans, and 48 European Americans). As a result, 56 polymorphisms were observed, including 9 core polymorphisms and 18 novel polymorphisms. Allele frequencies were exactly the same across the Asian populations, Korean, Han Chinese and Japanese, whereas several SNPs showed different genetic distributions between Asians and other ethnic populations (African American and European American). Additional in silico analysis was performed to predict the function of novel SNPs. One nonsynonymous SNP (+19323A>G, Asn151Asp) was predicted to change its polarity of amino acid (Asn, neutral to Asp, negative). These findings would be valuable for further research, including pharmacogenetic and drug responses studies.

Keywords: Ethnic Group, Pharmacogenetics, Dihydropyrimidine Dehydrogenase, Fluorouracil

INTRODUCTION

Pharmacogenetics focuses on identifying the role of a gene of interest that mediates drug-dependent mechanisms or triggers adverse effects. Therefore, dealing with the gene of interest is important to predict individual drug responses and toxicities. Genetic variations in genes of

Supplementary Materials:

- Supplementary Fig 1 (292K, pdf)
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Table 1
Allele frequency of DPYD in study (n=288)

*Alleles of core markers were verified from previous studies. (14,19).
monomorphic, † core SNP, ‡ major and minor alleles determined by frequency of all subjects, KR, Korean; HC, Han Chinese; JP, Japanese; AA, African American; EA, European American.

Notes

This research was supported by a grant (111K2M2P0616) from Ministry of Food and Drug Safety. The authors have no conflicts of interest to disclose.

Supplementary Material

Supplementary Fig. 1
Minor allele frequency of DPYD among Korean, Han Chinese, Japanese, African American and European American samples (upper panel). Fisher's exact test of allele distribution between Korean and other ethnic groups (lower panel). Relative physical coordinates of SNPs are shown at top of the figure. Bolded SNPs indicate pharmacogenetic core SNPs. Novel SNPs are labeled with their location and allele change. KR, Korean; HC, Han Chinese; JP, Japanese; AA, African American; EA, European American.

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Supplementary Table 1
Comparison of minor allele frequency of *9A (rs1801265) and *2A (rs3918290) between present study and previous studies

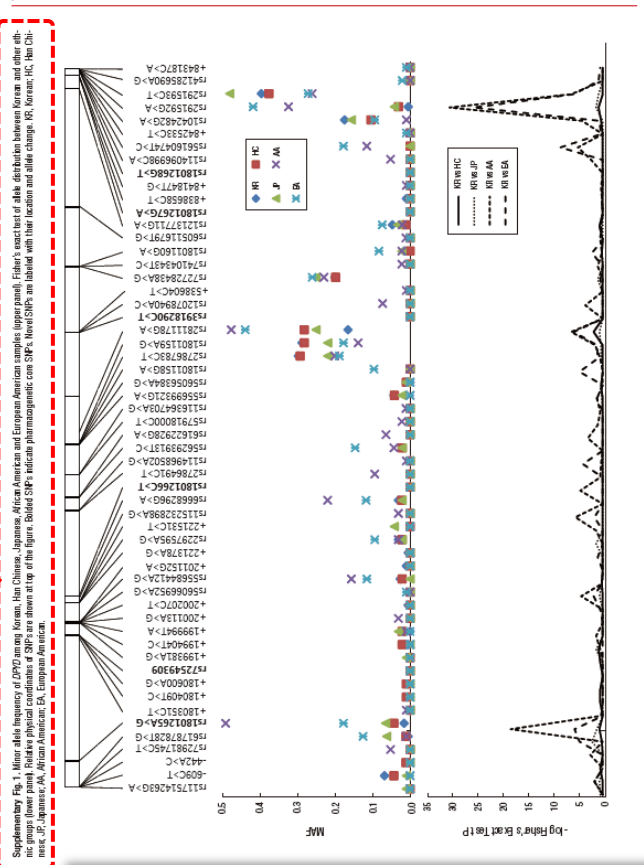
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Supplementary Table 2
Primer information of DPYD

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Supplementary Fig. 1. Minor allele frequency of DPYD among Korean, Han Chinese, Japanese, African American and European American samples (upper panel). Fisher's exact test of allele distribution between Korean and other ethnic groups (lower panel). Relative physical coordinates of SNPs are shown at top of the figure. Bolded SNPs indicate pharmacogenetic core SNPs. Novel SNPs are labeled with their location and allele change. KR, Korean; HC, Han Chinese; JP, Japanese; AA, African American; EA, European American.

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Supplementary Table 1. Comparison of minor allele frequency of *9A (rs1801265) and *2A (rs3918290) between present study and previous studies

		MAF	
		*9A (rs1801265)	*2A (rs3918290)
Present study	KR	0.016	-
	HC	0.043	-
	JP	0.065	-
	AA	0.49	-
	EA	0.177	-
Previous studies	KR	0.025 (24)	0 (24)
	HC	0.05 (25)	NR
	JP	0.037 (26)	0 (23)
	CA	0.16 (19), 0.21 (21), 0.34 (23)	0.013, 0.007 (23)

MAF, minor allele frequency; -, monomorphic; NR, not reported; KR, Korean; HC, Han Chinese; JP, Japanese; AA, African American; EA, European American; CA, Caucasian.

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DRhoGEF2 Regulates Cellular Tension and Cell Pulsations in the Amnioserosa during *Drosophila* Dorsal Closure

Dulce Azevedo,¹ Marco Antunes,¹ Soren Prag,¹ Xiaoyan Ma,² Udo Hacker,³ G. Wayne Brodland,⁴ M. Shane Hutson,² Jerome Solon,⁵ and Antonio Jacinto^{1,6*}

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Abstract

Coordination of apical constriction in epithelial sheets is a fundamental process during embryogenesis. Here, we show that DRhoGEF2 is a key regulator of apical pulsation and constriction of amnioserosal cells during *Drosophila* dorsal closure. Amnioserosal cells mutant for DRhoGEF2 exhibit a consistent decrease in amnioserosal pulsations whereas overexpression

...nce was estimated as the average density of sqm-metry in the selected area.

Supporting Information Go to >

Movie S1

AS cell pulsations in the WT. A short movie of an *UbiCadh-GFP;c381Gal4* embryo imaged using time-lapse confocal microscopy showing an early stage of dorsal closure. Note how AS cells pulsate. The total elapsed time is 37 min and the frame rate is 30 s/frame.

(MOV)

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Movie S2

AS cell pulsations in DRhoGEF2 maternal mutants. A short movie of an *UbiCadh-GFP/DRhoGEF2^(c104291)* embryo imaged using time-lapse confocal microscopy showing an early stage of dorsal closure. Note how AS cells pulsation is diminished compared to the WT. The total elapsed time is 37 min and the frame rate is 30 s/frame.

