

I SIMPOSIO NACIONAL de ONCOLOGÍA de PRECISIÓN

Vigo, del 28 de febrero al 1 de marzo de 2019

¿Llegará a desaparecer el diagnóstico histológico?

Dr. Enrique de Álava

Special Article

Expression Profiling of Human Tumors: The End of Surgical Pathology?

Marc Ladanyi,* Wing C. Chan,†
Timothy J. Triche,‡ and William L. Gerald*

**From the Department of Pathology, Memorial Sloan-Kettering*

information of immunohistochemistry. Nonetheless, it is widely believed that the latter shortcoming will be more than compensated by the sheer multiplicity of the gene

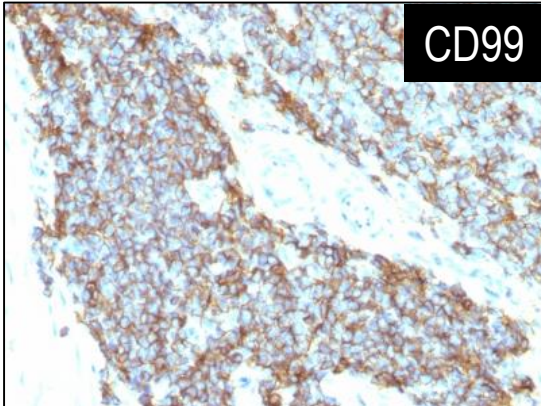
Will expression profiling evolve into another “ancillary” technique or will it come to be seen as an alternative to expert surgical pathology? At present, expression profiling studies are highly dependent on histopathology for validation,^{1,9} but it is conceivable that expression profiles may eventually become “disconnected” from the underlying morphology, assuming the role of clinically relevant entities.

32 year-old male, left forearm

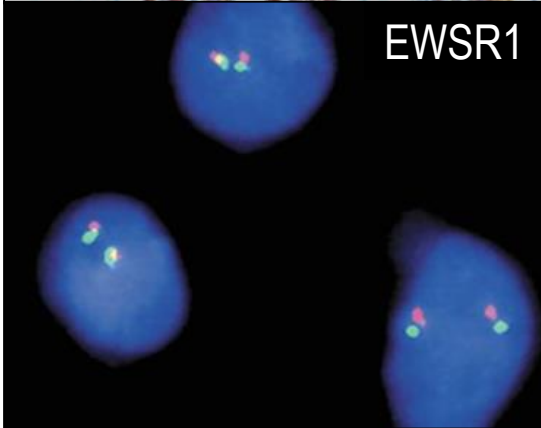
CIC- Rearranged sarcoma



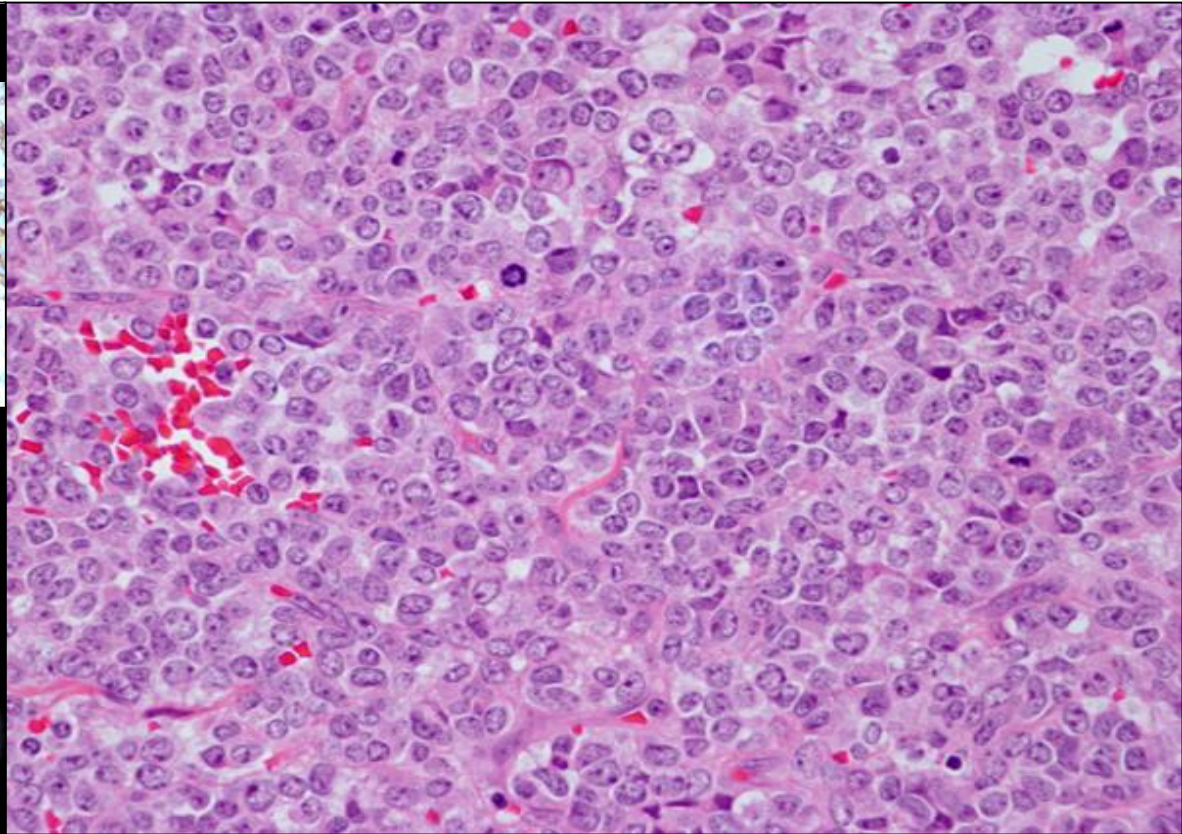
CICex20-DUX4ex1



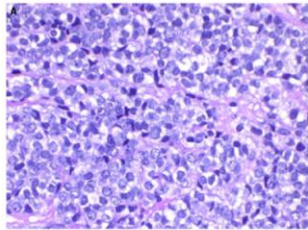
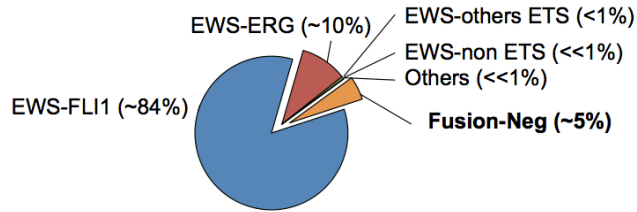
CD99



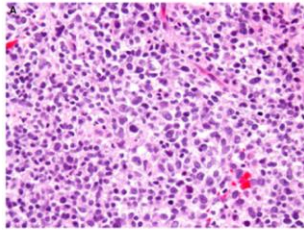
EWSR1



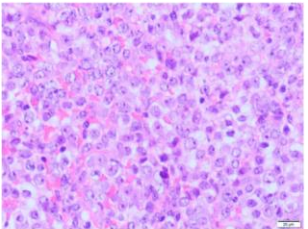
Diagnóstico diferencial de Sarcoma de Ewing y Ewing-like



