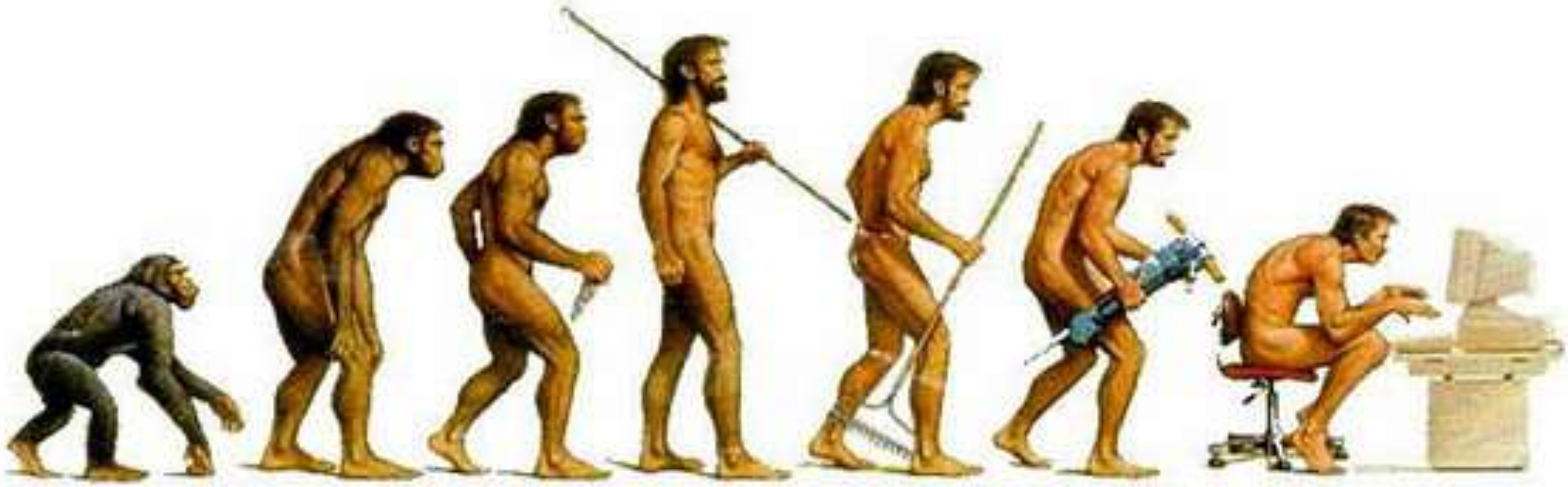
SPANISH SOCIETY OF PATHOLOGY
Zaragoza, May 2011

KEYNOTE LECTURE

Christopher D.M. Fletcher, M.D., FRCPath
Brigham and Women's Hospital and
Harvard Medical School, Boston MA

HOW SHOULD SURGICAL PATHOLOGY EVOLVE ?



DEFINITIONS OF EVOLUTION

A process of continuous change from a lower / simpler state to a more complex / better state

- A process of gradual (usually peaceful) social, political or economic advance
- A theory that various species have their origins in preexisting types and that differences are due to (? advantageous) modifications in successive generations
- A change in the inherited traits of a population of organisms through successive generations

“Organisms must be prepared to adapt or risk extinction. Since it cannot imagine or foresee the future, however, evolution has instead encouraged mechanisms that confer flexibility and has championed processes that allow for experimentation, while minimising the number of fatal mistakes.”

Debra Niehoff
The Language of Life
2005

KEY ELEMENTS OF MODERN SURGICAL PATHOLOGY (2011)

- Surgical pathology reports are more detailed and provide more diagnostic / prognostic information than ever
- Surgical pathology remains largely an interpretive skill – which is both a strength and a weakness
- Many clinicians are utterly dependent on surg path (even if they rarely admit it)
- Subspecialty expertise is increasingly expected by clinicians (and patients) and is becoming the norm

MAIN CLINICAL ROLES OF THE SURGICAL/CYTO- PATHOLOGIST

- **Diagnosis**
- **Prognosis**
- **Assessment of other clinical implications**
- **Target identification/assessment or prediction of treatment response**
- **Assistance in clinical decision-making**
- **Educating/guiding clinicians**

Has become increasingly cancer-centric

SURGICAL PATHOLOGY

MAIN STRENGTHS

- Has stood the test of time, currently irreplaceable
- Cheap, reliable, reproducible (most of the time)
- Currently the diagnostic gold standard

MAIN WEAKNESSES

- Subjectivity / grey areas
- Potential for error (analytic, also pre- and post-)
- Variable prognostic accuracy

Prone to Error: Earliest Steps to Find Cancer

By STEPHANIE SAUL
Published: July 19, 2010

Monica Long had expected a routine appointment. But here she was sitting in her new oncologist's office, and he was delivering deeply disturbing news.

TWITTER
SIGN IN TO E-MAIL
PRINT
SINGLE PAGE
REPRINTS
SHARE

Enlarge This Image

Michelle Litvin for The New York Times

Nearly a year earlier, in 2007, a pathologist at a small hospital in Cheboygan, Mich., had found the earliest stage of breast cancer from a biopsy. Extensive surgery followed, leaving Ms. Long's right breast missing a golf-ball-size chunk.

Now she was being told the pathologist had made a mistake. Her new doctor was certain she never had the disease, called ductal carcinoma in situ, or D.C.I.S. It had all been unnecessary — the surgery, the radiation, the drugs and, worst of all, the fear.

SELECTIVE PRESSURES TO ADDRESS

- How is clinical practice changing ?
- How are clinician expectations changing?
- How are patient expectations changing ?
- How are pathologists and their role perceived – and how best do we respond/adapt ?

Need to better define – and value – our role

OTHER KEY ISSUES TO ADDRESS

- How do we combat perceptions that much of the routine work that we do is outdated and of limited value ?
- Which elements of new technology are genuine opportunities and which are threats/potential replacements (or fakes) ?
- What elements of new technology merit inclusion in routine care ?
- What are the economic pressures and cost-benefit ratios in adding these tests ?

Need to better define – and value – our role

EVOLUTION IN PRACTICE OF PATHOLOGY

New technologies

New tests

New imaging capabilities

New ways to enhance patient safety

Increasing subspecialisation

‘….we are on the threshold of a new era in medical diagnostics and patient monitoring…. The following 4 technologies seem ripe for exploitation: (1) cDNA microarray technology, which permits the simultaneous assessment of thousands of genes; (2) microchip-based analytical chemistry….; (3) laser capture microdissection, which enables retrieval of selected populations of cells...for genomic and proteomic analyses, and (4) wireless medical informatics.’

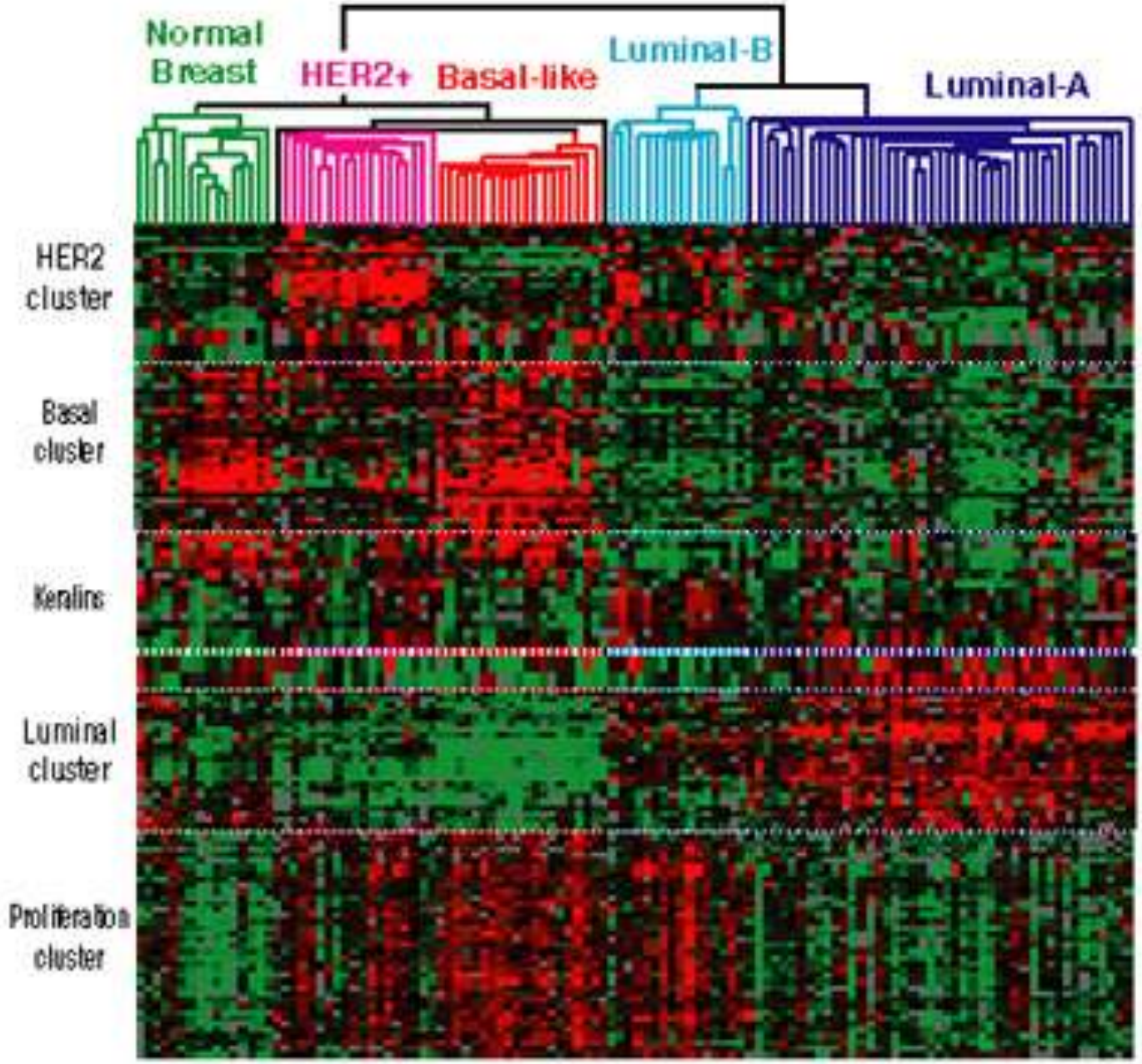
R. Weinstein MD, Hum Pathol, January 2000