(MOV)

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Movie S3

AS cell pulsations upon DRhoGEF2 overexpression. A short movie of an *UbiCadh-GFP;c381Gal4/UAS-DRhoGEF2* embryo imaged using time-lapse confocal microscopy showing an early stage of dorsal closure. Note how AS cells pulsate with a different behavior compared to the WT. The total elapsed time is 37 min and the frame rate is 30 s/frame.

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Movie S4

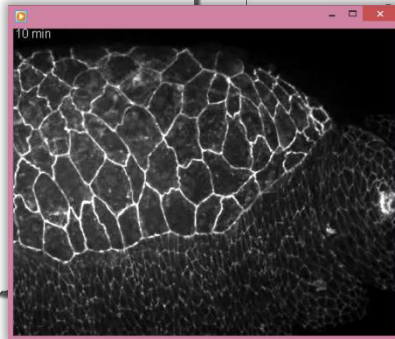
Germ-band retraction in WT. Movie of an *UbiCadh-GFP;c381Gal4* embryo imaged using time-lapse confocal microscopy showing germ-band retraction and beginning of DC. The total elapsed time is 300 min and the frame rate is 10 min/frame.

(MOV)

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Movie S5

Germ-band retraction in DRhoGEF2 maternal mutants. Movie of an *UbiCadh-GFP/DRhoGEF2^(c104291)* embryo imaged using time-lapse confocal microscopy showing



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DRhoGEF2 Regulates Cellular Tension and Cell Pulsations in the Amnioserosa during *Drosophila* Dorsal Closure

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Abstract

Coordination of apical constriction in epithelial sheets is a fundamental process during embryogenesis. Here, we show that DRhoGEF2 is a key regulator of apical pulsation and constriction of amnioserosal cells during *Drosophila* dorsal closure. Amnioserosal cells mutant

Abstract Introduction Results Discussion Methods Supporting Information Acknowledgments Author Contributions References

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AS cell pulsations in the WT. A short movie of an *UbiCadh-GFP;c381Gal4* embryo imaged using time-lapse confocal microscopy showing an early stage of dorsal closure. Note how AS cells pulsate. The total elapsed time is 37 min and the frame rate is 30 s/frame. doi:10.1371/journal.pone.0023964.s001 (MOV)

Movie S2

AS cell pulsations in DRhoGEF2 maternal mutants. A short movie of an *UbiCadh-GFP/DRhoGEF2^(c104291)* embryo imaged using time-lapse confocal microscopy showing an early stage of dorsal closure. Note how AS cells pulsation is diminished compared to the WT. The total elapsed time is 37 min and the frame rate is 30 s/frame.

II activity, or expression of a constitutively active form of the formin Diaphanous (Di^{CA}) that stimulates actin polymerization, exhibited precocious cell contraction through changes in the subcellular localization of myosin II, demonstrating the role of these Rho1 effectors in the regulation of AS cell pulsations [16].

The upstream regulator of the Rho signalling pathway, RhoGEF2, was initially characterised as a regulator of apical constriction during formation of the ventral furrow [17,18,19] and has subsequently been shown to coordinate contractile forces throughout morphogenesis in *Drosophila* by regulating the association of myosin II with actin to form contractile cables [20]. Here, we show for the first time that DRhoGEF2 plays a crucial role in AS apical constriction through the regulation of myosin II subcellular localization and control of the AS cells pulsating behaviour upstream of Rho signalling.

Results

1. DRhoGEF2 plays a role in Dorsal Closure

DRhoGEF2 has been shown to be expressed in AS cells [20] but the analysis of the function of DRhoGEF2 during dorsal closure has been precluded by its earlier role during gastrulation. We started by confirming that DRhoGEF2 is indeed localized at the right place and time to play a role in dorsal closure. In wild-type (WT) embryos, DRhoGEF2 protein accumulates along the leading edge of the dorsal-most epidermal cells and apically in AS cells (Fig. 1A). DRhoGEF2 localization in AS cells is increased cortically (Fig. 1A C), the outlines of the cells are marked by Armadillo).

To investigate whether DRhoGEF2 regulates apical constriction of AS cells during dorsal closure we took loss and gain of function approaches. *DRhoGEF2* maternal zygotic mutants showed significant changes of key components of the contractile machinery; myosin II was clearly reduced (Fig. 1G) and F-actin was more disorganized (Fig. 1H) in the AS cells when compared to WT (Fig. 1 D E). However, as DRhoGEF2 plays an important role during gastrulation [17,18], it was difficult to find embryos reaching dorsal closure stages, and the few that did were too abnormal for a more detailed analysis. To get around this limitation we used maternal mutants in which there is a paternal rescue allowing us to obtain embryos with reduced DRhoGEF2 function for analysing cell shape and dynamics. When stained for Arm to mark cell outlines (Fig. 1I), these *DRhoGEF2* maternal mutant embryos showed several tissue organization defects in the epithelial cells and in the AS. The leading edge of the dorsal-most epithelial mutant cells was irregular, in contrast to the WT (compare Fig. 1I with 1B). In the WT, all central AS cells showed similar exposed apical surface areas (Fig. 1B), whereas in the mutant, neighbouring AS cells presented very different apical areas (see arrows in Fig. 1I). In contrast to the mutant, overexpression of DRhoGEF2 in AS cells resulted in increased levels of myosin II and F-actin (compare Fig. 1J with 1D and Fig. 1K with 1E).

2. Cellular tension is affected in DRhoGEF2 mutants

In order to test whether DRhoGEF2 activity has a direct impact on tissue mechanics we assessed the cellular tension of the AS by performing a series of hole drilling experiments in embryos with reduced or increased DRhoGEF2 activity. We laser ablated a subcellular cylindrical hole through WT AS cells and we tracked the subsequent recoil of adjacent cells in order to calculate recoil parameters that allow us to evaluate cellular tension (see Fig. 2 (A I) and Materials and Methods, [11]). The mean initial recoil velocity (v_0), determined via a linear fit to the

first 100 ms of recoil, in the WT is $13.4 \pm 1.5 \mu\text{m/s}$ (Fig. 2M) whereas in the *DRhoGEF2* mutant it is $1.8 \pm 0.7 \mu\text{m/s}$, which represents a decrease in the mutant of almost one order of magnitude, indicating that the mutant is under less tension and/or is more viscous. This result is in line with the value obtained for the coefficient D , calculated using a power-law fit to the first 5 s of recoil (Fig. 2M). The lower value obtained for the mean D in the mutant (0.23 ± 0.09) is also an indication that the tissue is under less tension than the WT (1.34 ± 0.07). The values of exponent α suggest that the mutant tissue may be more fluid than WT (0.633 ± 0.232 vs 0.396 ± 0.015).