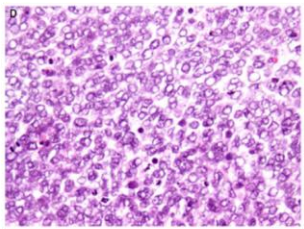
Classic ES



EWSR1-NFATC2



CIC-DUX4

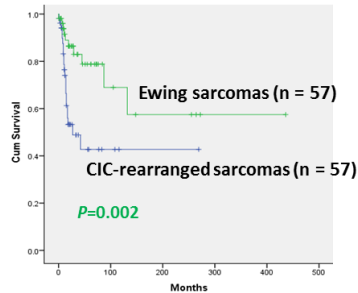


BCOR-CCNB3

	Ewing Sarcoma		Ewing-like Sarcoma	
Fusion Gene	EWSR1-ETS	BCOR-CCNB3	CIC-DUX4	EWS-NFATC2
Genetics	Translocation t(11;22) 85% Translocation t(21;22) 10%	Inversion X(p11.4;p11.22)	Translocation t(4;19) Translocation t(10;19)	Translocation t(20;22)
Age	Child Teenager Adult 36 40 25	26 50 25	20 30 50	25 75
Sex ratio	Male : female 1,4 : 1	2 : 1	2 : 1	7 : 1
Primary tumor tissue	Soft tissue : Bone 0.12 : 1	0.2 : 1	1 : 0	0.14 : 1
Metastases	Frequent: lung, bone, bone marrow	Frequent: lung, bone, bone marrow	Frequent: lung	Rare
Histology	SRBC tumors, CD99+	SRBC tumors, CD99 +/- CCNB3+	SRBC tumors, CD99 +/- ETV4+	SRBC tumors, CD99+
Prognosis	Poor if metastatic disease	Poor if metastatic disease	Poor	lymphocytes infiltrates unknown

Franck Tirode
INSERMU830 / Institut Curie

Antonescu CR, Amer J Surg Pathol 2017



poor response to
Ewing sarcoma neo-
adjuvant protocol

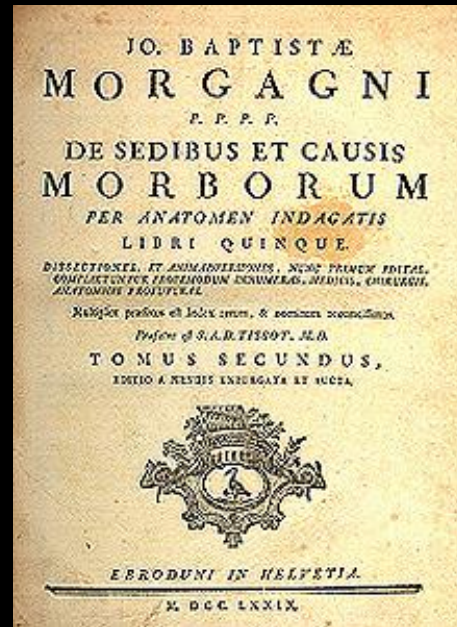
5-yr survival CIC : 43%
5-yr survival Ewing: 77%



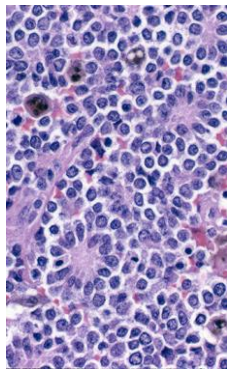
CICex20-DUX4ex1



G.B. Morgagni



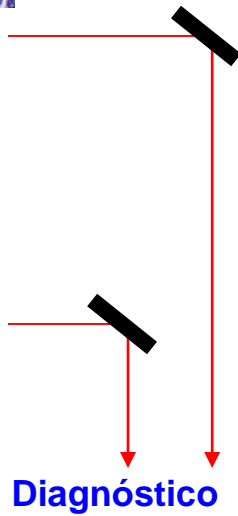
El asiento de las enfermedades son los órganos internos, y los síntomas varían de acuerdo con el órgano afectado