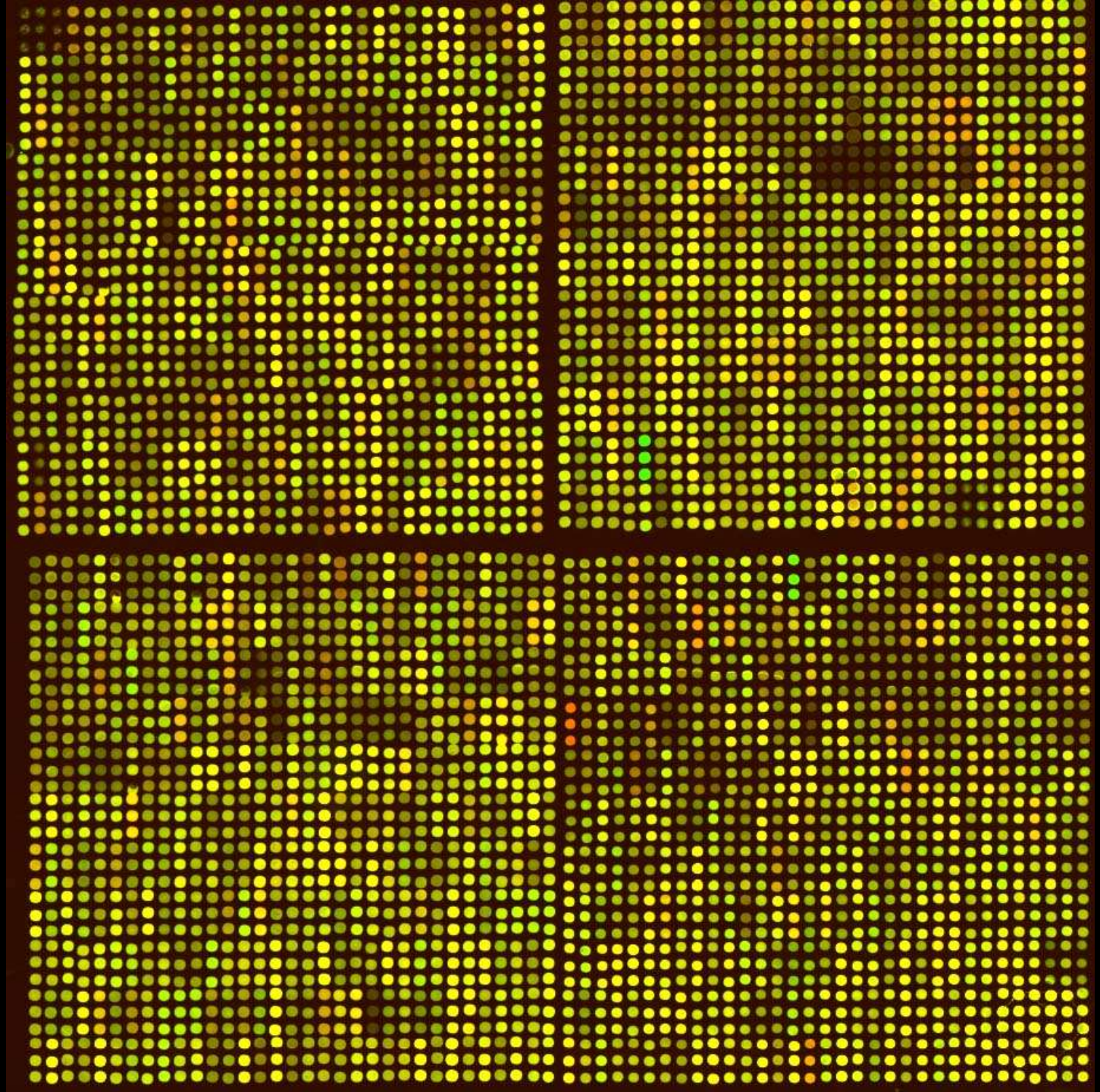
Science 1999; 286:531-537

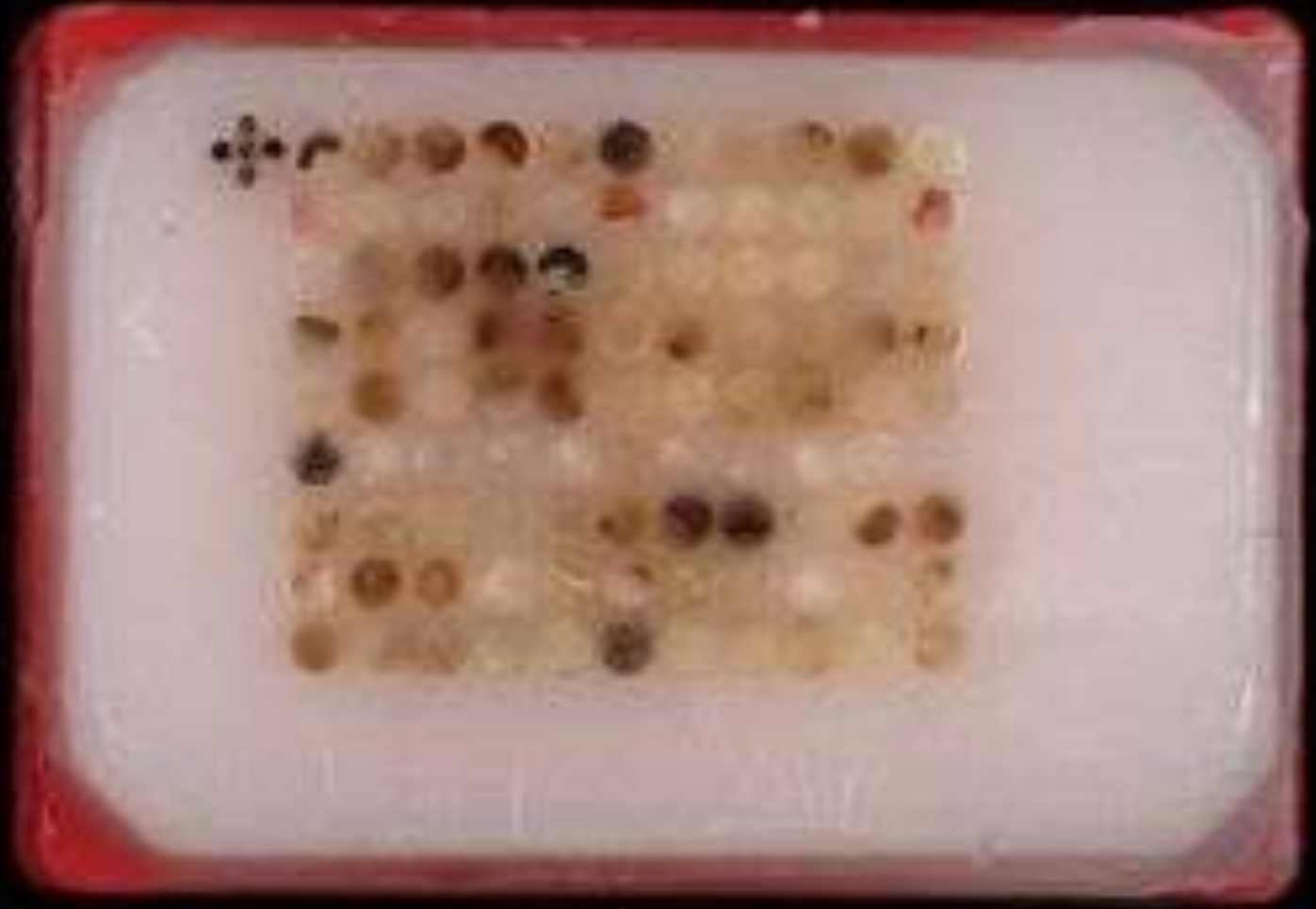
Molecular Classification of Cancer: Class Discovery and Class Prediction by Gene Expression Monitoring

T. R. Golub,[1,2*†] D. K. Slonim,[1†] P. Tamayo,[1] C. Huard,[1] M. Gaasenbeek,[1] J. P. Mesirov,[1] H. Coller,[1] M. L. Loh,[2] J. R. Downing,[3] M. A. Caligiuri,[4] C. D. Bloomfield,[4] E. S. Lander[1,5*]

Diversity of Breast Tumor Subtypes



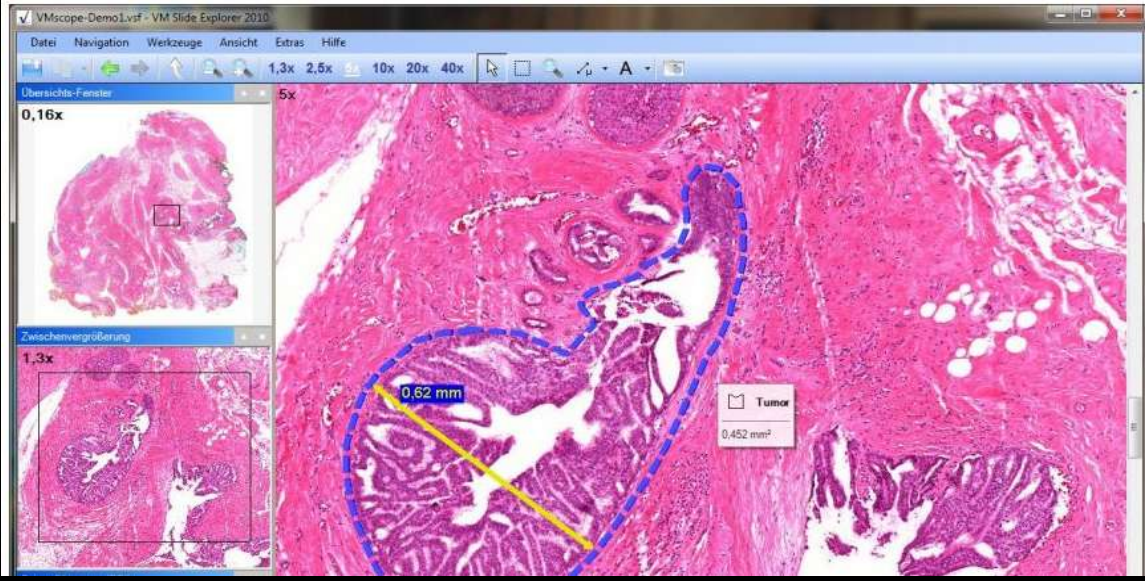




Courtesy of Veteran Association

efficiently on the monitor. Snapshots facilitate the generation of digital findings reports and screen presentations. The management of user profiles and the use of personal favorite folders for your slide collections accelerate your work.
VM Slide Explorer furthermore acts as plugin host. Developers can add own plugins using an interface. Already available are plugins for:

- TMA Analysis („VM TMA Evaluator")
- Point-of-Interest Manager
- Nucleus Segmentation
- Several image analysis functions



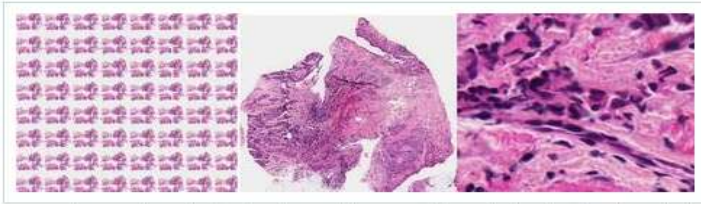
medGadget

internet journal of emerging medical technologies

Tuesday, May 8, 2007

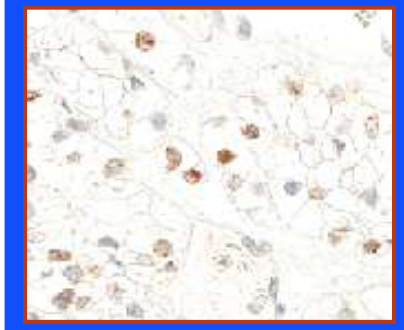
World's First: One Trillion Pixel Image

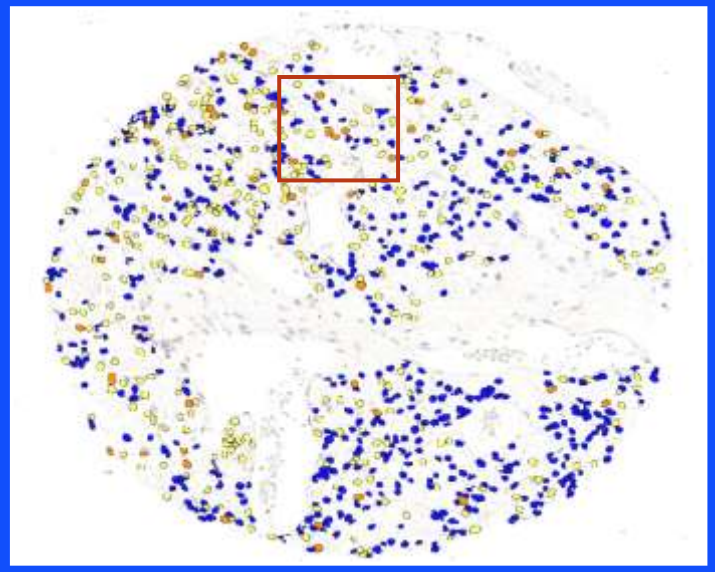
Filed under: Pathology

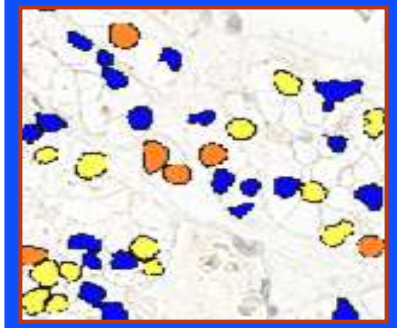


In a move rarely seen in an industry plagued by proprietary technologies, Aperio has released its latest digital pathology imaging file format to the open source software community. To debut this technology, they have taken the world's first terapixel image of 225 pathology slides from a sample of breast tissue, making it the largest image of a

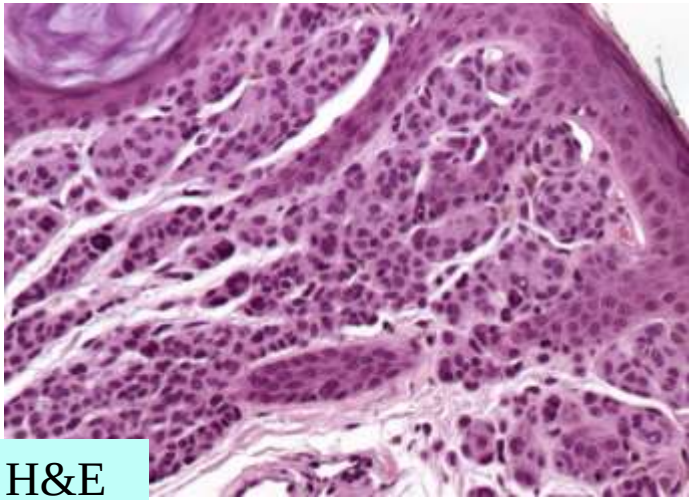
Quantification of nuclear HIF1α expression in RCC TMAs using the Aperio System



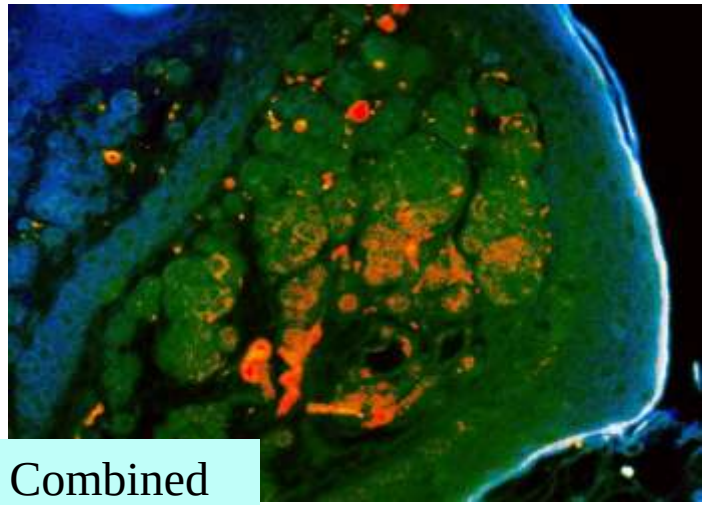




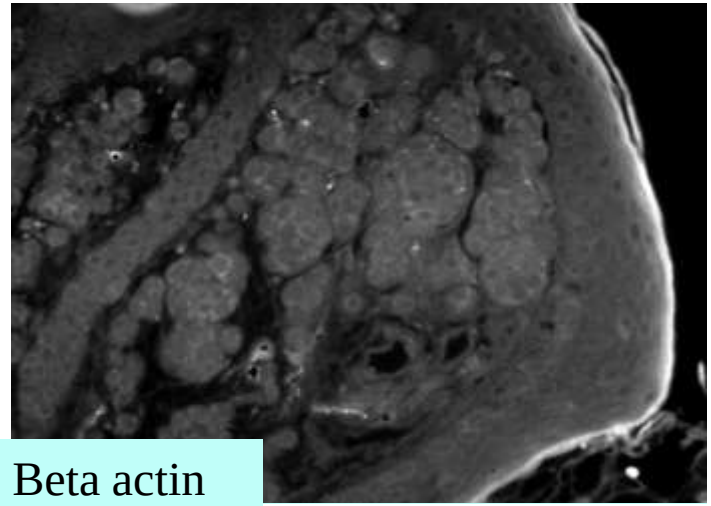
- The Aperio Nuclear Algorithm is utilized to quantify HIF1α expression in tumor cells.
- The algorithm generates a “mark up image” (B) in which negative nuclei are labeled in blue, 1+ nuclei are labeled in yellow, 2+ nuclei are labeled in orange, and 3+ nuclei are labeled in red.
- Percentages of negative, 1+, 2+, 3+ nuclei are calculated by the system.