The mean D and mean v_0 for WT and DRhoGEF2 overexpression is not significantly different (Fig. 2M, see also [11]), indicating that either the tension in DRhoGEF2 expressing cells is similar to WT or that an increase in tension is compensated by an increase in viscosity and stiffness. However, the variance of D is higher when overexpressing DRhoGEF2, consistent with a wider distribution of recoil displacements as shown in the respective graph (Fig. 2M, grey and yellow shadows). Interestingly the decrease in exponent α when DRhoGEF2 is overexpressed indicates a transition to a more solid-like tissue. Exponent α varies between 0 and 1 and lower values are characteristic of more solid materials [21]. Taken together, the results of the hole drilling experiments support the hypothesis that DRhoGEF2 regulates tissue tension in AS cells. In particular, the average tension in *DRhoGEF2* mutant cells seems to be lower than in WT, and the overexpression of *DRhoGEF2* results in a tissue that is less fluid and more solid-like.

3. DRhoGEF2 regulates AS pulsations

In order to find out whether DRhoGEF2 regulates AS pulsations, we investigated the dynamic behaviour of the AS cells in more detail by performing high speed time-lapse imaging with subcellular resolution (see Materials and Methods). The comparison of overall dorsal closure dynamics between WT and *DRhoGEF2* maternal zygotic mutants was not possible as the embryos with that genotype were extremely deformed. In *DRhoGEF2* maternal mutants, that were more amenable for time-lapse imaging, dorsal closure was slower than in WT but the phenotype was very variable (Fig. 3A B). When DRhoGEF2 was overexpressed specifically in AS cells dorsal closure also took longer to be completed but, as described above, the average apical surface of the AS cells was significantly smaller than WT and the AS seemed more densely packed (Fig. 3C). To quantify the dynamics of dorsal closure in the different genotypes, we focused on early dorsal closure stages, starting at stage 13. In the WT (Fig. 3A', **Supplementary Movie S1**), AS cells showed a cell pulsation period of 248 ± 64 s (Fig. 4B, upper graph) and an average cell area amplitude of $49 \pm 30 \mu\text{m}^2$ (Fig. 4A, upper graph), consistent with what has been previously described [8]. The analysis of *DRhoGEF2* maternal mutants revealed that the pulsation phenotype is variable, ranging from cells with almost no pulsations to cases that showed very irregular oscillations (see representative examples in Fig. 3B' and **Movie S2**). In this case it was not possible to calculate a meaningful average period or amplitude, as the majority of the cells do not exhibit a clear periodic behaviour. Therefore, we conclude that DRhoGEF2 is required for AS cell pulsations.

In *DRhoGEF2* overexpressing AS cells (Fig. 3C', **Movie S3**) the amplitude of pulsations is decreased to $26 \pm 13 \mu\text{m}^2$ compared to $49 \pm 30 \mu\text{m}^2$ in WT (Fig. 4A), and period, 387 ± 119 s, is longer when compared to 248 ± 64 s in WT (Fig. 4B). For this genotype the distribution of amplitudes is clearly skewed towards lower amplitudes, however, the distribution of the ratios amplitude/cell

Supporting Information

Movie S1 AS cell pulsations in the WT. A short movie of an *UbiCadh-GFP;381Gal4* embryo imaged using time-lapse confocal microscopy showing an early stage of dorsal closure. Note how AS cells pulsate. The total elapsed time is 37 min and the frame rate is 30 s/frame. (MOV)

Movie S2 AS cell pulsations in DRhoGEF2 maternal mutants. A short movie of an *UbiCadh-GFP;DRhoGEF2^{20942W}* embryo imaged using time-lapse confocal microscopy showing an early stage of dorsal closure. Note how AS cells pulsation is diminished compared to the WT. The total elapsed time is 37 min and the frame rate is 30 s/frame. (MOV)

Movie S3 AS cell pulsations upon DRhoGEF2 overexpression. A short movie of an *UbiCadh-GFP;381Gal4/UAS-DRhoGEF2* embryo imaged using time-lapse confocal microscopy showing an early stage of dorsal closure. Note how AS cells pulsate with a different behavior compared to the WT. The total elapsed time is 37 min and the frame rate is 30 s/frame. (MOV)

Movie S4 Germ-band retraction in WT. Movie of an *UbiCadh-GFP;381Gal4* embryo imaged using time-lapse confocal microscopy showing germ-band retraction and beginning of DC. The total elapsed time is 300 min and the frame rate is 10 min/frame. (MOV)

Movie S5 Germ-band retraction in DRhoGEF2 maternal mutants. Movie of an *UbiCadh-GFP;DRhoGEF2^{20942W}* embryo imaged using time-lapse confocal microscopy showing germ-band retraction. Note that some AS cells are bigger than WT. The total elapsed time is 500 min and the frame rate is 10 min/frame. (MOV)

Movie S6 Germ-band retraction in upon DRhoGEF2 overexpression. Movie of an *UbiCadh-GFP;381Gal4/UAS-DRhoGEF2* embryo imaged using time-lapse confocal microscopy showing germ-band retraction. Note that AS cells acquire a rounder shape from the beginning of germ-band retraction. The total elapsed time is 500 min and the frame rate is 10 min/frame. (MOV)

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Movie S7 Myosin coalescence in WT. A short movie of an *UbiCadh-GFP;Sph-mCherry;381Gal4* embryo imaged using time-lapse confocal microscopy showing an early stage of dorsal closure. Note that Myosin II coalescence is correlated with cell deformations. The total elapsed time is 1250 sec and the frame rate is 5 s/frame. (MOV)

Movie S8 Myosin coalescence in DRhoGEF2 maternal mutants. A short movie of an *UbiCadh-GFP;Sph-mCherry;DRhoGEF2^{20942W}* embryo imaged using time-lapse confocal microscopy showing an early stage of dorsal closure. Note the absence of Myosin II coalescence. The total elapsed time is 800 sec and the frame rate is 5 s/frame. (MOV)

Movie S9 Myosin coalescence upon DRhoGEF2 overexpression. A short movie of an *UbiCadh-GFP;UAS-DRhoGEF2;Sph-mCherry;381Gal4* embryo imaged using time-lapse confocal microscopy showing an early stage of dorsal closure. Note that Myosin II coalescence is more intense. The total elapsed time is 1185 sec and the frame rate is 5 s/frame. (MOV)

Movie S10 Rho1 activity upon DRhoGEF2 overexpression. A short movie of an *381Gal4/UAS-DRhoGEF2;UAS-PKNG58A;GFP* embryo imaged using time-lapse confocal microscopy showing an early stage of dorsal closure. Note that Rho1 activity is correlated with AS cells pulsation. The total elapsed time is 30 min and the frame rate is 30 s/frame. (MOV)

Acknowledgments

We thank Damian Brunner and Alfonso Martínez Arias for insightful discussions, Isabel Campos and Lara Carvalho for critically reading the manuscript. We acknowledge Dan Kiehart and Steve Rogers for reagents and fly stocks, José Rino and Antonio Temudo for microscopy assistance, and Inês Mateo and Ângela Dias for fly maintenance.