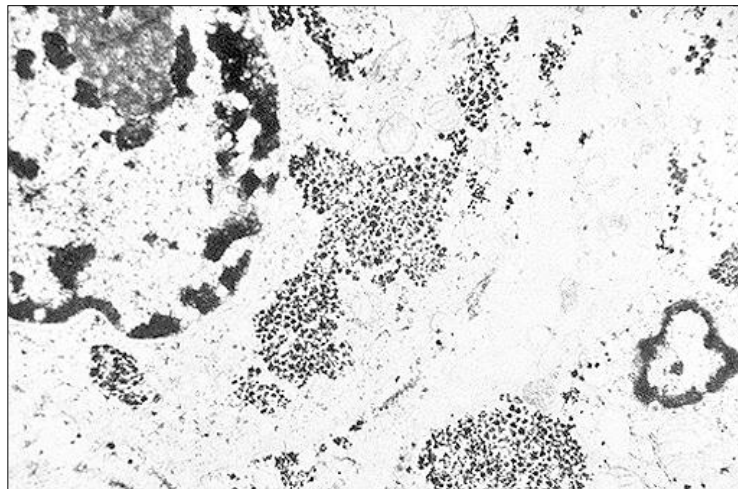
1970

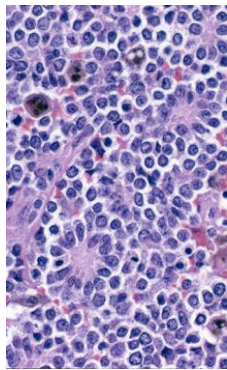
Fenotipo

Genotipo



Diagnóstico

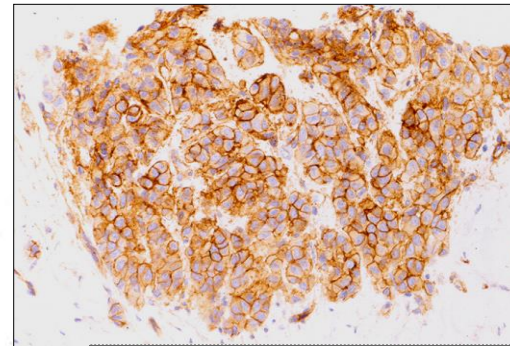




Fenotipo

1970

1990

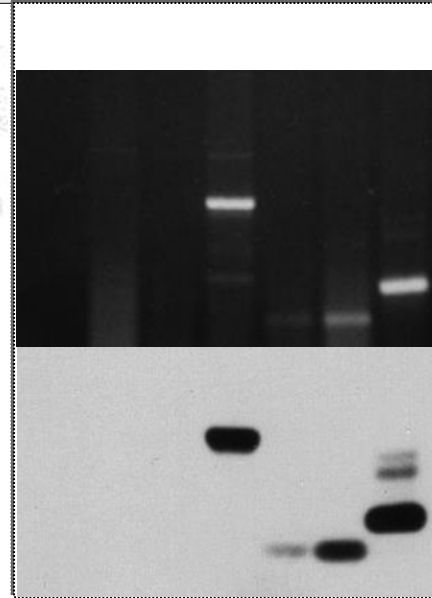


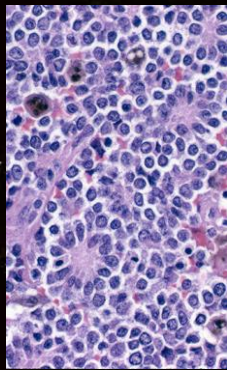
Genotipo



Diagnóstico

Diagnóstico
Pronóstico
Tratamiento





Fenotipo

1970

1990

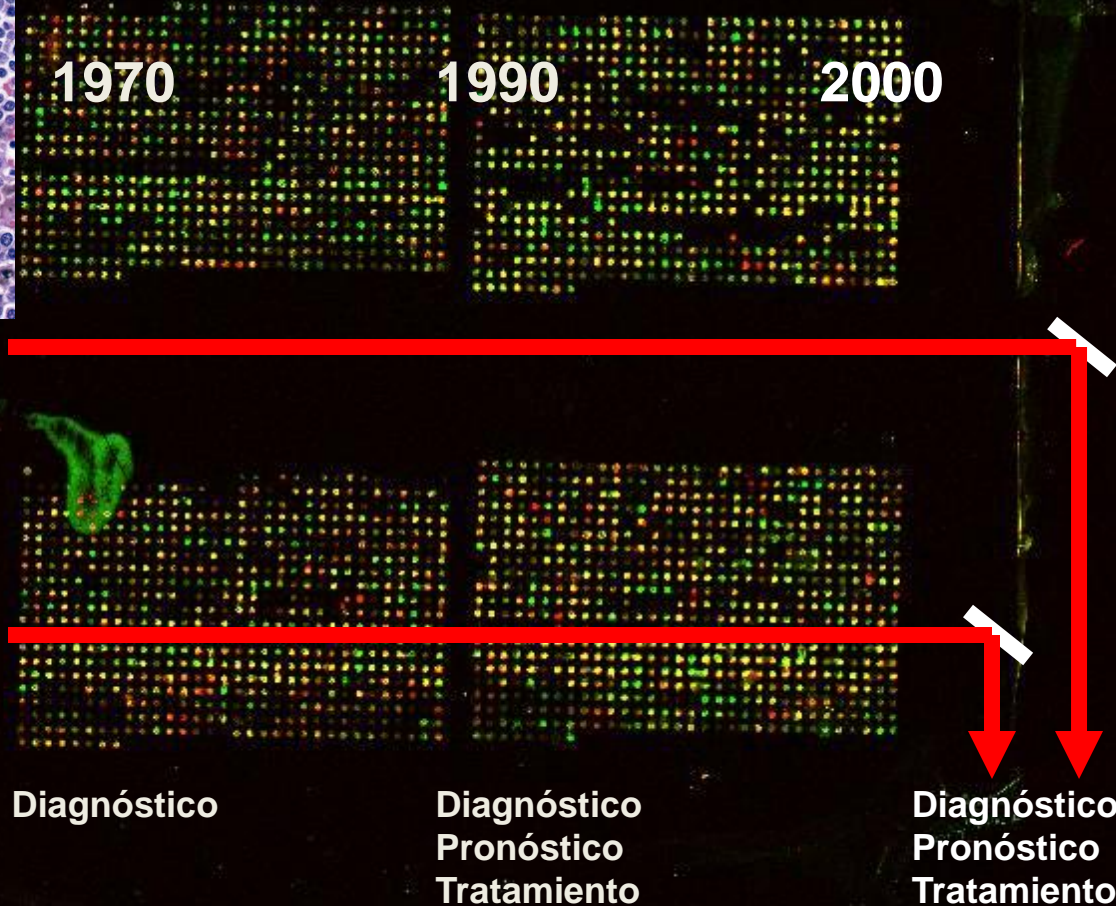
2000

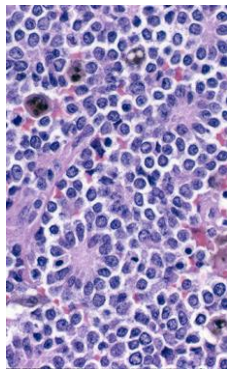
Genotipo

Diagnóstico

Diagnóstico
Pronóstico
Tratamiento

Diagnóstico
Pronóstico
Tratamiento



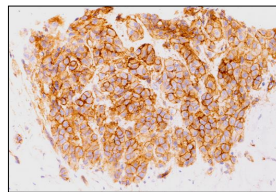


1970

1990

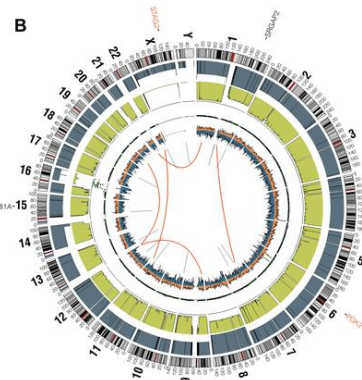
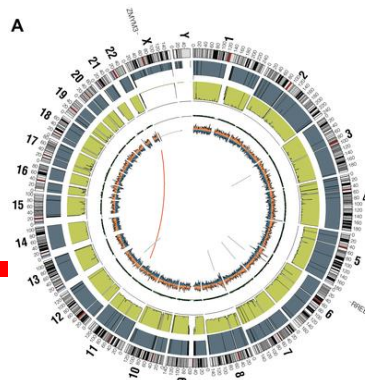
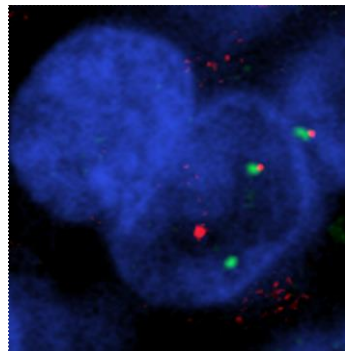
2000