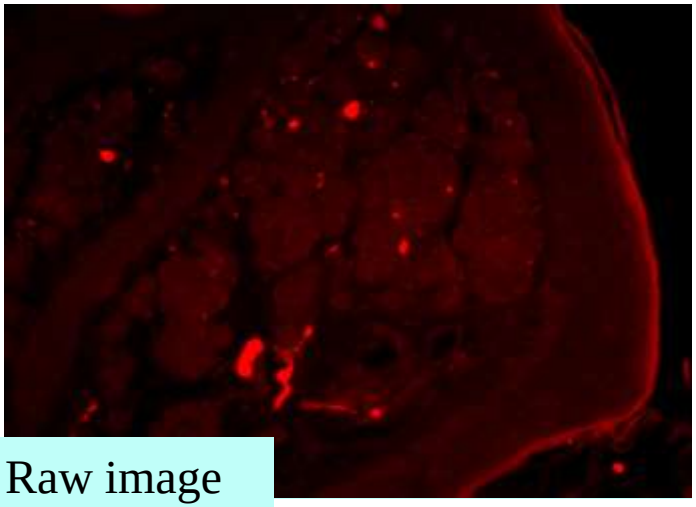
H&E



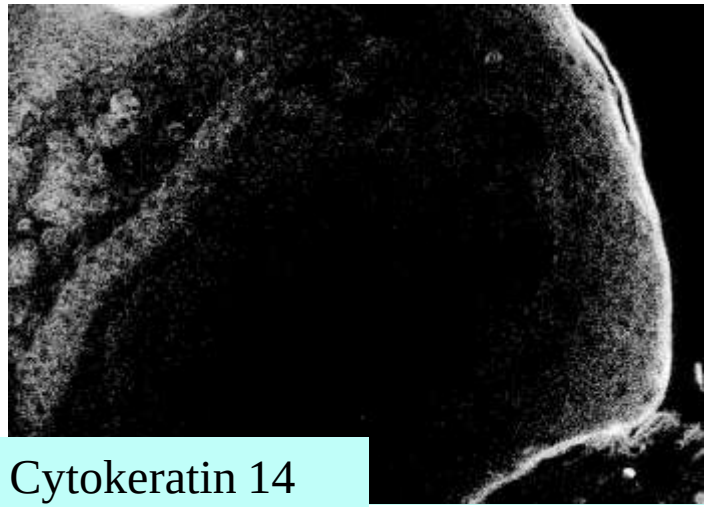
Combined



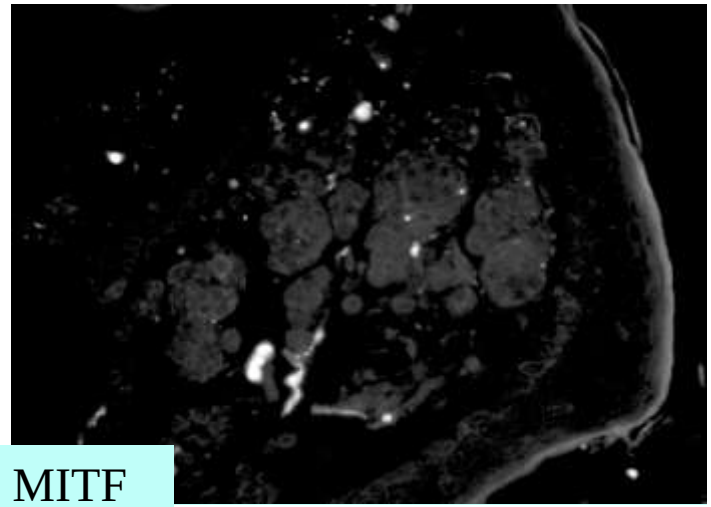
Beta actin



Raw image



Cytokeratin 14



MITF

β actin green, cytokeratin 14 blue, MITF red

The New England Journal of Medicine

VOLUME 347 DECEMBER 19, 2002 NUMBER 25

A GENE-EXPRESSION SIGNATURE AS A PREDICTOR OF SURVIVAL IN BREAST CANCER

MARC J. VAN DE VIJVER, M.D., PH.D., YUDONG D. HE, PH.D., LAURA J. VAN 'T VEER, PH.D., HONGYUE DAI, PH.D., AUGUSTINUS A.M. HART, M.SC., DORIEN W. VOSKUIL, PH.D., GEORGE J. SCHREIBER, M.SC., JOHANNES L. PETERSE, M.D., CHRIS ROBERTS, PH.D., MATTHEW J. MARTON, PH.D., MARK PARRISH, DOUWE ATSMA, ANKE WITTEVEEN, ANNUSKA GLAS, PH.D., LEONIE DELAHAYE, TONY VAN DER VELDE, HARRY BARTELINK, M.D., PH.D., SJOERD RODENHUIS, M.D., PH.D., EMIEL T. RUTGERS, M.D., PH.D., STEPHEN H. FRIEND, M.D., PH.D., AND RENÉ BERNARDS, PH.D.

Press Release

Our focus
Our values
History
Corporate Governance
Investor Relations
News and Events
Press Releases
News
Upcoming Conferences
Press Releases Archive

PRESS RELEASE - Agendia's MammaPrint breast cancer prognosis test cleared by U.S. Food and Drug Administration (FDA).

-- MammaPrint® is the first multi-gene expression test to receive market clearance by the FDA --

Amsterdam, The Netherlands, Tuesday 6 February 2007

Agendia's MammaPrint® breast cancer prognosis test is the world's first In Vitro Diagnostic Multivariate Index Assay (IVDMIA) to acquire market clearance from the U.S. Food and Drug Administration (FDA). Clearance of Agendia's 'de novo 510K' application for MammaPrint® provides the legal basis for offering this service in the United States. Agendia had previously received clearance from European authorities to market MammaPrint® in Europe and substantial progress has already been made there in market acceptance and reimbursement.

Vol 351:2817-2826 Dec 30 2004

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Multigene Assay to Predict Recurrence of Tamoxifen-Treated, Node-Negative Breast Cancer

Soonmyung Paik, M.D., Steven Shak, M.D., Gong Tang, Ph.D., Chungyeul Kim, M.D., Joffre Baker, Ph.D., Maureen Cronin, Ph.D., Frederick L. Baehner, M.D., Michael G. Walker, Ph.D., Drew Watson, Ph.D., Taesung Park, Ph.D., William Hiller, H.T., Edwin R. Fisher, M.D., D. Lawrence Wickerham, M.D., John Bryant, Ph.D., and Norman Wolmark, M.D.

genomic health | oncotype DX Breast Cancer Assay

The power of a quantitative Recurrence Score™ result.

Illuminating Breast Cancer Recurrence Risk

> Search GO | Take me to:

Home | Genomic Health | Contact Us | Register | Privacy | Terms and Conditions | Printer-friendly

- Healthcare Professionals
- Patients and Caregivers
- Laboratory Professionals

Medicare Contractor Establishes Reimbursement Coverage Policy for Genomic Health's Oncotype DX Breast Cancer Test

More women will have access to this important tool for making treatment decisions. Read more

Register for updates

Register

for more Information About Oncotype DX, call

Welcome to Oncotype DX™

Oncotype DX is a clinically validated laboratory test, ordered by physicians, that predicts the likelihood of breast cancer recurrence in women with newly diagnosed, early stage invasive breast cancer. Oncotype DX also assesses the benefit from chemotherapy.[1] To learn more about Oncotype DX, choose from the options below.

I am a Healthcare | I am a Patient or | I am a Laboratory

‘At present, it is not clear that the quantification of the level of expression of dozens or hundreds of genes provides more information about the potential of a cancer for metastasis, virulence, and response to therapy for an individual patient than does an optimal analysis of the standard and readily available histopathological prognostic factors.’

JA O’Shaughnessy
N Engl J Med
Editorial Aug 10 2006

MGH to use genetics to personalize cancer care

The Boston Globe

By Stephen Smith, Globe Staff | March 3, 2009

Cancer doctors at Massachusetts General Hospital plan within a year to read the genetic fingerprints of nearly all new patients' tumors, a novel strategy designed to customize treatment.

The hope is to spare patients from the traditional hit-or-miss approach to cancer care, when expensive drugs with harmful side effects are often given without knowing whether they will work.

Doctors will hunt for 110 abnormalities, carried on 13 major cancer genes, that can predict whether drugs already on the shelf or in development might thwart a patient's tumor. They will use robots - and lab machines nicknamed John, Paul, George, and Ringo - that are capable of swiftly identifying genetic quirks in 5,000 to 6,000 patients a year, replacing labor-intensive techniques that had been used only selectively for a handful of cancers.

Mass. General's decision to make gene testing standard in cancer treatment - it's believed to be the first hospital in the nation to do so - represents a major step in delivering personalized medicine to the masses. But doctors acknowledge that it is unclear whether screening patients for an expanded library of tumor defects will actually save money on drugs, or whether it will translate into longer lives.

"Right now, as an oncologist, much of what we do is really barely educated guesswork in terms of what therapy is going to be the best for a particular patient," said Dr. Leif Ellisen, a Mass. General breast cancer specialist. "We needed a new way to think about cancer diagnosis and cancer therapy."

Caris Target Now™

Caris Life Sciences'™ molecular profiling test, Caris Target Now™, examines the genetic and molecular changes unique to a patient's tumor so that treatment options may be matched to the tumor's molecular profile.

Caris Target Now helps patients and their treating physicians create a cancer treatment plan based on the tumor tested. By comparing the tumor's information with data from published clinical studies by thousands of the world's leading cancer researchers, Caris can help determine which treatments are likely to be most effective and, just as important, which treatments are likely to be ineffective.

The Caris Target Now test is performed after a cancer diagnosis has been established and the patient has exhausted standard of care therapies or if questions in therapeutic

CARIS TARGET NOW

- Overview
- How Caris Target Now Works
- The Evidence Behind Caris Target Now
- Caris Target Now Experts
- Ordering Information
- Caris Target Now Client Services
- The Caris Registry

FIND A DOCTOR

Enter your zip code to find a doctor who can help you determine if the Caris Target Now™ test is right for your cancer.

Enter your zip code

Find

Caris Target Now
PATIENT STORY

ON-Q-ITY

DIAGNOSE, MONITOR, SAVE.

Science

The future of cancer care lies in effectively diagnosing the disease, determining personalized therapies and monitoring and adjusting treatments in real time.

While defining and implementing individualized therapies for cancer patients is still in its infancy, the time has come to take advantage of emerging scientific advances to help save lives.

On-Q-ity's proprietary technologies prepare us to provide more frequent and effective monitoring of cancer progression by proactively measuring tumor biology and intelligently adjusting therapy as necessary throughout a patient's treatment lifecycle. Combining our DNA repair biomarkers with our ability to capture and analyze circulating tumor cells (CTCs) provides a complete view of an individual patient's pending treatment options and allows for more patient-friendly monitoring of the treatment's progress.

ANTICIPATED / PROMISED TESTS
HOW REALISTIC ?
AND HOW MEANINGFUL ?

Enhanced diagnostic accuracy/sensitivity
Detection of micrometastases
Detection of minimal residual disease
Detection of circulating tumour cells
Tumour genotyping/mutational screen
Genotype- (or kinome-) specific ('targeted') therapy
Genotyping for tumour susceptibility
Whole genome sequencing

COMPLICATING FACTORS REGARDING TECHNOLOGICAL ADVANCES

Cost / availability / access
Definition of role
Cost-benefit
Necessary infrastructure

PNAS 2008 (March 4); 105: 3521-3526

Transcriptome sequencing of malignant pleural mesothelioma tumors

David J. Sugarbaker*†‡, William G. Richards*†, Gavin J. Gordon*†, Lingsheng Dong*†, Assunta De Rienzo*†, Gautam Maulik*†, Jonathan N. Glickman§, Lucian R. Chirieac§, Mor-Li Hartman*†, Bruce E. Taillon¶, Lei Du¶, Pascal Bouffard¶, Stephen F. Kingsmore‖, Neil A. Miller‖, Andrew D. Farmer‖, Roderick V. Jensen**, Steven R. Gullans††, and Raphael Bueno*†

*International Mesothelioma Program, †Division of Thoracic Surgery, §Department of Pathology, Brigham and Women's Hospital and Harvard Medi School, 75 Francis Street, Boston, MA 02115; ¶454 Life Sciences, Inc., 20 Commercial Street, Branford, CT 06405; ‖National Center for Genome Resour (NCGR), 2935 Rodeo Park Drive East, Santa Fe, NM 87505; **Virginia Bioinformatics Institute, Virginia Polytechnic Institute and State University, Blacksburg, VA 24060; and ††RxGen, Inc., 100 Deepwood Drive, Hamden, CT 06517

Communicated by Elliott D. Kieff, Harvard University, Boston, MA, December 31, 2007 (received for review July 6, 2007)

Tuesday, February 26, 2008 New York 72°|57°

THE WALL STREET JOURNAL. | WORLD

WORLD NEWS | FEBRUARY 26, 2008

Study: More Complexity In Tailoring Cancer Drugs

Article | NEW Stock Quotes | Comments

Email Print Save This Like + More Text

By KEITH J. WINSTEIN

The genetic mutations in cancer cells may vary in every patient, a study found, suggesting that drugs will need to be tailored more finely to small groups.

The small study, by doctors at the Brigham and Women's Hospital in Boston and scientists from a gene-reading unit of Roche Holding AG, is among the first to look comprehensively at the genes in cancerous tumors to find which genes went awry. It's part of a new wave of medical studies using cheaper ways of reading DNA -- the chemical blueprint found in every cell -- that promise to change the understanding of disease.

The doctors, led by David Sugarbaker, a surgeon, examined four patients with a rare and deadly lung-sac cancer called pleural mesothelioma, which strikes about 3,000 people a year. The

New Genomic Cancer Care Alliance Formed to Study Whole-Genome Sequencing in Cancer Treatment

Leading oncology and genomic medicine institutions to sequence patients with broad range of difficult-to-treat cancers

CARLSBAD, Calif., Jun 03, 2010 (BUSINESS WIRE) --Life Technologies Corporation (NASDAQ: LIFE) today announced the creation of the Genomic Cancer Care Alliance to help people battling cancer gain access to treatment options found through analysis of their genomic information. Founding partners include Fox Chase Cancer Center, Scripps Genomic Medicine, and the Translational Genomics Research Institute (TGen).The announcement came during the Consumer Genetics Conference being held June 2-4 in Boston.

The Alliance will launch a pilot study aimed at determining whether whole-genome sequencing can better guide treatment decisions across a number of difficult-to-treat cancers. US Oncology, Inc., the nation's leading integratec oncology company, is expected to serve as the contract research and site management organization for the study.

The study builds upon a research trial announced earlier this year by Life Technologies, TGen and US Oncology to sequence the genomes of 14 patients diagnosed with triple negative breast cancer whose tumors have progressed despite multiple other therapies. In contrast to the breast cancer trial, this study is the first one to evaluate the use of whole-genome sequencing information in guiding treatment decisions across a wide range of cancer types.

"This is a groundbreaking initiative for oncologists and their patients that should demonstrate how whole-genome sequencing with analytics and counseling can identify a treatment plan customized specifically for each seriously ill patient," said Paul Billings, M.D., Ph.D., the Alliance's Chief Medical Officer, and a thought leader for more than 30 years in the application of genetics in medicine, who currently serves as Director and Chief Scientific Officer of the Genomic Medicine Institute at El Camino Hospital. "There is an urgent need to define and validate a complete medical workflow for genomic-based cancer care."

The New York Times

A Decade Later, Genetic Map Yields Few New Cures

By NICHOLAS WADE
Published: June 12, 2010

Ten years after President Bill Clinton announced that the first draft of the human genome was complete, medicine has yet to see any large part of the promised benefits.

The Genome at 10

First of Two Articles

Related

Health Guides: Genetics | Genes

Readers' Comments

Readers shared their thoughts on this article.