Author Contributions

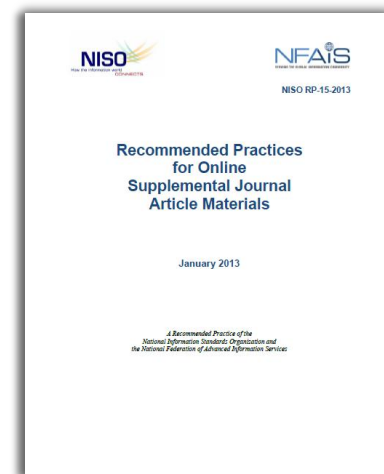
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Summary

Background
Methods
Results
Conclusions

Funding

Introduction

Methods

Participants

Measurement of vitamin D concentrations and bone-mineral content

Statistical analysis

Roles of the funding sources

Results



Table 1



Table 2

Table 3



Table 4

Discussion

Acknowledgements

Supplementary Material

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Volume 381, Issue 9884, 22–28 June 2013, Pages 2176–2183



Articles

Association of maternal vitamin D status during pregnancy with bone-mineral content in offspring: a prospective cohort study

Prof Debbie A Lawlor, PhD^{a,b}, Andrew K Wills, PhD^{a,b}, Abigail Fraser, PhD^{a,b}, Adrian Sayers, MSc^b, Prof William D Fraser, MD^d, Prof Jonathan H Tobias, PhD^c

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^cSchool of Clinical Sciences, University of Bristol, Bristol UK

^dNorwich Medical School, University of East Anglia, Norwich, UK

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Summary

Background

Maternal vitamin D status in pregnancy is a suggested determinant of bone-mineral content (BMC) in offspring, but has been assessed in small studies. We investigated this association in a large prospective study.

Methods

Eligible participants were mother-and-singleton-offspring pairs who had participated in the Avon Longitudinal Study of Parents and Children, and in which the mother had recorded measurements of 25 (OH)D concentration in pregnancy and the offspring had undergone dual-energy x-ray absorptiometry at age 9–10 years. 25(OH)D concentrations in pregnancy were assessed per 10·0 nmol/L and classified as

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Supplementary video. Professor Debbie Lawlor reports on the association of maternal vitamin D status in pregnancy with bone-mineral content in offspring, and discusses the implications for current clinical guidelines.

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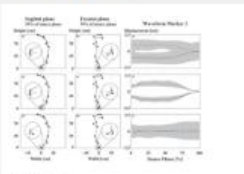
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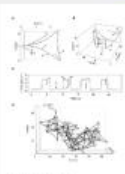
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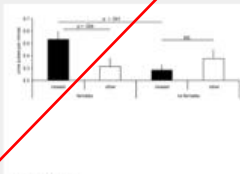
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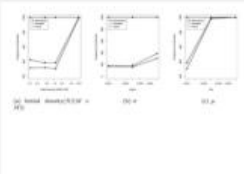
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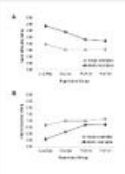
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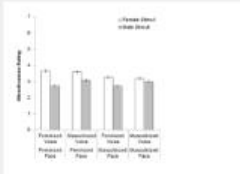
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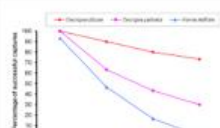
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Abstract
 Planktonic copepods display a large repertoire of motion behaviors in a three-dimensional environment. Two-dimensional video observations demonstrated that the small copepod *Clausocalanus furcatus*, one of the most widely distributed calanoids at low to medium latitudes, presented a unique swimming behavior that was continuous and fast and followed notably convoluted trajectories. Furthermore, previous observations indicated that the motion of *C. furcatus* resembled a random process. We characterized the swimming behavior of this species in three-dimensional space using a video system equipped with telecentric lenses, which allow tracking of zooplankton without the distortion errors inherent in common lenses. Our observations revealed unexpected regularities in the behavior of *C. furcatus* that appear primarily in the horizontal plane and could not have been identified in previous observations based on lateral views. Our results indicate that the swimming behavior of *C. furcatus* is based on a limited repertoire of basic kinematic modules but exhibits greater plasticity than previously thought.

Supporting Information

Video_S1.mov
Clausocalanus furcatus - HS pattern

A 3D plot showing the horizontal swimming pattern of *Clausocalanus furcatus*. The axes are labeled X (mm), Y (mm), and Z (mm). The plot shows a complex, convoluted trajectory in the horizontal plane. A play button is visible in the center of the plot. The time shown is 0.20s.

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Genomic and Epigenomic Landscapes of Adult De Novo Acute Myeloid Leukemia

The Cancer Genome Atlas Research Network
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BACKGROUND

Many mutations that contribute to the pathogenesis of acute myeloid leukemia (AML) are undefined. The relationships between patterns of mutations and epigenetic phenotypes are not yet clear.

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METHODS

We analyzed the genomes of 200 clinically annotated adult cases of de novo AML, using either whole-genome sequencing (50 cases) or whole-exome sequencing (150 cases), along with RNA and microRNA sequencing and DNA-methylation analysis.

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RESULTS

AML genomes have fewer mutations than most other adult cancers, with an average of only 13 mutations found in genes. Of these, an average of 5 are in genes that are recurrently mutated in AML. A total of 23 genes were significantly mutated, and another 237 were mutated in two or more samples. Nearly all samples had at least 1 nonsynonymous mutation in one of nine categories of genes that are almost certainly relevant for pathogenesis, including transcription-factor fusions (18% of cases), the gene encoding nucleophosmin (*NPM1*) (27%), tumor-suppressor genes (16%), DNA-methylation-related genes (44%), signaling genes (59%), chromatin-modifying genes (30%), myeloid transcription-factor genes (22%), cohesin-complex genes (13%), and spliceosome-complex genes (14%).

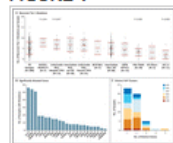
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Acute Myeloid Leukemia (AML).

FIGURE 1



Characterization of Mutations.