2020



Fenotipo

Genotipo



Diagnóstico

Diagnóstico
Pronóstico
Tratamiento

Diagnóstico
Pronóstico
Tratamiento

Diagnóstico
Pronóstico
Tratamiento

Clinical/image data

Biopsy/excision/cytology

Gross examination

**Paraffin
-embedded
tissue**

Diagnosis

Clinical/image data

Biopsy/excision/cytology

Gross examination

**Paraffin
-embedded
tissue**

**H&E,
IHC
FISH**

**Frozen
tissue/cells**

Pathology

**Take for
cyto or
cell culture**

PDX

3D- models

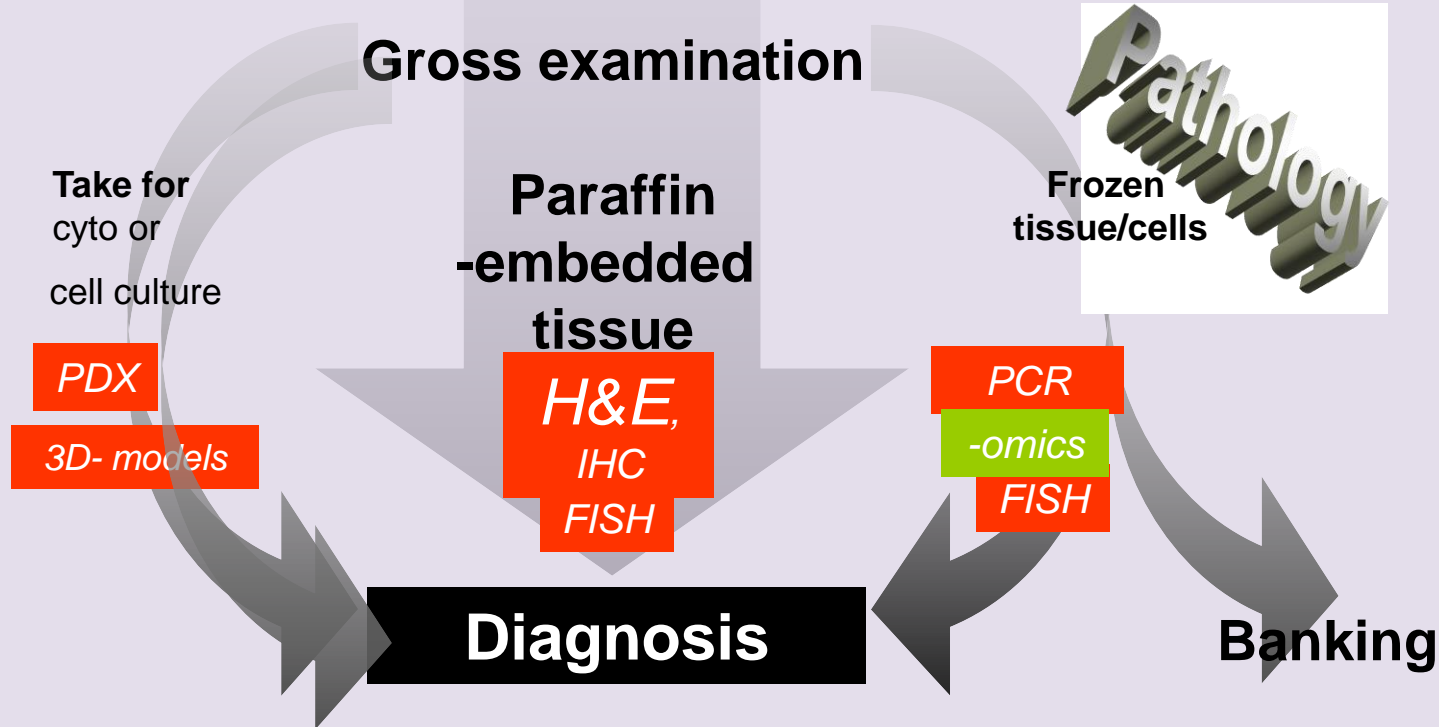
PCR

-omics

FISH

Diagnosis

Banking



Although the fact that the arrays could classify these lesions correctly is impressive, it is not that surprising that a technique that examines thousands of genes at a time can distinguish tumors that are morphologically as distinct as synovial sarcoma and malignant fibrous histiocytoma (MFH).

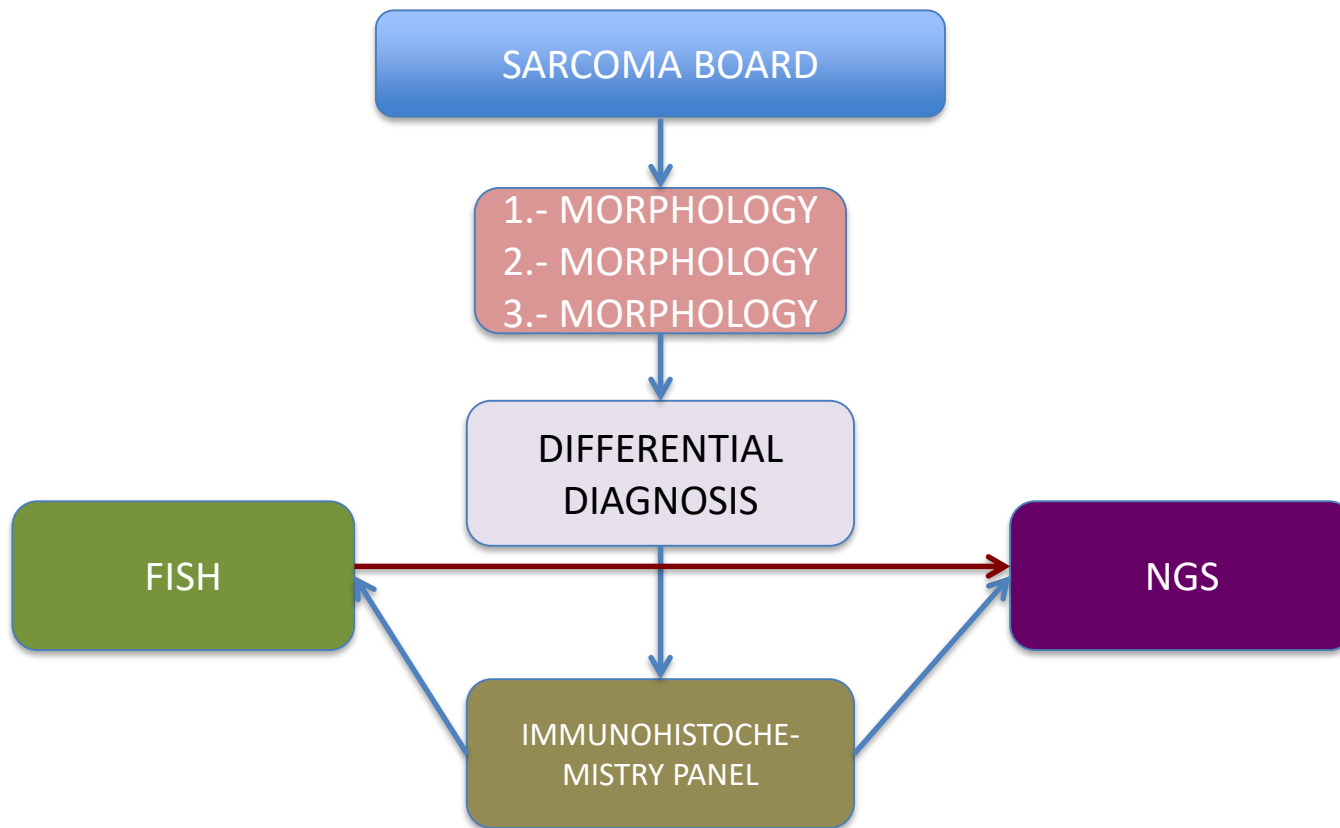
However, it is good to remember that it is not the purpose of gene arrays to classify lesions that can also be distinguished using conventional techniques such as light microscopy (as is sometimes proposed).../...

.../... The fact that arrays can do this is merely a verification that gene arrays work; they reflect what is seen under the microscope. The idea that gene array analysis will supplant histological examination is a simplification of the issue and in our opinion, wrong.

Rather, the real power of microarray analysis is to permit a genome-wide search for markers that may distinguish subtypes of tumors that remain inapparent by conventional techniques.

Van de Rijn et al. Am J Pathol 2002;161:1531

Sarcoma diagnostic algorithm 2018



Diagnóstico de precisión de Sarcomas con translocaciones en la rutina asistencial

Cartera de Biomarcadores en Cáncer Sistema Sanitario Público de Andalucía, SSPA Parte I