Read All Comments (149) »

For biologists, the genome has yielded one insightful surprise after another. But the primary goal of the $3 billion Human Genome Project — to ferret out the genetic roots of common diseases like cancer and Alzheimer's and then generate treatments — remains largely elusive. Indeed, after 10 years of effort, geneticists are almost back to square one in knowing where to look for the roots of common disease.

A Decade Later, Genetic Map Yields Few New Cures

By Nicholas WADE
NEW YORK TIMES
Published: June 12, 2010

“Genomics is a way to do science, not medicine,” said Harold Varmus, president of the Memorial Sloan-Kettering Cancer Center in New York, who in July will become the director of the National Cancer Institute.

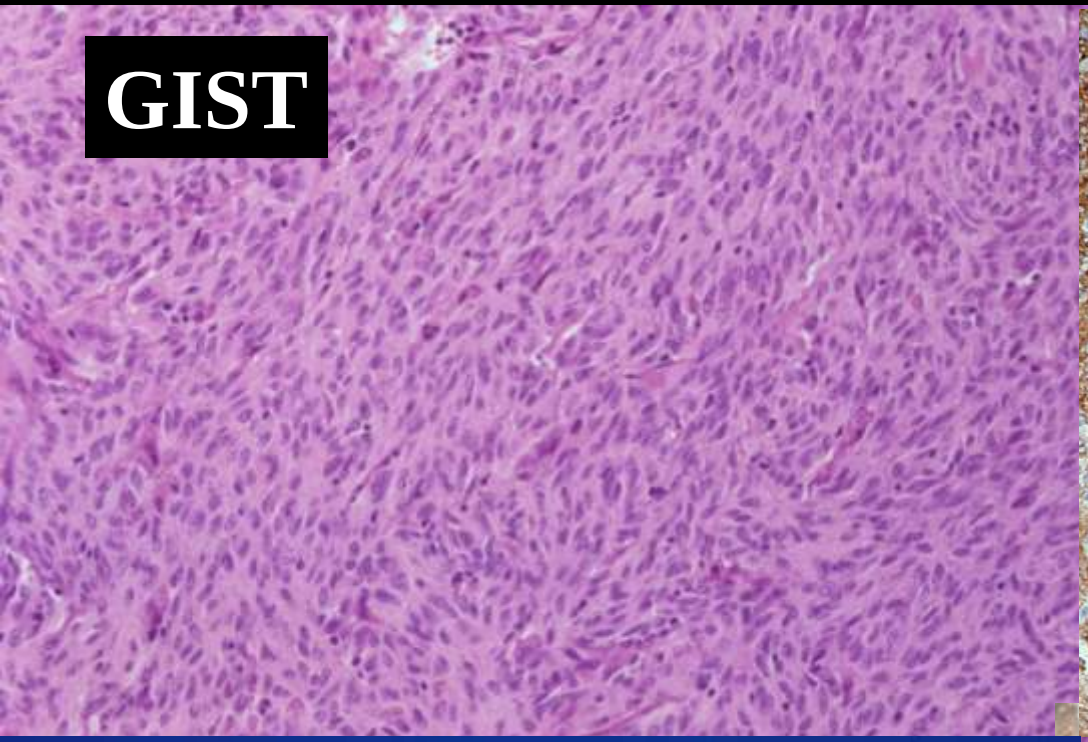
STATLINE
Federal and State News Briefs
September 30, 2010 • Volume 26, Number 20
Next Issue: October 14, 2010

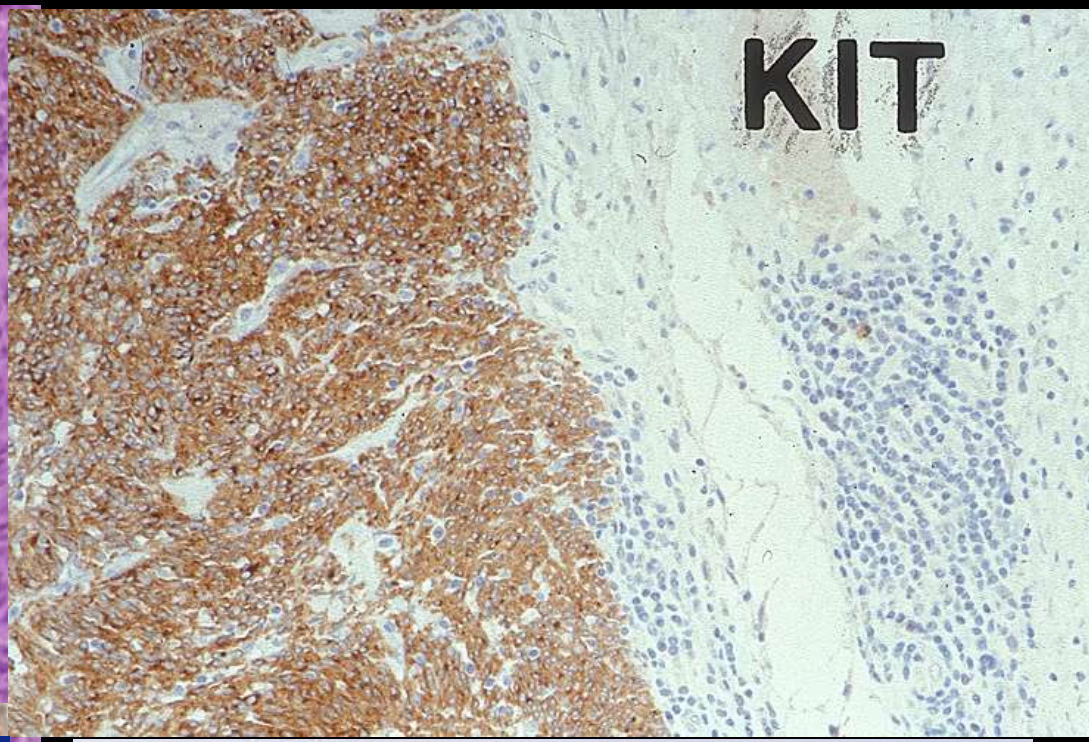
CAP Leaders Detail Strategies to Transform Future of Pathology

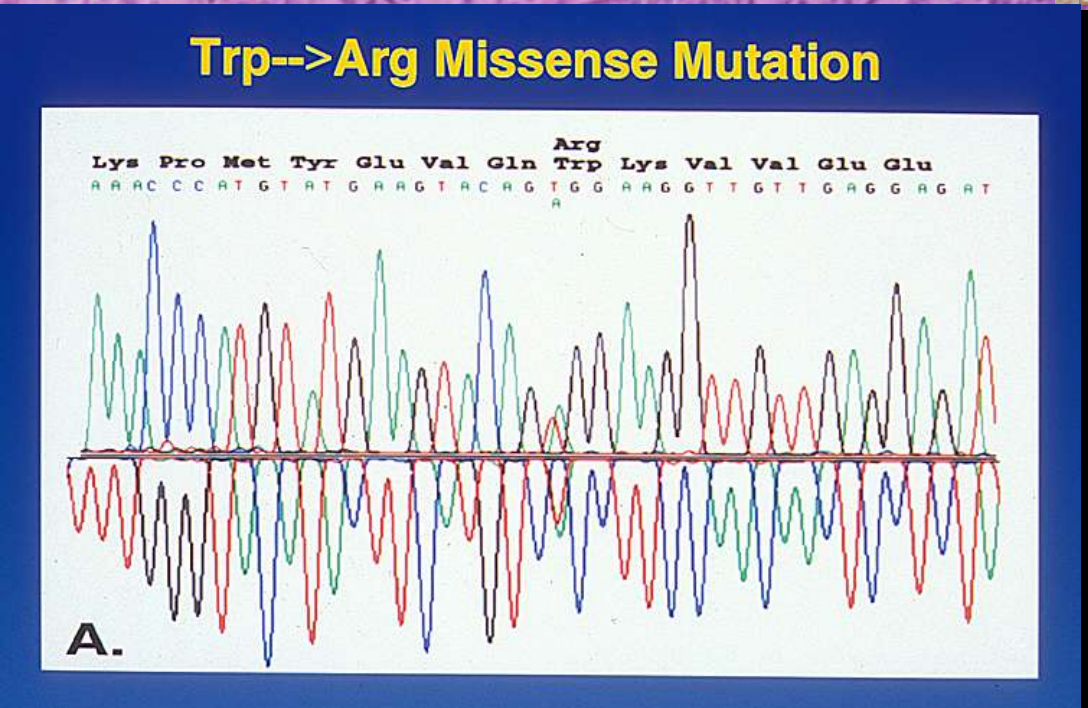
The seminal event of this week's CAP '10 annual meeting was the detailing of the College's plans for a Transformation initiative, focused on fostering new and enhanced roles for pathologists in the rapidly evolving health care landscape.

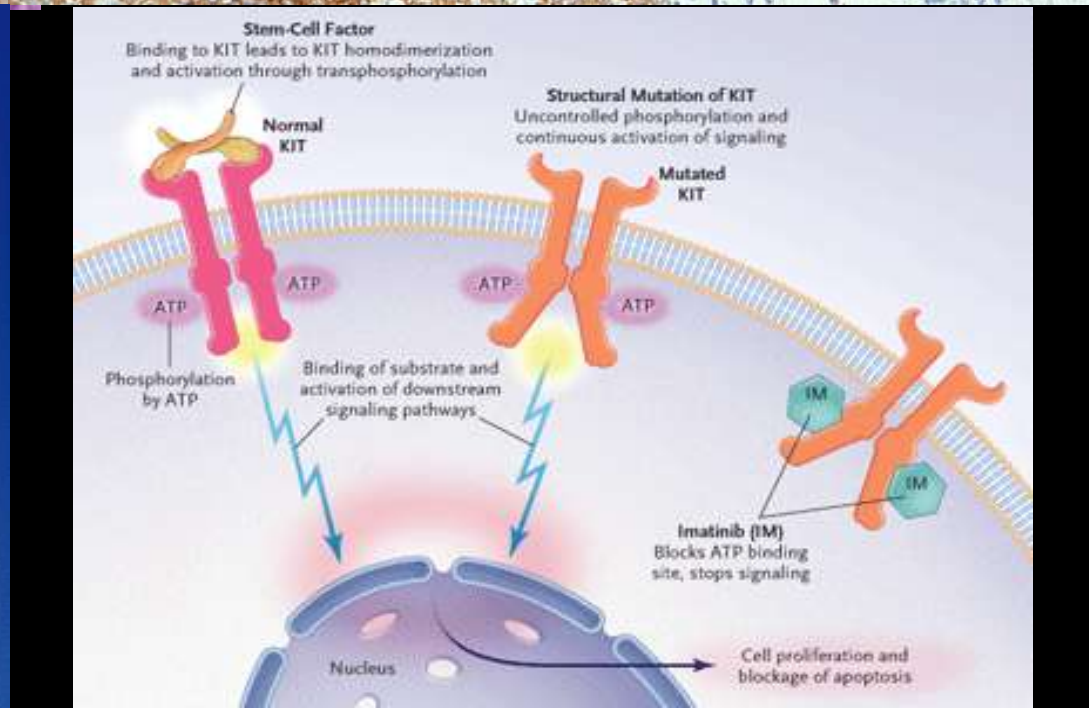
While CAP leaders have been calling for a Transformation push for some time, speakers at this multi-media plenary laid out why these initiatives are so important—i.e, the "Case for Change"—and what exactly these efforts will entail. Held Tuesday, Sept. 28, Chicago television journalist Phil Ponce moderated the event featuring panel discussions interspersed with video presentations from over 35 leading pathologists and other health care experts across the country who provided evidence supporting the Case for Change.

But pathologists need to seize ownership of these evolving areas—and fast, according to speaker Mark S. Boguski, MD, PhD, Associate Professor at Harvard Medical School's Center for Biomedical Informatics. "I predict that within three years whole genome analysis will be the standard of care for certain cancers," he explained. "The genome is the specimen of the future and pathologists, with their core competencies, have a singular opportunity to claim ownership of its clinical interpretation for medical application."


GIST


KIT


Trp-->Arg Missense Mutation
Lys Pro Met Tyr Glu Val Gln Arg Trp Lys Val Val Glu Glu
A.


Stem-Cell Factor
Binding to KIT leads to KIT homodimerization and activation through transphosphorylation
Normal KIT
Structural Mutation of KIT
Uncontrolled phosphorylation and continuous activation of signaling
Mutated KIT
ATP
ATP
ATP
ATP
Phosphorylation by ATP
Binding of substrate and activation of downstream signaling pathways
IM
IM
Imatinib (IM)
Blocks ATP binding site, stops signaling
Nucleus
Cell proliferation and blockage of apoptosis

GASTROINTESTINAL STROMAL TUMOURS
MUTATIONAL ANALYSIS

- **Approx. 75-80% have *KIT* mutations and 5-7% have *PDGFRA* mutations, irrespective of type/size**

	% of cases	Gleevec response
***KIT* exon 11**	**60-65**	**80-85%**
***KIT* exon 9**	**10-15**	**45-50%**
***KIT* exon 13**	**< 5%**	**Too few data**
***KIT* exon 17**	**< 5%**	**Too few data**
***PDGFRA* (exons 12/18)**	**~ 6%**	**Variable**

- **Tumours lacking either *KIT* or *PDGFRA* mutations still show 40-45% response – but progress sooner**
- **Gleevec response, predicted by mutation type, correlates with survival**
- **'Acquired' Gleevec resistance results from 2 mutations**

CYTOGENETIC ABERRATIONS IN SOFT TISSUE SARCOMAS

Tumor type	Cytogenetic changes	Gene fusion
Ewing's sarcoma/primitive neuroectodermal tumor	t(11;22)(q24;q12)	*FLI-1-EWSR1*
	t(21;22)(q22;q12)	*ERG-EWSR1*
	t(7;22)(p22;q12)	*ETV1-EWSR1*
	t(17;22)(q12;q12)	*EIAF-EWSR1*
	t(2;22)(q33;q12)	*FEV-EWSR1*
	t(16;21)(p11;q22)	*FUS-ERG*
Alveolar rhabdomyosarcoma	t(2;13)(q35;q14)	*PAX3-FOXO1A*
	t(1;13)(p36;q14)	*PAX7-FOXO1A*
Myxoid/round cell liposarcoma	t(12:16)(q13;q11)	*DDIT3-FUS*
	t(12;22)(q13;q11-12)	*DDIT3-EWSR1*
Desmoplastic small round cell tumor	t(11;22)(p13;q12)	*WT1-EWSR1*
Synovial sarcoma	t(X;18)(p11.2;q11.2)	*SSX1-SYT*
		SSX2-SYT
Clear cell sarcoma/ so-called angiomatoid 'MFH'	t(12;22)(q13;q12)	*ATF1-EWSR1*
	t(2;22)(q33;q12)	*CREB1-EWSR1*
Extraskeletal myxoid chondrosarcoma	t(9;22)(q22;q12)	*NR4A3-EWSR1*
	t(9;17)(q22;q11)	*NR4A3-TAF15*
Dermatofibrosarcoma protuberans/ giant cell fibroblastoma	t(17;22)(q22;q13)	*PDGFB-COL1A1*
Infantile fibrosarcoma	t(12;15)(p13;q25)	*ETV6-NTRK3*
Inflammy myofibroblastic tumor	2p23 translocations	*ALK* fusions
Alveolar soft part sarcoma	t(X;17)(p11;q25)	*ASPL-TFE3*
Low grade fibromyxoid sarcoma	t(7;16)(q33;p11)	*FUS-CREB3L2*
	t(11;16)(p13;p11)	*FUS-CREB3L1*

BUZZWORDS IN SURGICAL PATHOLOGY

Biomarkers

Personalised medicine

‘Theranostics’

WHAT IS A BIOMARKER ?