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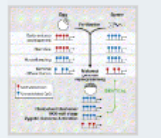
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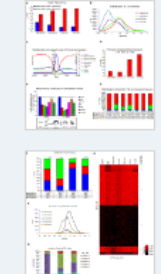
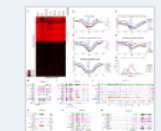
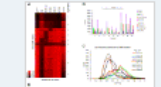


Table 1

DNAmE Comparison of TSS and zCGI Regions across Development



DNAmE Comparison of All DMRs across Embryo Development



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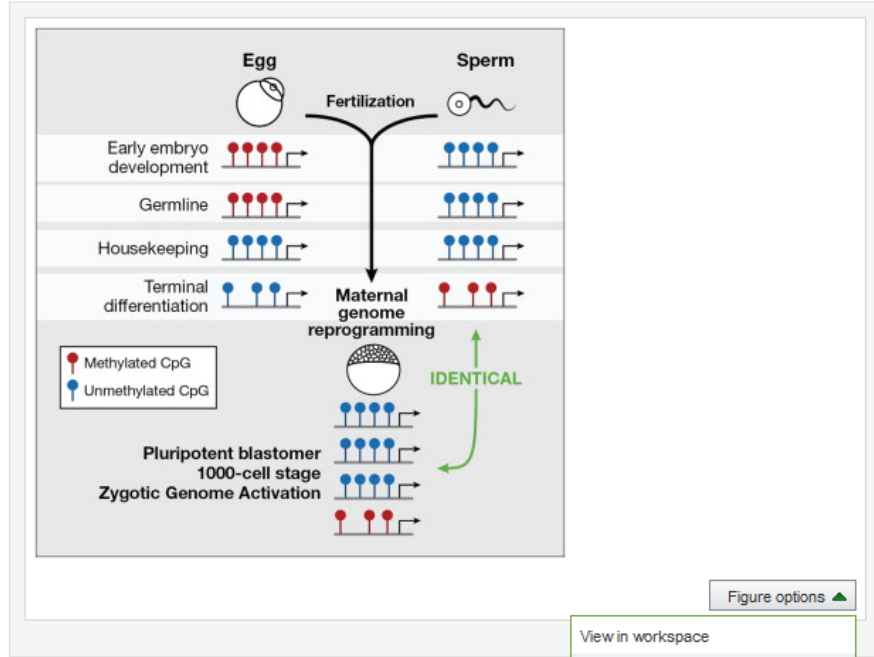


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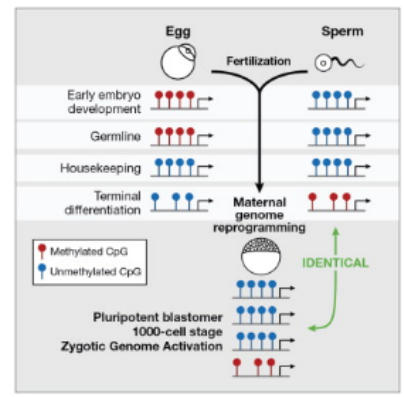
Introduction

Fertilization involves the joining of parental gametes to create a totipotent zygote. A central issue in developmental biology is to understand how totipotency is established—the enabling of all developmental decisions. Developmental decisions are often made via collaboration between signaling factors, transcription/chromatin factors, and miRNAs, which need to be expressed at the proper time in early development, and avoid silencing by repressive chromatin and DNA methylation. One mechanism for transcriptional competence of developmental genes is their packaging in “bivalent” chromatin, bearing (simultaneously) histone modifications normally associated with transcriptional activity (i.e., H3K4me3) and silencing (H3K27me3), along with underlying DNA hypomethylation (Laurent et al., 2010; Lister et al., 2009; Zhou et al., 2011). Interestingly, in vertebrate sperm, the vast majority of developmental genes of importance in the early embryo are already packaged in bivalent chromatin (lacking DNA methylation), including virtually all HOX, SOX, FOX, TBX, PAX, CDX, and GATA family transcription factors (Arpanahi et al., 2009; Brykczynska et al., 2010; Farthing et al., 2008; Hammoud et al., 2009; Weber et al., 2007; Wu et al., 2011a). This raises important questions regarding the extent to which DNA methylation and chromatin structures important for totipotency are simply inherited or must be established or reestablished in the early embryo.

In mice, bulk DNA demethylation occurs at the one-cell stage, preferentially affects the male pronucleus (Hajkova et al., 2008; Mayer et al., 2000; Okada et al., 2010; Oswald et al., 2000), and likely involves a 5-hydroxymethylcytosine (5hmC) intermediate catalyzed by TET enzymes (Gu et al., 2011; Iqbal et al., 2011). Recent approaches with DNAmE or reduced representation bisulphite sequencing (RRBS) reveal

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Pollcization: The Concept, Technical Details, and Outcome
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Symposium: Congenital Differences of the Hand

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Policization: The Concept, Technical Details, and Outcome

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Abstract

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Policization substitutes a functioning finger for a deficient thumb. The most indication is thumb hypoplasia with absence or instability of the carpometacarpal joint. However, there are additional causes that may negate thumb function, such as trauma, macrodactyly, multi-fingered hand, and a mirror hand. The technique of policization represents a consolidation of contributions from surgeons over the last 100 years. A meticulous stepwise approach from incision to closure is necessary to optimize outcome. Following policization, cortical plasticity and motor relearning play a pivotal role in function following policization with connections and adjacent sprouting from nearby cortical and/or subcortical territories. Occupational therapy is necessary to encourage large object acquisition followed by smaller objects and ultimately fine pinch. Policization is more reliable in patients with isolated thumb hypoplasia and a mobile index finger with robust extrinsic and intrinsic muscle-tendon units compared to and patients with radial forearm deficiencies and diminished index mobility.

Keywords: Policization, Thumb hypoplasia, Macrodactyly, Ulnar deficiency, Mirror hand.

Policization is an amazing operation that combines surgical skill with brain plasticity. The concept is to substitute a functioning finger for a deficient thumb. The deficient thumb is defined as one without ample function to contribute to prehension and grasp. The most common reason is hypoplasia with absence or instability of the carpometacarpal (CMC) joint, which obviates stability and function.¹⁻³⁰ However, there are additional causes that may negate thumb function, such as trauma, macrodactyly, multi-fingered hand, and a mirror hand. The more time I spend caring for children with congenital hand differences, the more likely I am to pursue policization as an option to reconstruct the hand impaired by thumb hypoplasia and other ailments. I firmly believe that the best substitute for a deficient thumb with small girth, unstable CMC joint, and/or insufficient extrinsic/intrinsic muscles is a mobile functional index finger. Adrian Flatt, MD (personal communication) has been an inspiration, mentor, and abounding with sage advice. He has extended congenital indications for policization to include a thumb smaller than a small finger and I concur! Reconstruction of a small hypoplastic thumb even with a stable CMC joint will pale in comparison to policization of a "normal" index finger. This decision requires a "heart to heart" conversation with the parents. The parents make the ultimate decision but the established surgeon has substantial influence. I spend substantial time explaining that "function trumps form" and that thumb ablation and index policization will result in enhanced function versus reconstruction of a small scrawny thumb. In addition, people are not very observant and a robust thumb with excellent function has better appearance compared to a small skinny thumb that contributes little to hand function. When in doubt, I recommend the parents discuss this decision with other parents who have made a similar difficult decision. This exchange is facilitated via a list of willing parents and