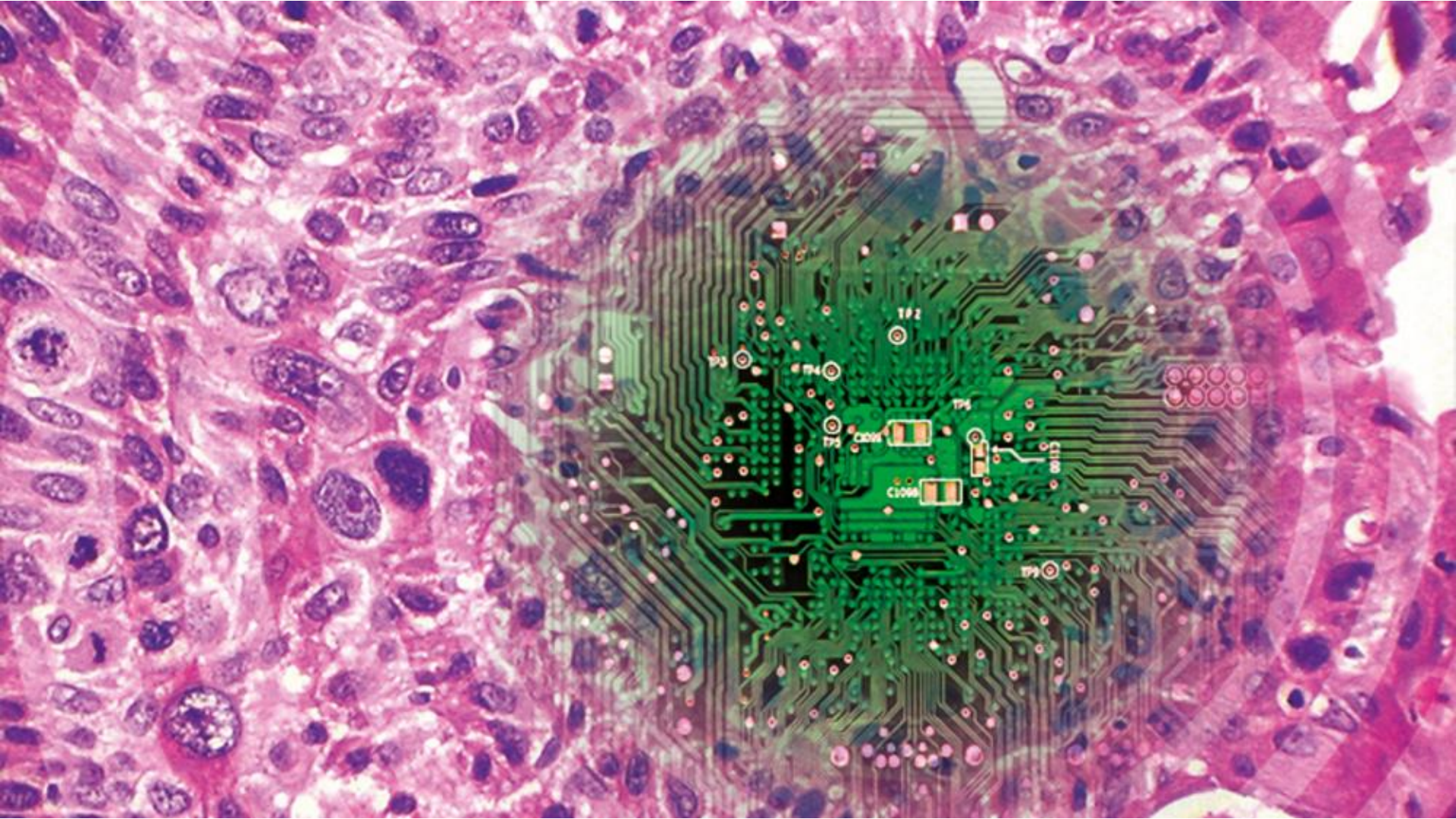
Enero 2019

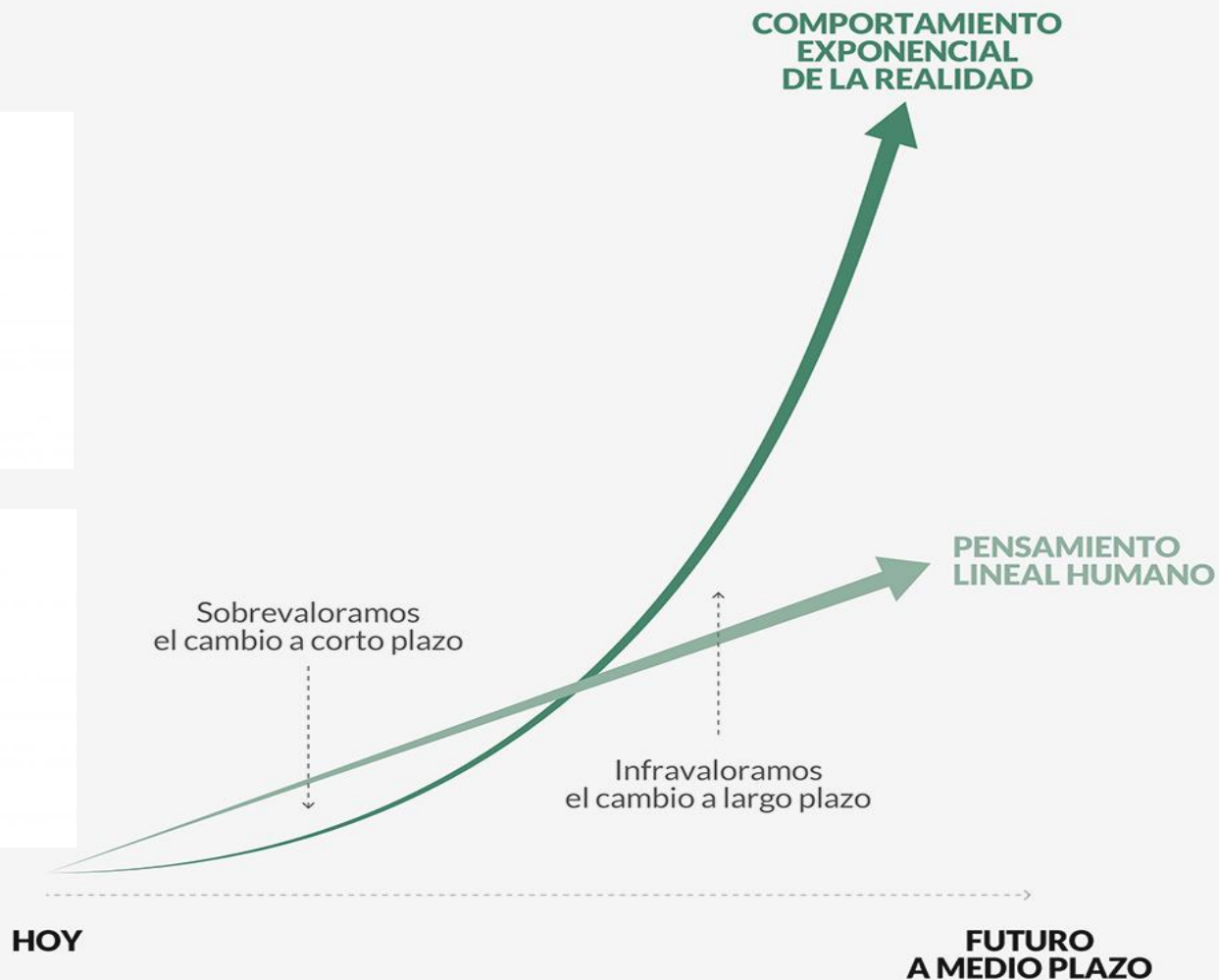
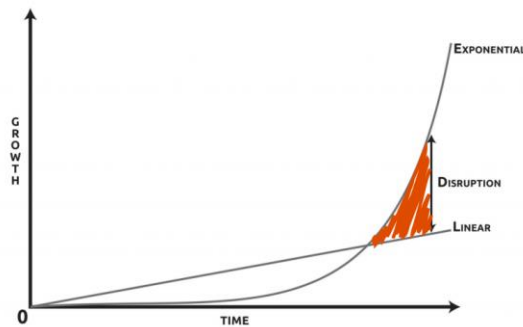
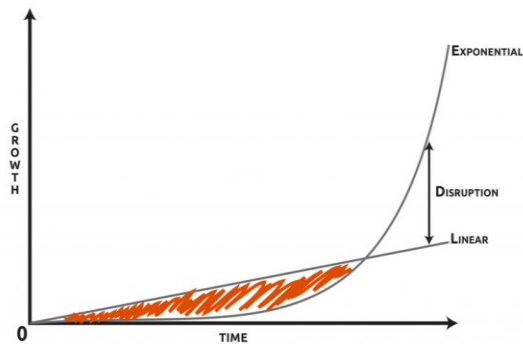
Hemos conseguido incorporar la secuenciación de
Sarcomas en la cartera de servicios del SAS