'A characteristic that is objectively measured as an indicator of normal biologic or pathologic processes or pharmacologic responses to a therapeutic intervention.'

NIH, 2001

Can be prognostic, predictive of treatment response or measure/monitor treatment response

TARGET IDENTIFICATION/VALIDATION

- Increasing focus/demand, using ever smaller tissue samples including FNAs
- Because of morphologic context, requires pathology expertise
- May increasingly require standardisation of methods and reagents
- Includes disease monitoring/ assessment of treatment response

‘Prediction of therapeutic response by molecular profiling is the logical and natural extension of the work of the surgical pathologist…. If we are unable to find a way to implement molecular profiling into our practices, surgical pathologists will be excluded from one of the most exciting and transformational developments to come around in a long time.’

Thomas Giordano
Am J Surg Pathol 2006

IMPACT OF TARGETED THERAPIES

Agent	Target	Disease	Survival
Trastuzamab (Herceptin)	HER2/neu	Breast ca	Localised MFS 90% vs 74% @ 4yrs Metastatic 25 vs 20 months
Imatinib (Gleevec)	KIT	GIST	Localised RFS 92% vs 80% @<2yrs Metastatic 55 vs <6 months
Gefitinib (Iressa)	EGFR	Lung ca	Metastatic O.S. -18.6 vs 17.3 mo - 30.5 vs 23.6 mo
Cetuximab (Erbitux)	EGFR	Colon ca	Metastatic O.S. - 11 vs 7 months (depends on *KRAS* status)

Average costs:

Herceptin & Gleevec $60K/yr; Cetuximab $30K for 8 week course

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 19, 2010 VOL. 363 NO. 8

Improved Survival with Ipilimumab in Patients with Metastatic Melanoma

F. Stephen Hodi, M.D., Steven J. O'Day, M.D., David F. McDermott, M.D., Robert W. Weber, M.D., Jeffrey A. Sosman, M.D., John B. Haanen, M.D., Rene Gonzalez, M.D., Caroline Robert, M.D., Ph.D., Dirk Schadendorf, M.D., Jessica C. Hassel, M.D., Wallace Akerley, M.D., Alfons J.M. van den Eertwegh, M.D., Ph.D., Jose Lutzky, M.D., Paul Lorigan, M.D., Julia M. Vaubel, M.D., Gerald P. Linette, M.D., Ph.D., David Hogg, M.D., Christian H. Ottensmeier, M.D., Ph.D., Celeste Lebbé, M.D., Christian Peschel, M.D., Ian Quirt, M.D., Joseph I. Clark, M.D., Jedd D. Wolchok, M.D., Ph.D., Jeffrey S. Weber, M.D., Ph.D., Jason Tian, Ph.D., Michael J. Yellin, M.D., Geoffrey M. Nichol, M.B., Ch.B., Axel Hoos, M.D., Ph.D., and Walter J. Urba, M.D., Ph.D.

ABSTRACT

BACKGROUND

An improvement in overall survival among patients with metastatic melanoma has been an elusive goal. In this phase 3 study, ipilimumab — which blocks cytotoxic T-lymphocyte–associated antigen 4 to potentiate an antitumor T-cell response — administered with or without a glycoprotein 100 (gp100) peptide vaccine was compared with gp100 alone in patients with previously treated metastatic melanoma.

Drs. Hodi and O'Day contributed equally to this article.

The authors' affiliations and participating investigators are listed in the Appendix. Address reprint requests to Dr. Hodi at the Dana–Farber Cancer Institute, 44 Binney

THE WALL STREET JOURNAL. | BUSINESS

Europe Edition ▾ | Today's Paper • Video • Blogs • Journal Community

SEPTEMBER 15, 2010, 7:01 P.M. ET

UK Body Rejects Novartis' Gleevec For Higher GIST Dosing

LONDON (Dow Jones)--Britain's cost watchdog NICE Thursday said it will not recommend Novartis AG's (NOVN.VX) oncology medicine Gleevec at doses of 600 or 800 milligrams per day for people with inoperable and/or metastatic gastrointestinal stromal tumors, whose disease has progressed after being treated with a lower dosing of the drug, which is also called imatinib.

Gastrointestinal stromal tumors, or GIST, are a rare kind of tumor which predominantly occur in the stomach or bowel. If they become malignant and are confined to one area of the stomach or bowel, they can often be removed surgically, but some cannot.

The National Institute for Clinical Excellence, which determines what medicines can be used by the publicly-funded National Health Service, said in a statement that "increased doses of imatinib are not an appropriate use of NHS resources for people with unresectable and/or metastatic GIST whose disease has progressed after taking 400 milligrams per day imatinib."

NICE's chief executive Andrew Dillon said: "this review looks specifically at increased doses of imatinib after treatment with milligrams per day imatinib has stopped working...The independent Appraisal Committee found that since the original guidance was published in October 2004, there have been no new good quality clinical and cost effectiveness data produced on doses of 600 or 800 milligrams per day imatinib given after disease progression on a dose of 400 milligrams per day. On this basis, we cannot recommend these higher doses of imatinib for use on the NHS."

If a daily Gleevec dose of 400 milligrams per day was given for a year, the drug cost would be around GBP19,500 per patient per per year, NICE said. A 600 milligrams per day dosing regime would cost some GBP29,300 annually and that would rise to GBP39,067 for 800 milligrams per day.

POTENTIAL "ENHANCEMENTS" TO DIAGNOSTIC PATHOLOGY REPORTS

- **Electronic access**
- **Inclusion of images**
- **Inclusion of/links to peer-reviewed refs**
- **Provision of frequently-asked questions and answers (for patients)**
- **Links to internet resources – but much information on-line is of dubious quality…**

May provide patient education/insight

CARIS Dx
8400 ESTERS BLVD. SUITE 190
IRVING, TEXAS 75063
866-588-3280 • FAX: 866-628-3280

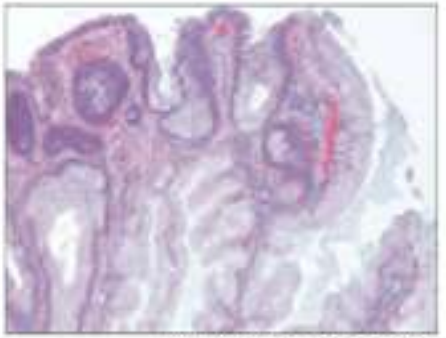
SURGICAL PATHOLOGY REPORT

PATIENT INFORMATION		COLLECTED	22 APR 2007	ORDERED BY
PATIENT, JANE FEMALE, AGE 48 DOB 17 FEB 1959 **ACCESSION #: DS00-0000**		RECEIVED	23 APR 2007	MATTHEW THOMAS, M.D. ABC ENDOSCOPY CENTER 12345 STREET NAME YOUR TOWN, USA 54321 (123) 456-7890
		REPORTED	24 APR 2007	
		MRN/CHART	0000000	
		OTHER CLINICIAN	BOB SMITH, M.D.	

FINAL DIAGNOSIS

A. **Ascending Colon:**
- **SESSILE SERRATED ADENOMA ("SESSILE SERRATED POLYP") WITH LOW-GRADE ADENOMATOUS DYSPLASIA.**
See Comment.

COMMENT: Patients with Sessile Serrated Adenomas, especially with cytologic dysplasia, are at increased risk for the development of adenocarcinomas showing microsatellite instability. This progression may occur at a more rapid rate than with traditional adenomas. Complete endoscopic excision is recommended if clinically appropriate and if not already performed. If unresectable, repeat colonoscopy at a shortened interval (e.g., 1 year) with sampling of suspicious areas or surgical resection may be indicated. (See REFERENCE below.)



000-0000-A - Ascending Colon

B. **Sigmoid Colon:**
- **TUBULAR ADENOMA.**

CLINICAL INDICATIONS/HISTORY

Screening colonoscopy. Paternal history of colonic adenocarcinoma age 50.

FINDINGS/SPECIAL REQUESTS

2cm polyp in ascending colon. 3mm polyp in sigmoid colon.

GROSS DESCRIPTION

A. The first container is labeled "ascending colon". It contains a polypoid piece of light tan mucosal tissue measuring 2.1cm. in greatest dimension. The polyp margin is inked black, sectioned, and submitted in cassettes A1 and A2. Due to large size of polyp, specimen will be processed overnight for optimal fixation.

B. The second container is labeled "sigmoid colon". It contains one piece of light tan mucosal tissue 0.3 cm. in greatest dimension. The specimen is submitted in cassette B.

MICROSCOPIC EXAMINATION

Microscopic examination performed, supportive of the FINAL DIAGNOSIS above.

REFERENCE

1) Goldstein NS. Small Colonic Microsatellite Unstable Adenocarcinomas and High-Grade Epithelial Dysplasias in Sessile Serrated Adenoma Polypectomy Specimens: a study of eight cases. Am J Clin Pathol 2006; 125(1): 132-145. 2) Rashid A and Issa J. CpG Island Methylation in Gastroenterologic Neoplasia: A Maturing Field. Gastroenterol 2004; 127(5): 1578-1588. 3) Snover D, et al. Serrated Polyps of the Large Intestines: a morphologic and molecular review of an evolving concept. Am J Clin Pathol 2005; 124(3): 380-391.

MODERN PATHOLOGY

Letter to the Editor

Modern Pathology (2010) **23,** 1298–1300; doi:10.1038/modpathol.2010.108

The FAQ initiative explaining pathology reports to patients

Jonathan I Epstein[1]

[1]Department of Pathology, The Johns Hopkins Medical Institution, Baltimore, MD, USA

Correspondence: Jonathan I Epstein, E-mail: jepstein@jhmi.edu

To the Editor: Concern has been expressed by pathologists about the lack of visibility of our profession and our role as clinicians by both the general public and the medical community, despite the fact that our contribution to the care of patients with cancer and other diseases has never been greater. In an attempt to reach the goal of enhanced visibility, an international group of patient-centric pathologists organized by Juan Rosai met in Sirmione, Italy on 2–4 May 2008. One outcome of this meeting concerned the recognition that patients are becoming more active participants in their health care. Not only are they using the internet to research their disease and find specific pathologists to offer second opinion reviews, but increasingly patients are also reading their pathology reports.

EVOLUTION OF PATIENT SAFETY IN SURGICAL PATHOLOGY

Barcoding

Specimen / slide tracking

Laboratory automation

Electronic documents / scanning

Checklists

Synoptic reports

SELECTIVE PRESSURES TOWARDS SUBSPECIALISATION

- Increasing complexity / detail in routine surgical pathology
- Virtual impossibility of credible expertise across all surgical pathology
- Increasingly specialised clinical care
- Tertiary care model of clinical care
- Patient expectations
- Almost inevitably better service

ADVANTAGES OF TOTAL SUBSPECIALISATION

- Enhancement of diagnostic expertise
- Reports more accurately tailored to clinical need
- Clinical perception of better/more responsive service
- Recognised point person for questions and conferences
- Standardised reporting style/format

DISADVANTAGES OF TOTAL SUBSPECIALISATION

- Faculty expansion / cost
- Non-specialist cross-coverage
- Logistical issues/short rotations for trainees
- Potential loss of flexibility for junior faculty
- Potential undermining of other faculty
- Loss of faculty with broad interests
- Fragmentation of pathology service
- Need more space/equipment

What impact do new technologies, the rapid pace of innovation and change, and the associated hype have on the expectations and beliefs of clinicians and patients ? And how (or to what extent) should that influence the way surgical pathology evolves ?

SOCIETAL CHANGES / PRESSURES

Medicine is increasingly patient-driven

Unrealistic wishes to "never give up"

Doctors increasingly don't/won't say no

Death is viewed as an option

50% (? more) of lifetime healthcare costs are in last 6 months of life

25% of entire Medicare budget in the USA is spent on last 6 months of life

Limited cost-benefit analysis

Why do MDs so often say yes ?

Should MDs be contributing to prevailing unrealistic patient expectations and high expenditures?

Why do many MDs say that they would not want the same tests/treatment ?

Ethical concerns

HOW ARE CLINICIAN EXPECTATIONS CHANGING ?

- Want more detailed information
- Want results more quickly
- Want access to new “sexy” tests
- Want to offer their pathology service/report as “special”
- Want more treatment guidance
  - not only target identification

Often driven by patient demand

“What about the margins ?”

“Do we need to re-excise ?”

“What grade is it ?”

“What is the margin status (or grade) of that metastasis I resected ?”

“Please send it for that [new and often not validated] test”

BELIEFS OR 'HYPE' WHICH GET GENERALISED

- Narrow margin + radiation is as good, if not better, than wide margin
- Value of resecting metastatic disease or debulking uncontrolled disease
- Value of hunting for the unknown primary
- Presence of a "treatable" protein, mutation or pathway is always clinically significant
- Targeted therapies may be curative

CONUNDRUM FOR SURGICAL PATHOLOGY

- Pathologic assessment is more informative (diagnosis / prognosis) than ever before
- Pathologic diagnosis is so reproducible that it consistently leads to discovery / validation of molecular or genetic signatures
- Clinicians often don't have specific treatment or other ability to stratify patients based on the data which we provide
- Increasing assumption (with limited evidence) that clinicians should instead treat / inhibit a mutation or pathway (if present)

HOW ARE PATIENT EXPECTATIONS CHANGING ?

- Want to read (and understand) their pathology reports
- Want detailed information - quickly
- Expect subspecialty expertise
- Increasingly seek to request tests
- May want to communicate directly with pathologist

Often driven by information from internet or patient support groups

In the minds of many patients in developed countries, modern medicine offers:

“Science”
“Black and white answers”
“Personalised treatment”
“A cure which is just around the corner”
“A way to avoid death”

Often little understanding and web-based misinformation

MacDonald’s

MacDonald's
Starbucks

MacDonald's

Starbucks

"Cool", "Awesome"

MacDonald's
Starbucks
"Cool", "Awesome"
Celebrity culture

MacDonald's
Starbucks
"Cool", "Awesome"
Celebrity culture
Morbid obesity

MacDonald's
Starbucks
"Cool", "Awesome"
Celebrity culture
Morbid obesity
"Death is optional"

SHARED WEAKNESS OF HUMAN NATURE

Fashion

Assumption that something new must be better

Follow the promise of “objectivity”

Belief in hype / exaggeration (? based on hope)

WHAT SHOULD WE BE ?