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Table 2	Policization Factors
	Factors that influence policization outcome
	Status of finger
	Age of surgery
	Technical factors: incision, technique, dressings, etc.
	Surgeon
	Rehabilitation

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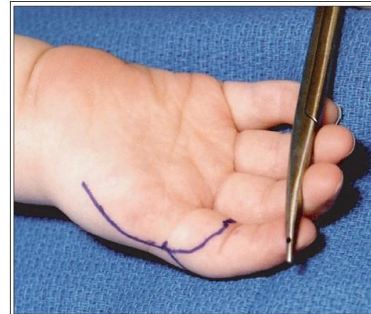


Fig. 1
Volar skin design (Courtesy of Shriners Hospital for Children, Philadelphia).

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Table 2
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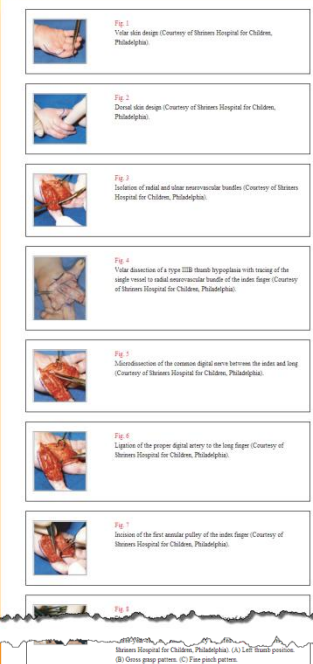
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Table 1	Surgical Approach to Policization
Table 2	Policization Factors



Policization

Scott H. Kozin, MD

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BRAIN PLASTICITY

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Cortical plasticity and motor relearning play a pivotal in functional following policization. There is a large region of the sensorimotor cortex (SMC) homunculus dedicated to the hand. Researchers are trying to understand the changes in SMC following injury, repair, and reconstruction.⁵⁾ Techniques include transcranial magnetic stimulation, electroencephalography, magnetoencephalography, functional magnetic resonance imaging (MRI), structural MRI, and positron emission tomography.⁵⁻⁹⁾ Human cortical plasticity is a complex process that involves the unweaving of previously ineffective connections and sprouting of intact afferents from nearby cortical and/or subcortical territories.

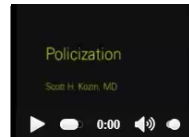
Giroux et al.¹⁰⁾ have demonstrated that after hand transplantation, the original SMC map for hand activation is restored. The transplantation reverses the SMC loss following the initial hand amputation. Similarly, successful toe transfer produces temporal activation within the SMC cortex consistent with cortical plasticity.¹¹⁾ Functional MRI has demonstrated that a patient learning to use their toe transfer lead to an expansion in their motor cortical representation. Practice magnifies the changes within the SMC cortex. As the new motor skill is mastered, there is a subsequent decrease in the amount of cortical representation.^{5,11)} Functional MRI studies have provided evidence that that motor reorganization continues to evolve over time and may be modified by training and experience for a protracted time.¹²⁾ These findings suggest that prolonged therapy and training may be necessary to maximize cortical reorganization and functional outcome.

The effects of policization have yet to be studied with reference to cortical plasticity. The locale and quantity of homunculus thumb representation before and after policization is an intriguing question. Without a doubt, functional changes occur in the SMC cortex as the

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index finger transforms into a thumb. The initial rehabilitation likely involves cortical plasticity with the development of new connections and adjacent sprouting from nearby cortical and/or subcortical territories.

TECHNIQUE

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The current technique of pollicization represents a consolidation of contributions from surgeons over the last 100 years.¹³⁻¹⁵ My personal technique stems from direct interaction with other congenital hand surgeons, especially Marybeth Ezaki, Peter Carter, and Terry Light. Their surgical nuances have been incorporated into my current procedure, which has been fairly consistent for the last 10 years. I must profess that my technique will likely undergo further subtle modifications as I learn more from congenital hand colleagues.

A stepwise approach is used for multiple reasons (Table 1).¹⁶ First of all, multiple steps are required for completion of the procedure and this approach avoids "missing" a crucial step. Secondly, I operate at a teaching institution and this methodical approach is "teachable" to interested fellows. I will detail the basic surgical approach and highlight special circumstances that require surgical alterations related to the underlying diagnosis and anatomy encountered.

Table 1
Stepwise Approach to Pollicization

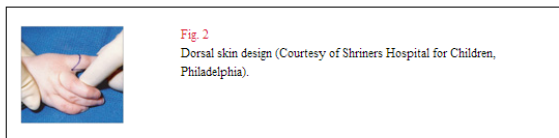
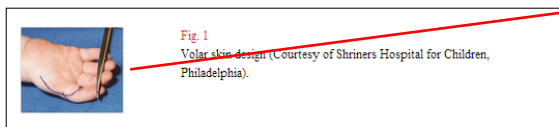
POLLICIZATION FOR THUMB HYPOPLASIA (TYPES IIIB, IV, OR V HYPOPLASIA)

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Following general anesthesia, the child is placed in the supine position. A pediatric tourniquet (Delfi Medical Innovations, Vancouver, Canada) is placed on the upper arm. The pediatric size is smaller in diameter, avoids irritation in the antecubital fossa, and extends the surgical field. Preoperative antibiotics are routinely administered. The extremity is prepped and draped in sterile fashion.

The skin incision must be nimble to allow easy index finger transposition and creation of an adequate thumbweb space (Figs. 1 and 2). I currently use a modified design by Marybeth Ezaki and Peter Carter that allows more glabrous skin to be placed along the palmar aspect of the index finger.¹⁶ This improves the appearance of the index finger once in the thumb position, such that the index looks more like a thumb compared to other incisions.