NEOPLASIAS DE HUESO Y PARTES BLANDAS
Línea somática
FOS-B: hemangioma epiteliode
ROS-1: tumor miofibroblástico inflamatorio
CAMTA-1: hemangioendotelioma epiteliode (HEE)
EWSR1 22q12: sarcoma de Ewing
FOXO1-FKHR: rabdomiosarcoma alveolar
SYT/SS18: sarcoma sinovial
FUS 16q11: liposarcoma mixoide/sarcoma fibromixoide bajo grado/histiocitoma
CHOP 12q13: liposarcoma mixoide
RMSE 11q15.5: rabdomiosarcoma embrionario
MDM2: liposarcoma pleomórfico
RB-1: miofibroblastoma, lipoma fusocelular....
CDk4: liposarcoma bien diferenciado/ desdiferenciado
TFE3: hemangioendotelioma epiteliode y Sarcoma alveolar
NGS secuenciación masiva de fusiones génicas
USP6: quiste óseo aneurismático
NR4A3: condrosarcoma mixoide extraesquelético
JAZF1: sarcoma del estroma endometrial de bajo grado
YWHAE: sarcoma andometrial de alto grado
STAT-6: tumor fibroso solitario, por inmunohistoquímica
IDH1/2: condrosarcoma
BCOR: sarcomas con reordenamiento de BCOR, por inmunohistoquímica
ETV4 : sarcomas CIC-DUX, por inmunohistoquímica
H3G34W: tumor de células gigantes
H3K36M: condroblastoma
H3K27ME: tumor maligno de vaina neural periférica
WWTR1: hemangioendotelioma epiteliode

THE NEXT
BIG
THING

A 3D, golden-colored sign with the words "THE NEXT BIG THING" stacked vertically. The letters are thick and blocky, with a metallic sheen. The sign is set against a bright blue sky with soft, white light rays emanating from behind it, creating a sense of optimism and forward momentum.





THE 3 DIMENSIONS OF DISRUPTION



The intersection and interaction of Emerging Technologies, Innovative New Business Models, and Exponential Adoption Curves is leading to large scale disruption of industries at an unprecedented rate.



D/SRUPTION

disruption

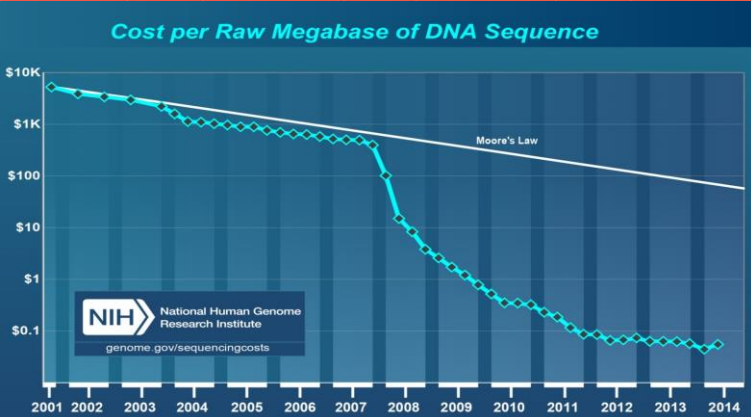
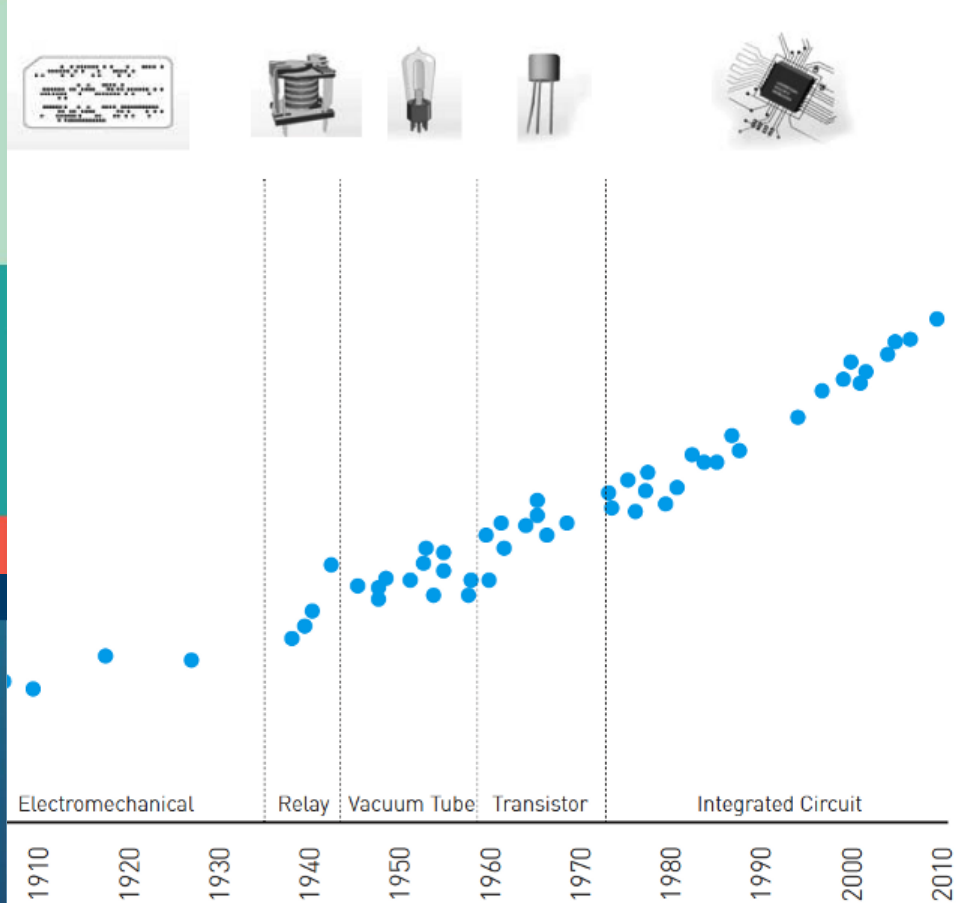
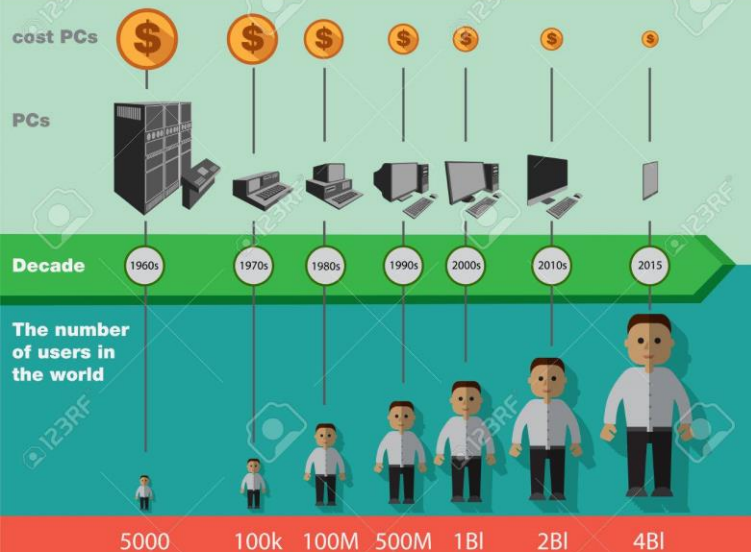
20 years later and all of these things fit in your pocket.