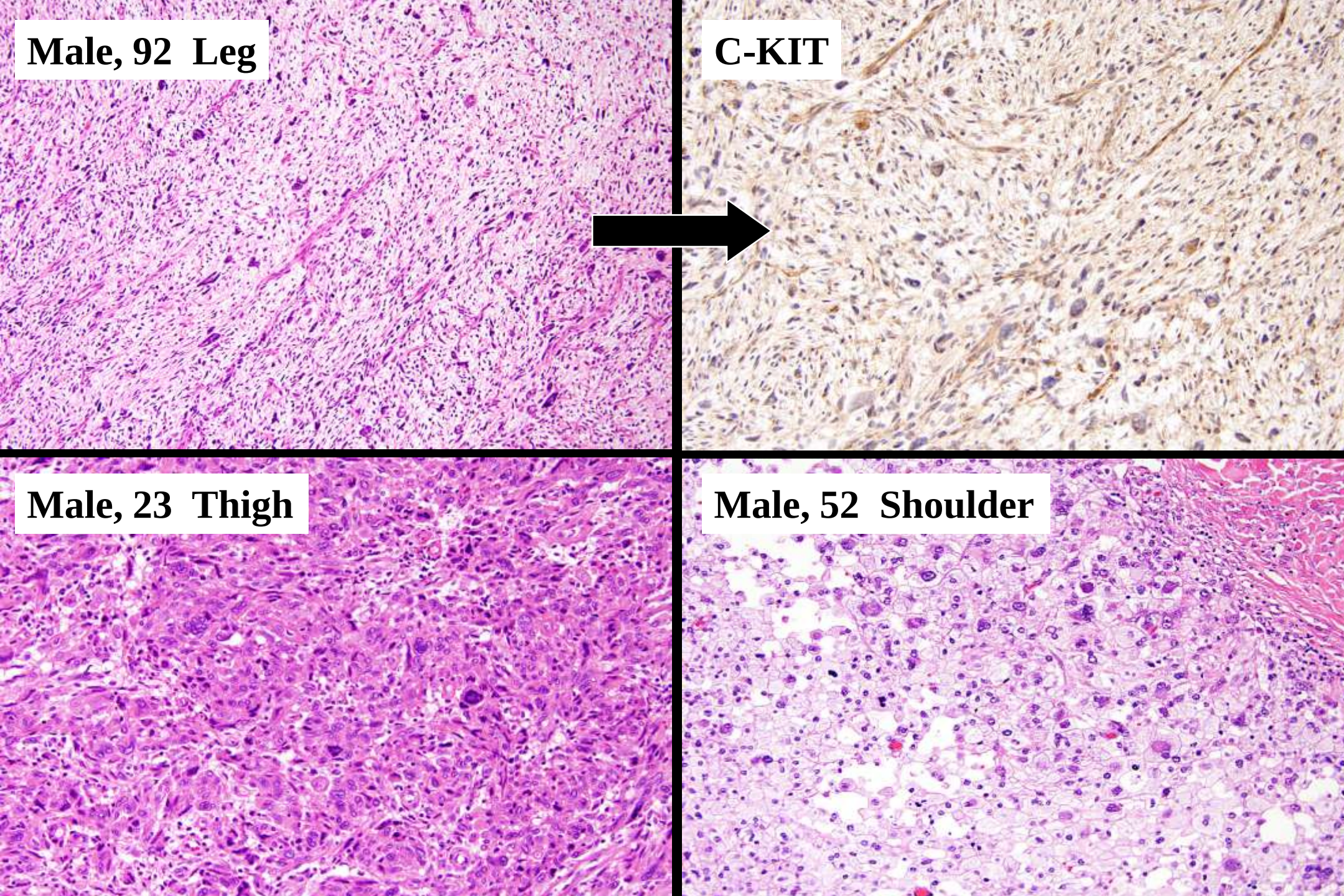
Passive purveyors of data (and tests)

OR

Integrated member / guiding hand in the clinical team – seeking to enable informed choices for clinician and patient

EXAMPLES OF INAPPROPRIATE TESTS - USUALLY CLINICIAN-REQUESTED

- **Immunostaining for c-kit (CD117) as justification for treating with imatinib**
- **Immunostaining for ER/PR to justify hormonal therapy in non-breast ca**
- ***EGFR* mutational analysis in squamous cell carcinoma of lung**
- **Speculative mutational analysis to allow use of novel inhibitor in the absence of data (eg *EGFR, ALK etc*)**


Male, 92 Leg
C-KIT
Male, 23 Thigh
Male, 52 Shoulder

WHAT ROLE DOES/SHOULD THE PATHOLOGIST HAVE IN ANCILLARY TEST SELECTION ?

- Phenotypic or molecular genetic test requested by clinician without any reasoned basis
- Molecular testing to prove a diagnosis
- Chemosensitivity testing requested by either clinician or patient
- Gene expression profiling (also genome sequencing) requested by clinician or patient
- Kinome assay (usually in a research lab)

"Personalised medicine"

L.a.n.c.e. Home | Intro | Contact | Download | Literature | Links | Imprint

The reason why
The principle
Examples from the lab
What is important?
The advantages

Intro | Preface

Individualized chemotherapy planning requires clinical experience.

Essential for a successful chemosensitivity test is not only a valid lab technique. The individual choice of the regimen to be tested and the transfer of lab results into clinical decisions-making processes is at least equally important. This makes high clinical competence concerning chemotherapy of tumor patients indispensable.
L.a.n.c.e. offers both. Our clinical directors are not only scientists of international format, but also renowned tumor specialists in their respective fields with long lasting clinical experience acquired at University hospitals.

Precision Therapeutics®
The Science of Individualizing Cancer Therapy

Contact PRECISION: info@precisionthe

HOME | ▶ CHEMOFX | ▶ ABOUT PRECISION THERAPEUTICS | ▶ NEWS & EVENTS | ▶ CONTACT US

CHEMOFX®
A product of Precision Therapeutics, Inc.

Her cancer is being treated with 10 different chemotherapies.
But she isn't.

By testing multiple chemotherapies on a patient's cancer cells before treating a cance patient, ChemoFx® helps determine the chemotherapies that are more likely to be effective and helps guide the physician away from therapies that are more likely to b ineffective- giving cancer patients a powerful advantage in the fight against cancer.

What is ChemoFx?

ChemoFx® is a drug response marker. It's a test that quantifies an individual cancer patient's probable tumor response to various chemotherapeutic and biologic agents— providing both sensitivity and resistance information. As such, ChemoFx® provides valuable insights that help guide physicians' treatment decisions and give both physic and patients an edge against cancer.

Chemosensitivity Testing

Chemosensitivity or Extreme Drug Resistance requires live tissue cells for testing.
We have been doing throat cultures and pus cultures for decades. Finding out what will kill the bugs and what won't has been the "standard of care" in infectious disease for yonks. Why can't we grate some fresh cancer tu grow tissue cultures of the tumor, and then sprinkle different chemotherapy agents over the cultures...to see what kills the growing cells, and what doesn't?

We CAN do this. There are different methods including, among others, the human tumor colony-forming assay (HTCA), the succinate dehydrogenase inhibition (SDI) test, the fluorescent cytoprint assay, the adenosine trip assay (ATP assay), Differential Staining and Cytotoxicity (DiSC) Assays, and the MTT assay. It is a bit more complicated than making cookies, but the live tissue cultures of the cancer can be used to do the following:

1. Determine what chemotherapy drugs work well on the cultures. Because of LMS tumor cell heterogeneity, development of resistance, and generally poorly effective chemotherapy agents, this may not be of as much one would wish.
2. Determine what chemotherapy drugs are useless for this tumor.
3. Check out new cancer drugs on the tumor, to see if it works for that kind of tumor?
4. Check a test's predictions against what actually happened when the tumor owners were given the chemotherapy agents. [Seeing how good the test is].
5. Suggest prognosis for patients, depending upon whether their tumor is chemosensitive or chemoresistant.

ISSUES OF UTILISATION

What tests do we provide ?
Who decides ? (Clinicians/patients ??)
How do we cover/recoup costs before tests are fully accepted ?
Which tests are truly useful ?
Which are ‘window dressing’ ?
- or simply offer false hope ?

Pathology should embrace new technology, should engage in validation & cost-benefit analysis and should be responsible for incorporation of the results – but only where appropriate

SURGICAL PATHOLOGIST AS PATIENT ADVOCATE

- Accurate diagnosis is major determinant of treatment
- Issues of caution vs. overconfidence
- Guiding surgeon / oncologist
- Rational test selection
- Patient questions/demands are increasing - educational opportunity
- Realistic appraisal of disease

Dear dr. Christopher,
Good afternoon.
Sorry to disturb you.
I'm the father of Paola ..... for which you carried out an analysis on the material related to a pelvic mass on behalf of dr. .... , which was attending also her surgery on the 3rd february 2007 in Rio de Janeiro by dr. Jose..... .
On this respect plse refer to your analysis result dd 28th february 2007.
Subsequently of that my daughter being submitted to a daily sections of physiotherapy in order to improve the lost movement of her right foot in consequence of the surgery, and also on the last week she completed a period of 45 days for thirty sections of radiotherapy made at the hospital Sirio Libanes (Sao Paulo) under the surveliance of dr. ..... .
Understood that the radiotherapy was made by the use of IMRT system.
Apparently, there was no major problems unless the loose of her weight in approx. 4 kgs which i belive will be recovered soon.
In near future she is scheduled to made the first examination (magetic ressonance) after the surgery.
The reason of my e-mail to you, is to know your opinion about the necessity or not of a further treatment (chemitherapy), and if possible to know the best indicated way, and consequences which she could from such additional tratment.
Resuming, in your opinion, at this stage or in a future, she need to do such additional treatment.
Thanks in advance for your assistance.

Dear Dr. Fletcher,

I am a researcher at UCSF and my husband is a Harvard doctoral student. You recently (5/2/07) consulted on a diagnosis for my husband (Sean _ of low-grade myxofibrosarcoma with Dr. Andrew ' at UCSF. It looked from the pathology report that it was not 100% clear if the tumor was an atypical lipoma or a sarcoma. Thus, we are unsure what treatment options are available and most appropriate for this conditio or with whom we should consult. Is there a doctor you would recommend we seek who specializes in the treatment of sarcomas? We would be grateful for any referrals and/or sources we could look to for information about prognosis, future screening, etc.

Best regards,

Dear Dr. Fletcher:
Parden me for contacting you directly but I thought you would be very interested to have the information that I would like to share with you. My husband, Roger F. was diagnosed with "undefined cancer of an unknown primary" and also with a menengioma tumor in 1999. You sent a letter to the pathology department of General Hospital at the time (I am scanning my copy of that letter and attaching it to this e-mail. You mentioned at the time that you "would be very interested to hear of any follow-up in this unusual case." Well, I am also enclosing a report that we got a copy of recently (also regarding my husband and stating he now has "metastatic meningioma") from General Hospital. This report states that Dr. Chistopher Fletcher of Brigham and Women's Hospital has reviewed all material and concurs. I am now taking care of my husband with the help of hospice. I know that you are a very busy man, but I thought in light of what you stated in the first letter you would find it interesting that 7 years later this happened to him.

2. Are there other treatments, conventional or not conventional that are known to deal
well with this disease?
3. Do you know another case of this specific sarcoma in XXXXXX ? If so, can you connect me with this person?
4. Do you know another research about this sarcoma, which can explain me more about the disease – its origin, main characteristics, etc.?

My name is XXXXX YYYYYY. You examined my tumor and found it to be a low grade fibromyxoid sarcoma. You made clear that a re-excision is necessary. How urgent is the surgery? I am asking because I made plans to study in Nepal for four months. I have a flight ticket for next monday. I would really like to go so it's important to me to know how much the risk of metastasis is increasing if I postpone the surgery to december.