The limb is gently exsanguinated to facilitate identification of the vasculature (Fig. 3). The palmar skin is incised first and the radial neurovascular bundle isolated. In children with type IV or IIIB thumb hypoplasia, the single vessel within the digit can be traced to radial neurovascular bundle of the index finger (Fig. 4). Dissection then proceeds further ulnar to identify the common digital vessels to the index-long web space. The proper digital nerves to the ulnar side of the index and the radial side of the long finger are isolated. Proximal

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Table 1
Stepwise Approach to Pollicization

Step	Technique	Rationale
Exsanguination	Moderate	Vessel identification
Skin incision	Evaki design	More glabrous skin along palmar aspect of thumb and excellent thumb-index web space
Isolation palmar neurovascular bundles	Lupe magnification and meticulous dissection	Preserve sensibility and circulation to index
Microdissection of common digital nerve	Intra-fascicular dissection	Mobilize nerve for tension free pollicization
Ligate proper digital artery to radial side of long finger	Ligature clip	Allows constant visualization throughout the procedure
Release A1 pulley to index finger		Prevent buckling of flexor tendons after pollicization
Incise intermetacarpal ligament		Allows repositioning of the index finger
Elevation of dorsal skin with preservation of dorsal veins		Delaying dorsal exposure allows veins to be filled with blood
Extensor tendons freed from adjacent		Confirm appropriate line of pull to index finger pollicization
Extensor and flexor tendons are not shortened		Adapt and shorten over time
Elevation of the first dorsal and palmar muscles from the index metacarpal and metacarpophalangeal joint with a strip of extensor hood	Sharp dissection	Muscles will be advanced to proximal interphalangeal joint and length is necessary
Identify and tag the radial and ulnar lateral bands about the proximal interphalangeal joint	Pull on lateral band until desired function is evident and tag band with suture	Prior to bony resection, identification is easier
Shorten the index finger by removing the majority of the metacarpal bone, including physis ablation	Fine bladed saw to cut metacarpal perpendicular to bone through its metaphyseal portion Distal cut directly through physis (epiphysis)	Index too long for a thumb Physis ablation prevents continued metacarpal growth
Reposition index metacarpophalangeal joint into hyperextension	Fixation of the index metacarpophalangeal joint into hyperextension using a non-absorbable suture placed through the epiphysis and dorsal capsule	Prevents unwanted thumb carpometacarpal joint hyperextension
Kirschner wire is passed anterior to the metacarpal epiphysis, into the proximal phalanx, and out the proximal interphalangeal joint	Wire driver	This Kirschner wire is used as a joystick for index finger positioning and ultimate fixation
Align the index finger into the thumb position with 45-degree of abduction and between 100 and 120-degree of pronation	Metacarpal epiphysis is aligned anterior to its remaining base and Kirschner wire drilled retrograde across the metacarpal base to secure the position	Replicate thumb position
Tendon transfer to restore intrinsic function to the pollicization	First dorsal interosseous sutured into the radial lateral band and the first palmar interosseous sutured into the ulnar lateral band	Maximize function in grasp and pinch
Inset skin with absorbable suture	Skin inset advanced and inset along the palmar aspect of the "thumb"	Index appearance similar to thumb
	Inset web space skin	Avoid suture line in thumb-index web space

Ensure circulation, protect pollicization, decrease chances of inadvertent dressing removal

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Fig. 1
Volar skin design (Courtesy of Shriners Hospital for Children, Philadelphia).

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PubMed search results for "The burden of allergic rhinitis" by Nathan RA. The abstract discusses the financial burden of allergic rhinitis (AR) and its association with sleep-disordered breathing, psychiatric disorders, and increased medication costs. It notes that AR is associated with a 1.8-fold increase in medication costs and a 1.8-fold increase in visits to health practitioners. The abstract also mentions that AR is associated with sleep-disordered breathing, a condition that can have a profound effect on mental health, including increased psychiatric disorders, depression, anxiety, and alcohol abuse. Furthermore, sleep-disordered breathing in childhood and adolescence is associated with increased disorders of learning performance, behavior, and attention. In the United States, AR results in 3.5 million lost workdays and 2 million lost school days annually. Patients struggle to alleviate their misery, frequently self-adjusting their treatment regimen of over-the-counter and prescription medications because of lack of efficacy, deterioration of efficacy, lack of 24-hour relief, and bothersome side effects. Ironically, health care providers overestimate patient satisfaction with therapy. Therefore, improvement in patient-practitioner communication may enhance patient adherence with prescribed regimens.

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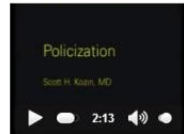
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BRAIN PLASTICITY

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Long-term complications are more prevalent. Any unsatisfactory outcome requires an analytical approach to find the root of the problem (Table 3). Additional surgery may or may not be available to improve the status and function of the thumb.^{31,32}

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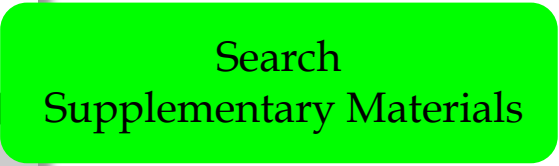
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Volar skin design (Courtesy of Shriners Hospital for Children, Philadelphia).



Fig. 2
Dorsal skin design (Courtesy of Shriners Hospital for Children, Philadelphia).



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Clinical approach to quality of life in children with end-stage renal disease
Cho MH.

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Lee YM, Bae SG, Lee SH, Jacobs DR, Lee DH.

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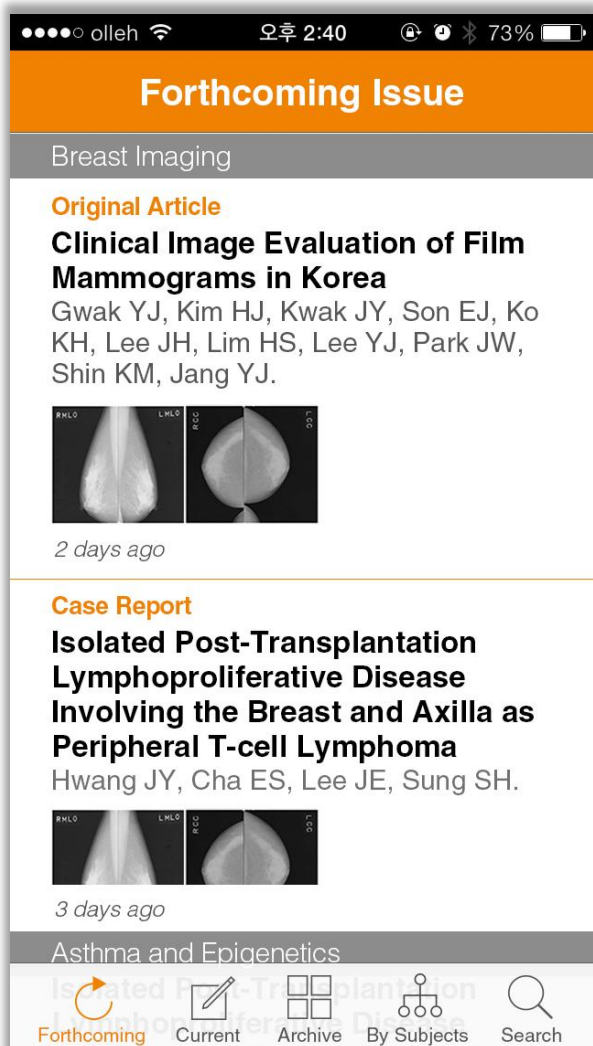
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Mutant p53-Notch1 Signaling Axis Is Involved in Curcumin-Induced Apoptosis of Breast Cancer Cells

Bae YH, Ryu JH, Park HJ, Kim KR, Wee HJ, Lee OH, Jang HO, Bae MK, Kim KW, Bae S



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Current Issue

Volume 54(11), November 2013

Review Articles

- 721 Androgens Modulate Endothelial Function and Endothelial Progenitor Cells in Erectile Physiology
 Traish AM, Galoosian A.
- 732 Current Surgical Management of Vesicoureteral Reflux
 Baik M, Kim KD.