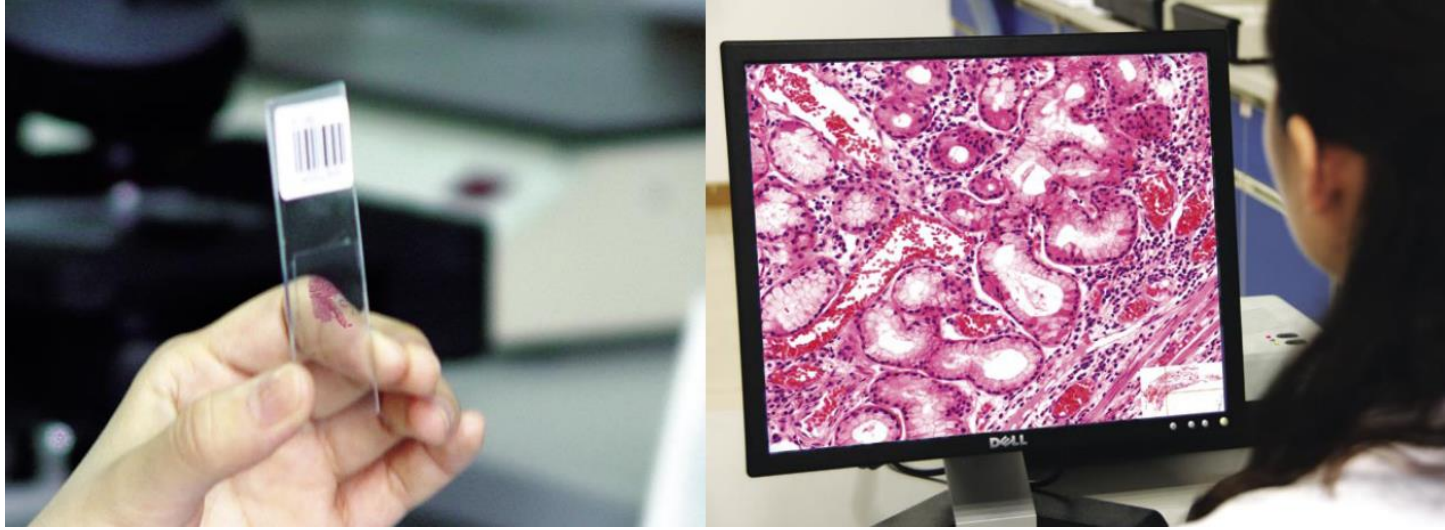


mfigueroa/9GAG

Follow @9GAG on Instagram!

Evolution of computers





El patólogo ya no tiene por
qué estar donde están los
portas

5 Key criteria for evaluating Digital Pathology

The adoption of digital pathology is evolving and offers functionality that goes far beyond the microscope. These new opportunities significantly increase workflow efficiency. They move time-consuming tasks to the computer and allow the pathologist to spend more time on reviewing cases. Here are five key criteria when evaluating a solution for digital pathology.

1 Optimized workflow



Access to all relevant patient data in one workstation.

Minimum mouse mileage and clicks through seamless integration of control and interface.



High-speed image display through web technology and serverside rendering.

Improved ergonomics, avoiding shoulder and neck problems.



2 Collaboration with other specialists



Easily share information across department boundaries.

Tailored dynamic worklists and support for multi-disciplinary team meetings.



Sharing of workload and second opinions.

Strategy towards integrated diagnostics.



3 Availability anytime, anywhere



View, present and discuss from any workstation.

Vendor Neutral Archive (VNA) for centralized storage.



Scalable to handle growth of users and production.



4 More consistent reviews



Automated image analysis for frequent cases.

Support for counting and percentage calculations.



Teaching functionality with easy tag and search.

Compare with patient history data.



5 Integration with healthcare IT solutions

Support for standards like HL7 and DICOM to integrate with EMRs, LIS, etc.



Vendor agnostic approach.

Part of the full enterprise image management strategy.



Review Article

Do we see what we think we see? The complexities of morphological assessment

Peter W Hamilton,^{1*} Paul J van Diest,² Richard Williams³ and Anthony G Gallagher⁴

¹Centre for Cancer Research and Cell Biology, Queen's University of Belfast, Belfast, UK

²Department of Pathology, UMC Utrecht, Utrecht, The Netherlands

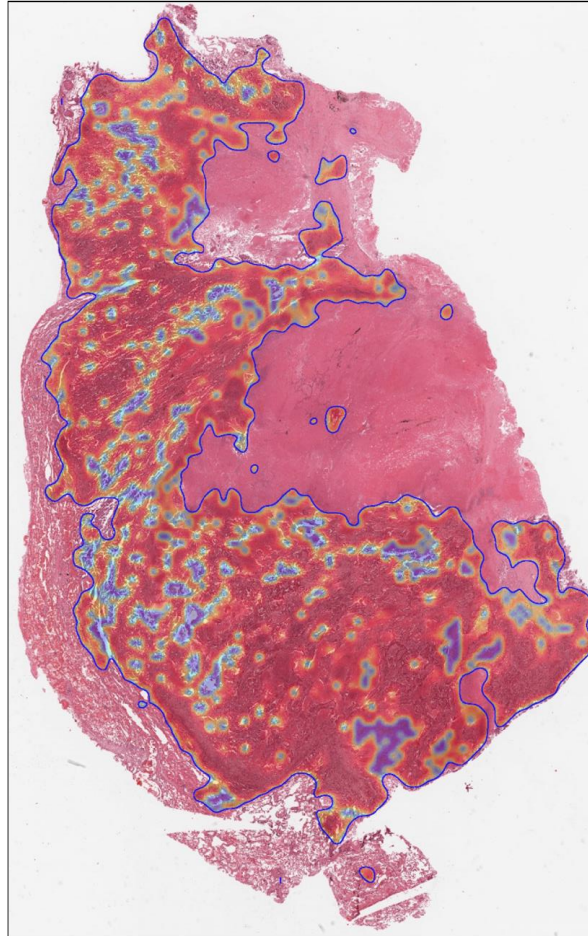
³Department of Anatomical Pathology, St Vincen's Hospital and The University of Melbourne, Melbourne, Australia

⁴National Surgical Training Centre, Royal College of Surgeons Ireland, Dublin, Ireland

- Ilusiones ópticas
- Variabilidad en la comprensión del significado de algunas claves visuales
- Variabilidad en las estrategias espaciales de búsqueda
- Variabilidad en las estrategias cognitivas
- Variabilidad en el peso que se da a un rasgo concreto
- Variabilidad en umbrales de detección
- Variabilidad de la identificación de eventos infrecuentes
- Capacidad de procesamiento simultáneo limitada
- Cansancio
- El papel de la intuición y lo difícil que es trasmitirla
- ...