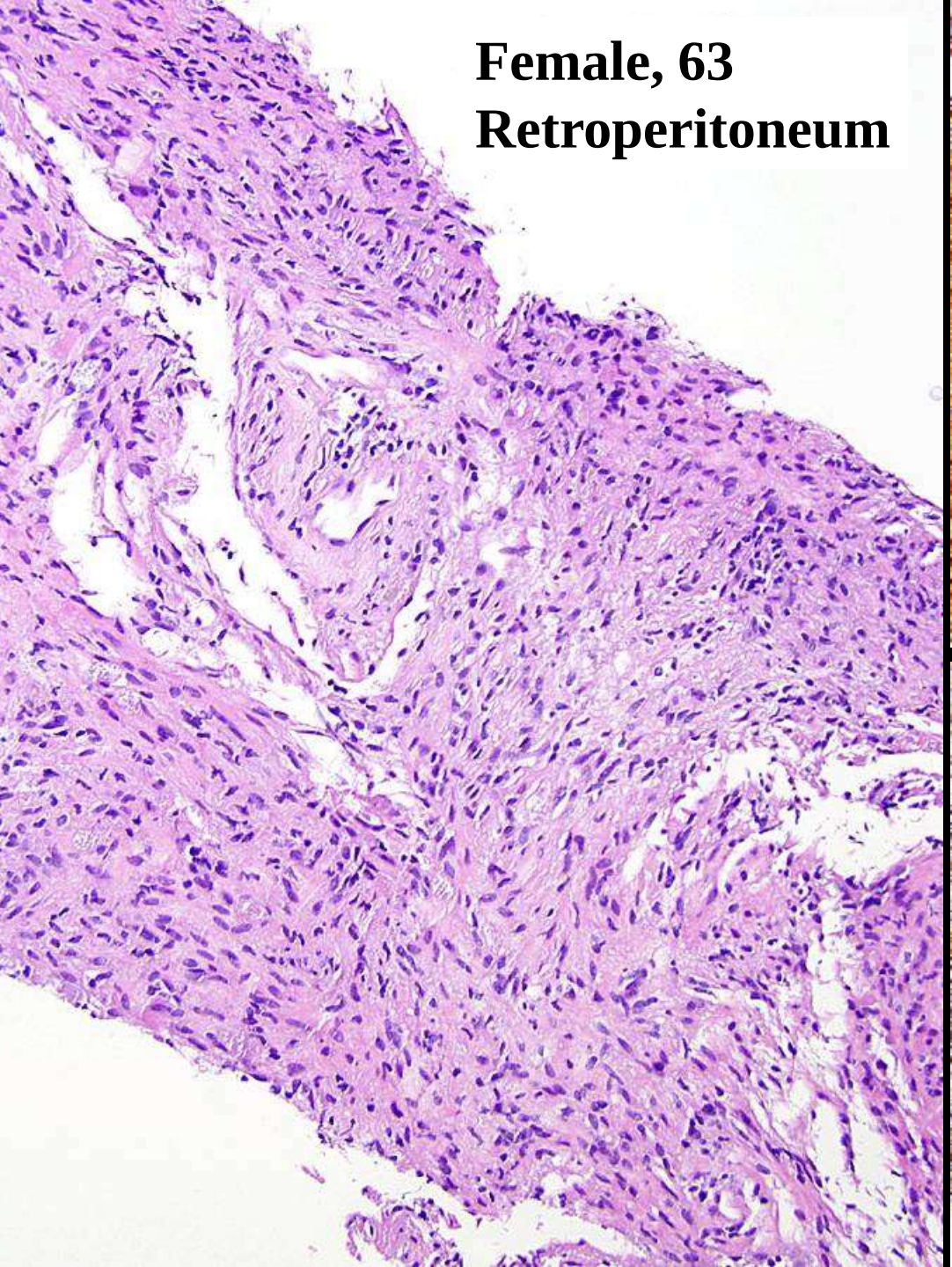
Dear Dr Flecher,

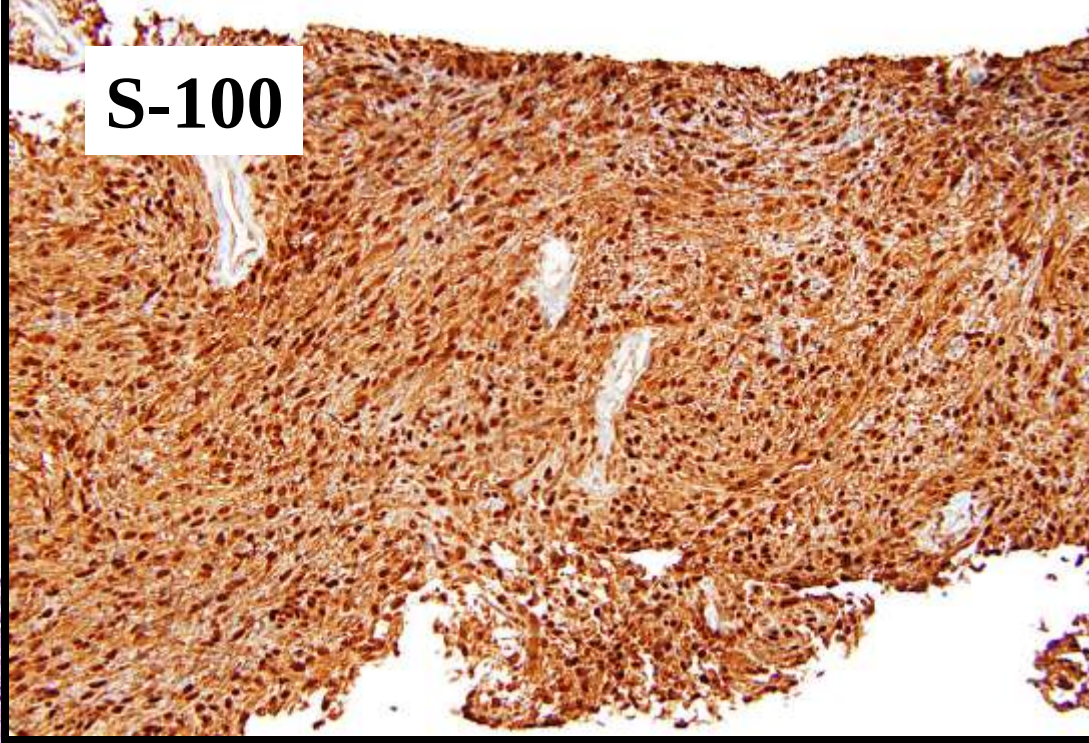
I know you are out of the office, but I am requesting treatment recommendations on a consultation . It is your reference number BS09-XXXXXXX.

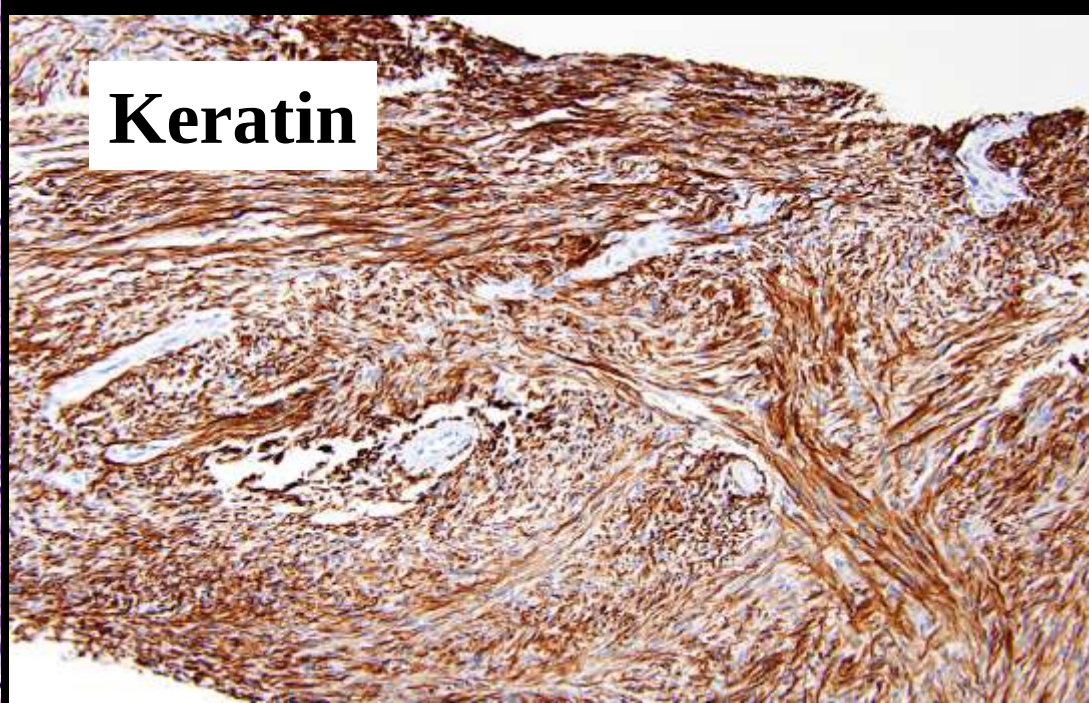
Your interpretation was malignant spindle cell neoplasm most suggestive of keratin-negative spindle cell squamous cell carcinoma. From my research a complete excision with close clinical follow up is what I will suggest . Do you agree?

CLINICAL RESOURCE UTILISATION AS A FORM OF PATIENT ADVOCACY

- A 63 year old woman develops acute non-specific abdominal discomfort
- She attends the emergency room
- CT scans of chest and abdomen are performed
- Retroperitoneal “adenopathy” is identified
- Patient returns the following week for a needle biopsy by interventional radiology


Female, 63
Retroperitoneum


S-100


Keratin

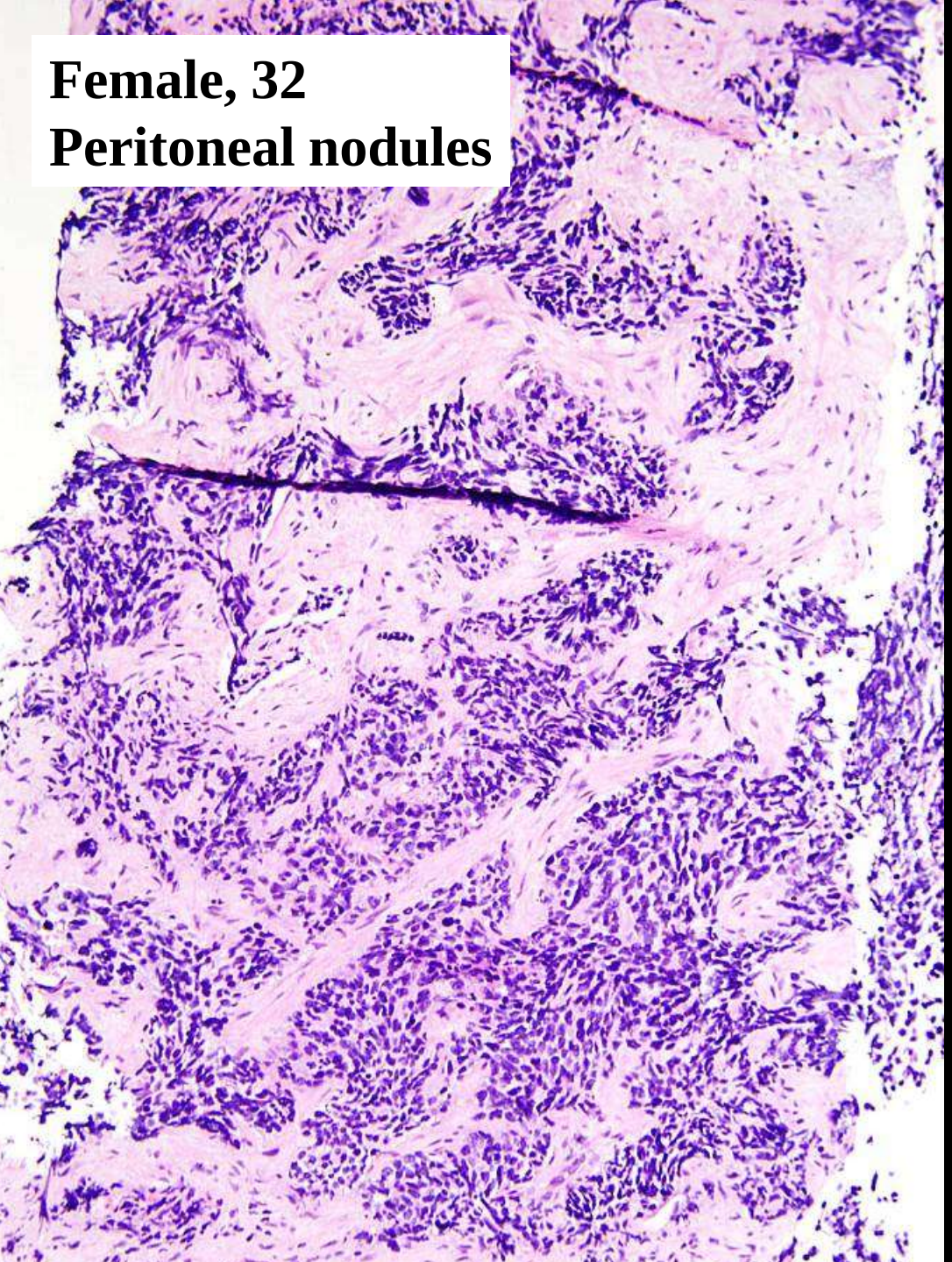
PAST MEDICAL HISTORY:

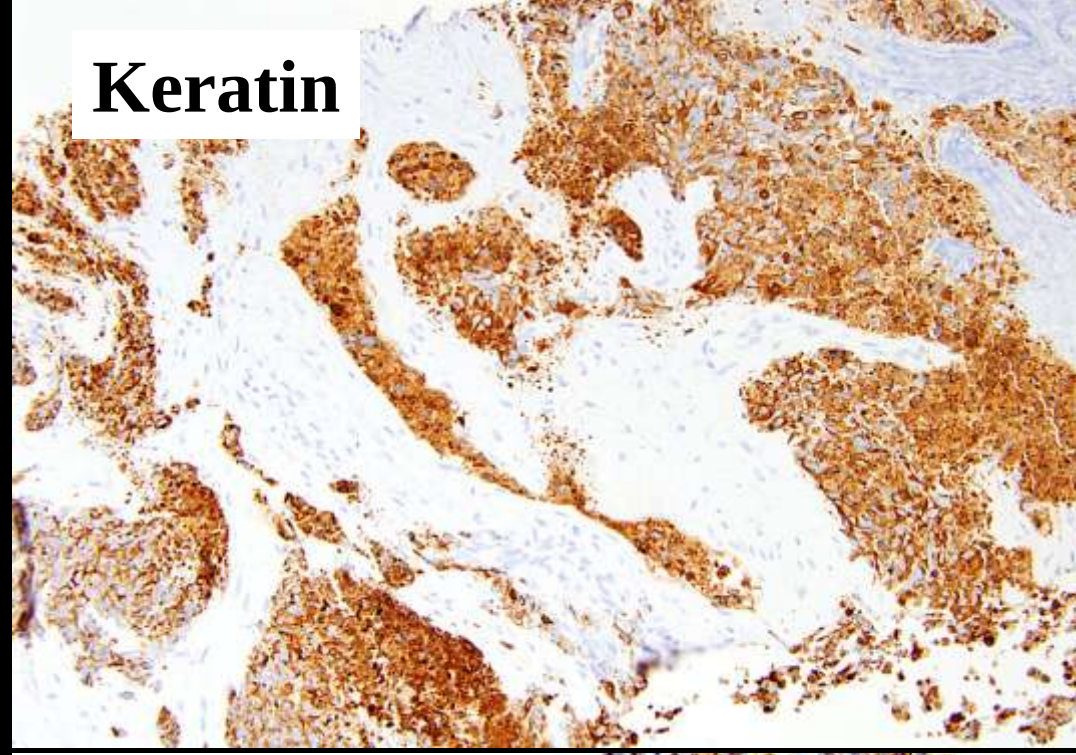
1. Type 2 diabetes mellitus.
2. Hypercholesterolemia.
3. Morbid Obesity.
4. Hypothyroidism.
5. Osteoarthritis.
6. Gout.
7. Diastolic CHF.
8. COPD.
9. Gastroesophageal reflux disease.
10. Obstructive sleep apnea not on any treatment. Intolerant of BiPAP.
11. Depression and anxiety.
12. Restless leg syndrome.