Original Articles

Urological Oncology

- 738 Comparative Analysis of Radiologically Measured Size and True Size of Renal Tumors
 Lee KB, Kim SI, Cho DS, Park SK, Jang HI, Kim SJ.
- 744 Factors Affecting the Time to Recurrence After Radical Nephrectomy for Localized Renal Cell Carcinoma
 Son HS, Jeon SH, Chang SG.
- 750 Impact of Treatment With Statins on Prostate-Specific Antigen and Prostate Volume in Patients With Benign Prostatic Hyperplasia
 Lee SH, Park TJ, Bae MH, Choi SH, Cho YS, Joo KJ, Kwon CH, Park HJ.

Laparoscopy/Robotics

- 756 Retropubic Versus Robot-Assisted Laparoscopic Prostatectomy for Prostate Cancer: A Comparative Study of Postoperative Complications
 Ryu J, Kwon T, Kyung YS, Hong S, You D, Jeong IG, Kim CS.

Voiding Dysfunction/Female Urology

- 762 Effect of Urgency Symptoms on the Risk of Depression in Community-Dwelling Elderly Men
 Lee YI, Kim JW, Bae SR, Paick SH, Kim KW, Kim HG, Lho YS, Park HK.
- 767 Elimination of Hunner's Ulcers by Fulguration in Patients With Interstitial Cystitis: Is It Effective and Long Lasting?
 Ryu J, Pak S, Song M, Chun JY, Hong S, Choo MS.

Endourology/Urolithiasis

- 772 Predictive Value of Preoperative Unenhanced Computed Tomography During Ureteroscopic Lithotripsy: A Single Institute's Experience
 Kim S, Choi SK, Lee SM, Choi T, Lee DG, Min GE, Jeon SH, Lee HL, Chung JY, Joh JH, Yoo KH.

Sexual Dysfunction

- 778 An Evidence-Based Evaluation of Health Information on Erectile Dysfunction From 10 Nationwide Daily Newspapers in Korea
 Hah YS, Lee JY, Lim SK, Cho KS, Choi YD.

Pediatric

- 783 Efficacy of an Enuresis Alarm, Desmopressin, and Combination Therapy in the Treatment



Highlights
 articles/issues

Video Interview with Author
 Ryu J, et al. Retropubic Versus Robot-Assisted Laparoscopic Prostatectomy for Prostate Cancer: A Comparative Study of Postoperative Complications. *Korean J Urol.* 2013 Nov;54(11):756-761.

[Interview with Author] Retropubic

Grade	Description
1	Any deviation from the normal postoperative course with no specific treatment required.
2	Requiring pharmacologic treatment with drugs other than such as allowed for grade 1 complications. Blood transfusions and total parenteral nutrition are also included.
3	Complications requiring reoperation, re-urologic intervention, or re-urologic therapy.
4	Any life-threatening complication requiring intermediate or intensive care for single organ dysfunction.

Hot Articles

- Effect of Urgency Symptoms on the Risk ..
- Impact of Treatment With Statins on ..
- Androgens Modulate Endothelial Function ..

Reviewer of the Month

In Rae Cho, M.D., Ph.D. in November 2013
 Dr. Cho is a professor of the Department of Urology, Inje University College of Medicine and director of the Department of Urology, Ilsanpaik Hospital.

KJU Today

- KJU Editorial Board Meeting was held on November 6, 2013
- KJU Editorial Board workshop was held on July 20, 2013.
- BJU-KJU Luncheon Meeting was held on June 8th, 2013.

Publisher/Editor의 역할

A.2 Roles and Responsibilities Related to Supplemental Materials

Many parties play a role in maintaining the record of scholarship and supplemental material. For convenience in this document, we have separated the parties into two segments: Primary Publishing and Related Parties, and described their responsibilities in the two tables below.

A.2.1 Primary Publishing

Publisher	Editor	Peer Reviewer	Author(s)
Educate other parties about requirements for posting and curating content.	<u>Set editorial policy.</u>	Follow journal guidelines for reviewing Supplemental Materials.	Be aware of Journal expectations and follow them to the best of their ability.
<u>Provide appropriate resources for managing supplemental content.</u>	Make final decisions on content.	Inform the editor in a timely fashion if unable to review any content.	Provide context and demonstrate that the Supplemental Materials add substance to scholarship in the field.
Provide systems and policies to facilitate the decision-making process.	Determine whether supplemental content is integral to the article. ³	Alert the editor to instances in which integral data are not provided, but are needed to understand the manuscript.	Be responsible for providing Supplemental Materials at the same level of quality as the article.
Be clear about the level of delivery and preservation that can be provided.	Set expectations for acceptable content with an understanding of what is entailed in vetting, delivering, and preserving content.		Be aware of trusted repositories in the field and knowledgeable about their practices.
Encourage authors to post Additional Content in endorsed archives that ensure good preservation and provide bidirectional linking to the journal. ⁴	Encourage authors to post Additional Content in endorsed archives that ensure good preservation and provide bidirectional linking to the journal. ⁴		Be aware of and adhere to policies of your institution and funder for sharing of research data.



NISO RP-15-2013

Recommended Practices
for Online
Supplemental Journal
Article Materials

January 2013

A Recommended Practice of the
National Information Standards Organization and
the National Federation of Advanced Information Services

A.2.2 Related Parties

Libraries	Abstracting and Indexing Services	Repository Administrators
May serve as a repository for the research done by university researchers.	Indicate the availability of Supplemental Materials if the journal publisher has provided clear indication they exist.	Make deposited content accessible by assigning persistent identifiers, such as a DOI or another unique identifier.
Include Supplemental Materials with journal article interlibrary loan when the journal publisher has provided clear indication they exist.	Include the formats and file types of Supplemental Material if the publisher has provided identifiable metadata.	Include DOIs for any journal articles that link to content in their repository.
	Include the publisher-provided DOI or other identifier.	Manage bidirectional links between the deposited content and the article.

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