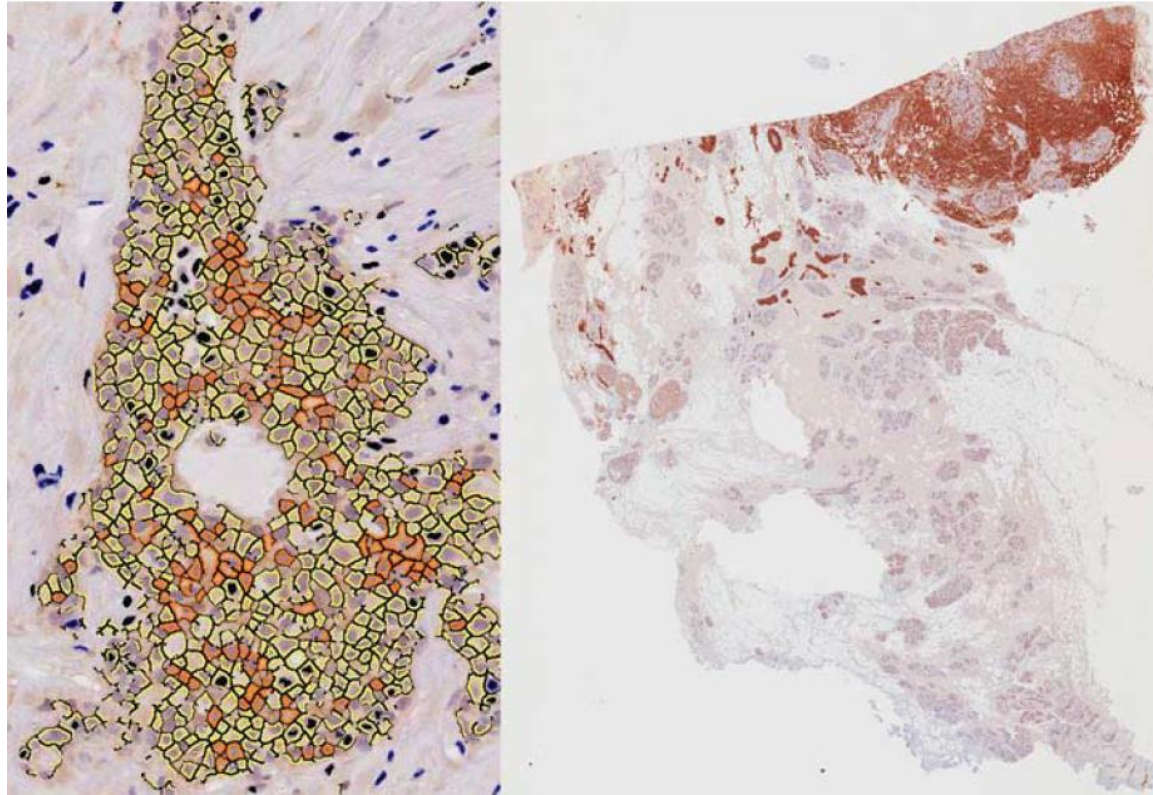
Dos aplicaciones en marcadores más 'moleculares'

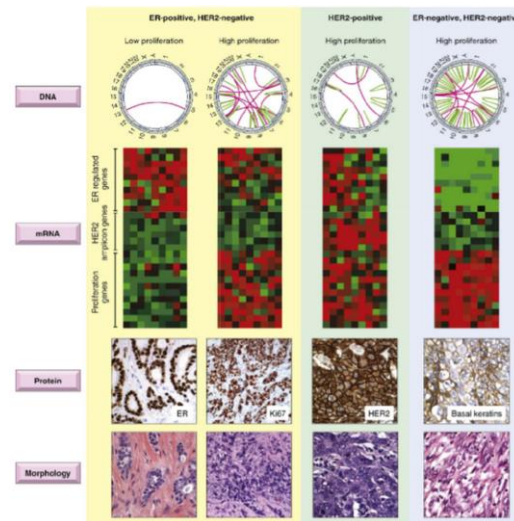
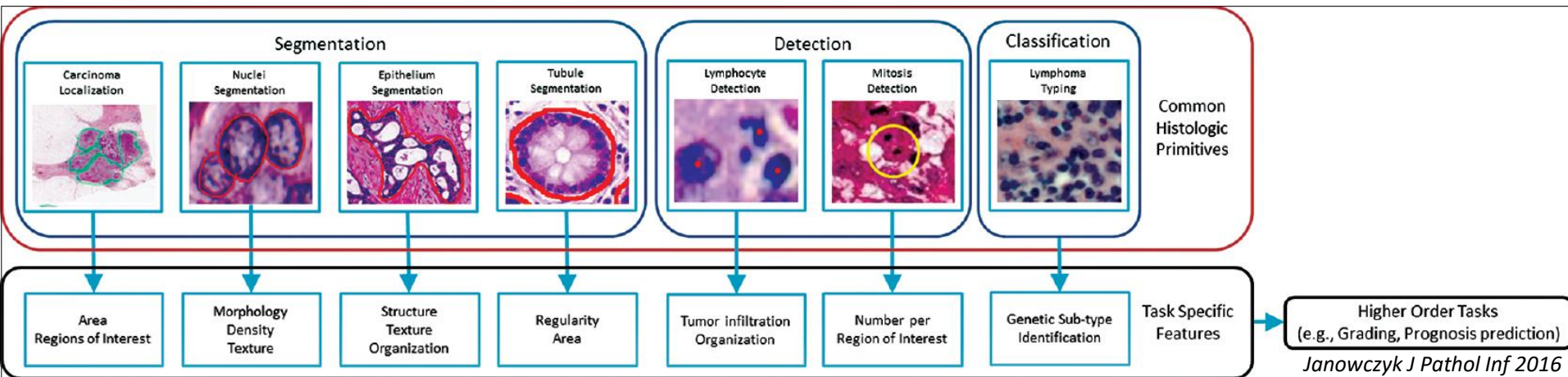
- Porcentaje de **tumor** respecto al total de la **muestra**
- Porcentaje de **células tumorales** respecto al total de **tumor**



Evaluating tumor heterogeneity in immunohistochemistry-stained breast cancer tissue

Steven J Potts¹, Joseph S Krueger¹, Nicholas D Landis¹, David A Eberhard^{2,1}, G David Young¹,
Steven C Schmechel³ and Holger Lange¹ *Laboratory Investigation* (2012) **92**, 1342–1357;





I SIMPOSIO NACIONAL de ONCOLOGÍA de PRECISIÓN

Vigo, del 28 de febrero al 1 de marzo de 2019

¿Llegará a desaparecer el diagnóstico histológico?

Dr. Enrique de Álava

La Medicina de Precisión...

Comienza por una
Patología de Precisión

A photograph of a city skyline at sunset. The sun is a bright, glowing orb on the horizon, casting a warm orange and yellow light across the sky. The city below is in silhouette, with various spires and buildings visible. On the right side, a tall, prominent tower with a pointed top stands out. The text '¡Gracias!' is written in a large, white, sans-serif font in the center of the image.

¡Gracias!



@EnriqueAlava
@Lab_HUVR