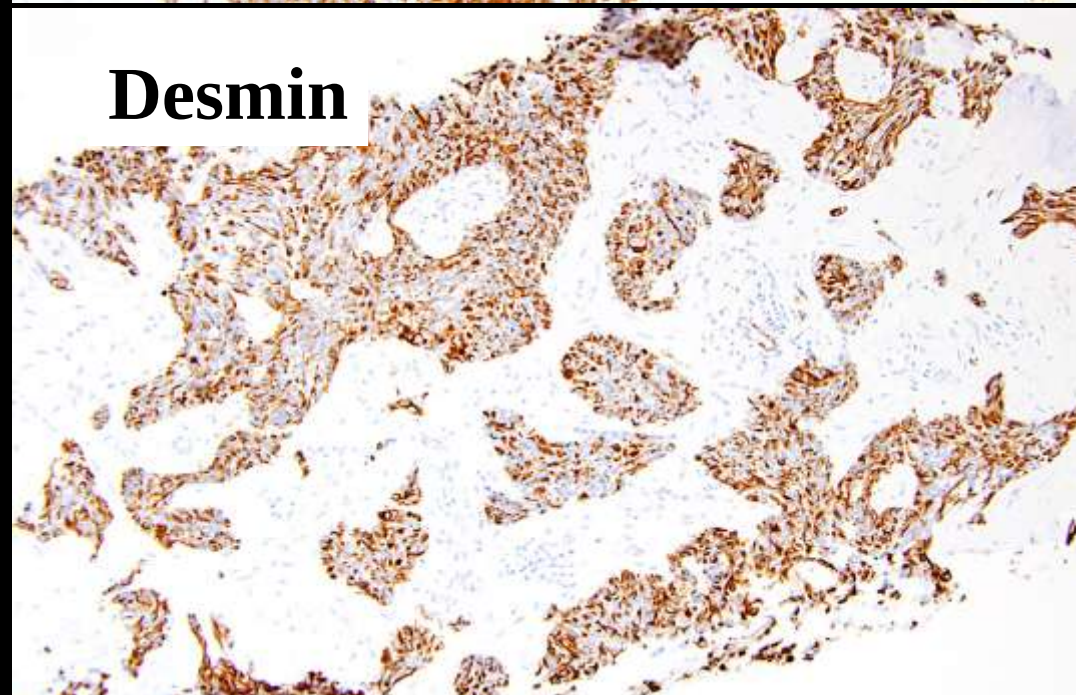
The patient denied any history of coronary artery disease.

MEDICATIONS:

1. Lasix 40 mg twice a day.
2. Sinemet 25/250 two tablets daily at bedtime.
3. Allopurinol 100 mg at bedtime.
4. Glipizide 5 mg daily.
5. Metformin 500 mg twice daily.
6. Paxil 20 mg daily.
7. Lipitor 80 mg daily.
8. Digoxin 0.25 mg every other day and 0.125 mg every other day.
9. Nitrostat sublingual as needed for pain.
10. Colchicine 0.6 mg twice daily.
11. Klor-Con 20 mEq twice daily.
12. Advair Diskus 250/50 one puff twice daily.
13. Fish oil capsule 500 mg 3 times daily.
14. Synthroid 250 mcg daily.
15. Lisinopril 10 mg daily.
16. Protonix 40 mg daily.
17. Lidoderm patch 5% to the left hip daily.
18. Darvocet-N 100 1/2 tablet twice a day as needed for pain.
19. The patient said she takes ibuprofen 800 mg 3 times daily.


Female, 32
Peritoneal nodules


Keratin


Desmin

Huge variation around the world (and even within same geographic region) in healthcare resources / infrastructure (incl. money, people, available technology and available therapeutic options) , as well as in education / training

As we consider how our specialty and our role may evolve, what about PUBLIC / LAY PERCEPTIONS OF PATHOLOGISTS ?…..

‘You cut people up, don’t you ?’

‘Not a proper doctor’

‘Not a physician’

‘What you do is creepy’

‘It must be depressing dealing with death all day’

‘How can you do a job like that ?’

Pathologist

Carcass-inspired crepitant grind with underlying absurdist melody.

Pathologist - Grinding Opus of Forensic Medical Problems (1993)

Grinding Opus of Forensic Medical Problems

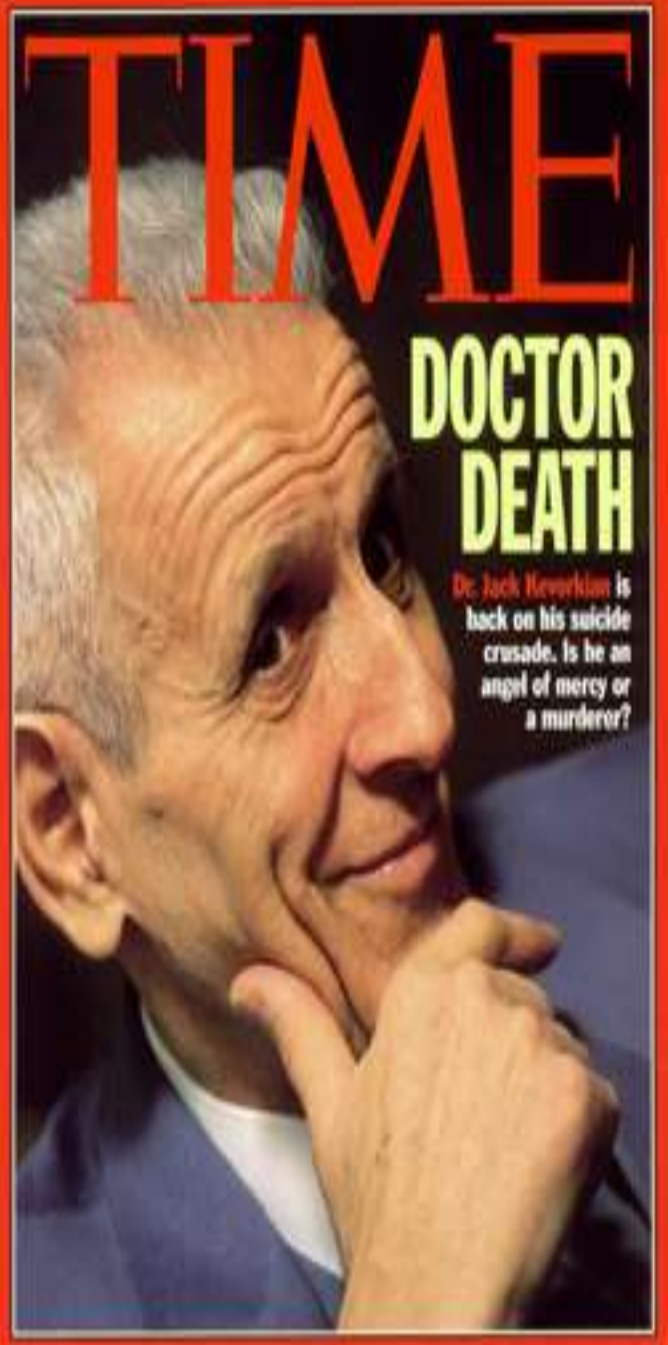
M.A.B. 1993

Production: Thick wooden-room-y but clear production.

Review: It would be a mistake to characterize this album simply as a Carcass clone, although the influence in theme and music is unmistakeable, as it takes a fusion of the best of two eras of Carcass and to it adds a musicality and sense of life that was not present in the original. The variations in structure and death metal-influenced use of introductory material and sense of melody from later Carcass (Necroticism) is preserved, but the use of distinctive melodies that sound borrowed from 1940s club hits of earlier Carcass (Reek of Putrefaction) is expanded upon here to give the music a sage, august character.

Tracklist:

1. Paroxysmal Prelude
2. Cannibalistic Disfigurement
3. Putrescene
4. Cadavers in medical Jurisprudence
5. Uterogestation to Abortion
6. Exhumed Dead Body
7. Infectious Agonizing Parasitism
8. Gynaecological Sickness



“A pathologist is a nice, warm person who looks at cold, dead people. Two thousand of them – pathologists, not dead people – were in San Francisco the other day, talking about dead people they have known. Sometimes a pathologist looks at dead tissue from living people. It’s a living. Anyway, the members of ASCP held a big slide show inside a ballroom at the Hilton Hotel. When a pathologist puts on a slide show, there are no pictures from his summer vacation. It’s a ballroom, but it’s no ball.”

Rubinstein, San Francisco Chronicle, Apr. 2, 1990

“The histopathologist probably has the most extensive involvement with the largest number of patients, but with the least visibility and the least recognition.”

Start et al. *J Clin Pathol* 1995; 48:398-401

WHO AMONG THE FOLLOWING ARE MOST COMMITTED TO IMPROVING PUBLIC HEALTH ?

Doctors	62%
Environmental health officers	61%
Medical research charities	49%
Medical researchers (academic)	44%
Medical researchers (pharma)	20%
Politicians	17%
Pathologists	12%
Health insurance companies	7%

Royal Coll Pathol (UK) 2005

WHY ARE PATHOLOGISTS SO UNDER-RECOGNISED ?

‘Part of the problem is the media and its portrayal of the laboratory and the pathologist who work in it as a ‘black box’. How often have you heard the phrase “we are waiting for the results?” What you are really waiting for is the pathologist to make the diagnosis… There is often an incorrect conclusion that the surgeon or internist makes the diagnosis… the definitive and final diagnosis always rests with the pathologist.

Paul Shitabata, M.D.
thedoctorsdoctor.com

Thursday August 20th 2009

Home

This week's print edition

Daily news analysis

Opinion

World politics

Special reports

Business and finance

Markets and data

Science and technology

About our new page

All science and technology

Technology Quarterly

Technology Monitor

Books and arts

Science & Technology

Apology: Lighting up cancer

Apr 30th 2009

From *The Economist* print edition

We would like to apologise to the world's pathologists for suggesting that the histological examination of excised tumours is carried out by "technicians", as suggested last week in "Illuminating surgery". The pathologists who perform this work are of course, physicians who specialise in the examination of tissue samples.

THE PLACE OF PATHOLOGY IN CONTEMPORARY MEDICINE

Given the unparalleled scope and clinical importance of the information that we provide …

- **Why is pathology often seen as one of the less respected medical specialties among our peers?**
- **Why do most patients not know, understand or recognise what we do ?**
- **Why do we struggle to garner resources from institutions or Departments of Health ?**

THE PLACE OF PATHOLOGY IN CONTEMPORARY MEDICINE

Some simplistic answers…

- **Many clinicians don't understand what we do or how we do it….**
- **Many (? most) patients don't know we exist or that we contribute to patient care….**
- **Many hospital organisations/administrators don't know what we do, firmly believe that we're overstaffed and don't understand why we can't be automated….**

THE PLACE OF PATHOLOGY IN CONTEMPORARY MEDICINE

Some possible explanations …

- Ours is primarily a ‘service’ role – by nature responsive to a need/request
- Poor advocacy/representation on our part
- Generally limited patient contact (with some notable exceptions – eg FNA, multidisciplinary clinics or patient-driven consultation)
- Clinicians often don’t advertise (? even mention) our role – because it diminishes their own
- Possible negative connotations relating to ‘pathologist’ involvement

Given the amount of valuable information that we can provide:

- Surgical pathologists are definitely clinicians
- Surgical pathologists have an obligation to engage in the clinical care process
- Surgical pathologists can often provide the objective voice of common sense

EVOLUTION OF SURGICAL PATHOLOGIST'S ROLE

- **Patients need to be more aware of the role / importance of pathology**
- **Pathologists need to be more visible**
- **Pathologists need to be willing to educate patients, not just clinicians (e.g. FAQs)**

HOW DO WE IMPROVE THE PUBLIC PERCEPTION GOING FORWARD?

- Continue to explain to clinicians, patients, friends, family, etc. what we do – no need to hide / apologise !
- Don’t avoid patient contact – instead take the opportunity when presented
- Don’t be shy of reminding people of our huge influence on clinical decisions
- Take any opportunity to educate the media
- Better ‘marketing’ by major professional bodies / associations

CHRISTOPHER FLETCHER, ESPECIALISTA EN ANATOMÍA PATOLÓGICA

«El médico ya no toca al paciente, sólo le dice: 'hágase una placa'»

«Cada vez que firmamos un diagnóstico estamos causando un drama familiar; no lo olvidemos»

FERMÍN APEZTEGUIA f.apezteguia@diario-elcorreo.com/BILBAO

Con 35 años, Christopher Fletcher se convirtió en el catedrático más joven de la Universidad de Harvard. Hoy, 14 años después, está considerado como el mayor experto del mundo de su especialidad, la Anatomía Patológica. Ayer visitó Bilbao para dar una charla en el hospital de Basurto.

-Perdone mi entrada; ¿qué es esto de la

CONCLUSIONS

1. Emerging technologies and therapeutic advances are enhancing the role of the surgical pathologist
2. Anatomic pathologists are the ideal providers and integrators of increasingly subspecialised or novel diagnostic and prognostic information
3. Societal expectations are affecting the role of the surgical pathologist, sometimes in an unrealistic way
4. Surgical pathologists have the capacity to influence these developments and to help to provide a balanced view
5. Pathologists must better recognise their role and do a better job of educating others
6. Huge variation in available resources lead to sensations of unreality and disassociation between the “haves” and “have nots” - we need to be aware and also realistic

EVOLVING ROLES OF SURGICAL PATHOLOGIST

Sophisticated diagnostician/prognosticator

Integrator of information

Increasing role in treatment guidance

Patient advocate

Advocate for professional integrity

“From inability to let well alone; from too much zeal for the new and contempt for what is old; from putting knowledge before wisdom, science before art and cleverness before common sense, from treating patients as cases, and from making the cure of the disease more grievous than the endurance of the same, good Lord, deliver us.”

Sir Robert Hutchison
1871-1960
***BMJ* 1953**

SOME QUESTIONABLE OBSESSIONS OR BELIEFS RELATED TO MODERN SURGICAL PATHOLOGY

- Speed/turn-around time – eg same day tissue processing and immunohistochemistry
- Assessment of resection margins at 1-2 mm resolution is clinically important/relevant
- Identification of predictive ‘biomarkers’ – often with little scientific justification/basis
- Predictive/prognostic gene expression profile – tiny case numbers/little diagnostic uniformity
- ‘Kinome’ assays – “find me a target” – usually with little or no scientific underpinning

WHAT HAS LED TO THESE CHANGES ?

- Demise of paternalistic medicine
- Patients becoming better informed
- Medicine becoming “client”-driven
- Increasing range of treatment options
- Direct impact of pathologic interpretation on treatment selection

Clinicians not always best equipped to provide interpret^{n} of pathology report

LOCAL ADVANTAGES OF PARTIAL SUBSPECIALISATION

- General surgical pathologists still see broad range of specimens
- Junior faculty generally do not subspecialise too early
- Residents generally sign out with 1 person
- Subspecialty expertise / consultations available as required
- Divisions / services well integrated / cohesive
- Clinical services have point person(s) when required
- Allows ‘niche’ area / focus for publications

POTENTIAL CONSEQUENCES OF LIMITED / INCORRECT PUBLIC PERCEPTION

- Erosion of professional status
- Undervaluation of professional activity (both perceptual and financial)
- Failure to attract medical students to the specialty
- Continued inability to attract significant institutional resources / space
- Possible morale issues

NEED FOR INTEGRATION OF (OFTEN NEW) INFORMATION

Imaging

Biomarkers – diagnosis, prognostic, predictive

Molecular/genetic/genomic data

Proteomic data (?)

etc.

Is it safe/appropriate for molecular / genetic test results to go directly to clinicians ?