

# VolitionRx

SMI BioNetworks Summit 2014

Biomarker - Pharma partnering

An ideal partnership ?

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20A

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Seminaire

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Belgium

[www.volitionrx.com](http://www.volitionrx.com)

***A VolitionRx Company***

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# Origins and Current Status

- Belgian R&D facility, US OTC listed
- Nucleosomics® Core Technology Platform
- \$10M equity funding and €1.47M regional funding
  
- Experienced management team
- Core team of 7 scientists
- Kit production
- Chief Operations Officer
- Former Eppendorf lab



Namur Citadel and the river Meuse

# VolitionRx - Clinical Networks

## Cancer Banks

- Wales - 500 patient retrospective study in breast cancer
- Manchester - 100 patient prospective study - renal, bladder and prostate

## Hvidovre Hospital, University of Copenhagen, *Denmark*

- Retrospective 5000 patient study – Colorectal population screening
- Prospective 11 000 patient study – Colorectal population screening

## Bonn University Hospital, *Germany*

Retrospective 800 patient study – various cancers (completed)

- Retrospective 1500 cohort study - Lung cancer
- Prospective 4000 cohort study - various cancers and controls
- **Neo-adjuvant therapy stratification – breast cancer**

## Mont-Godinne Hospital, *Belgium*

- 250 patient longitudinal study - early detection/prognosis of CRC.

# Introduction

- Understanding impact of early diagnosis and prognosis
- Pinpointing opportunities for biomarker integration
- CDx as enabling technology not a market restraint
- Surrogate biomarkers
  - efficacy monitoring
  - therapy switching
- Engaging with partners
  - Patients - Resource/Benefactor
  - CROs - Customers
  - Suppliers - Manufacturing

# Impact of Early Diagnosis

Cancer	Incidence	Rank	Mortality	Rank	5-yr survival		Ratio
					Distant	Local	
Lung	215, 021	1	161, 841	1	4%	53%	15X
PCa	186, 320	2	28, 660	5	3%	100%	31X
Breast	182, 460	3	40, 481	3	23%	98%	4X
CRC	153, 861	4	50, 640	2	12%	90%	8X

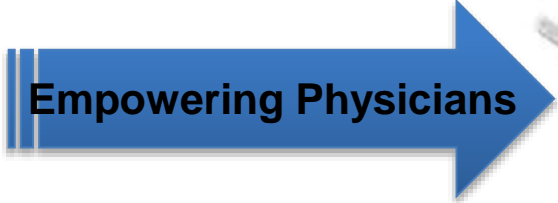
- More Treatment options - Better for Patient
  - Better for Payers
  - Better for Payers
  - Better for Payers

Analysis by PwC (PWC Diagnostics 2011); survival rates from US National Cancer Institute; incidence and mortality data from GLOBOCAN 2008 (IARC)

# Impact of Early Diagnosis



- Easily implemented Screening
- Point of Care diagnosis



High Sensitivity  
(identifies patients with disease)  
Rapid Specialist referral and treatment selection

High Specificity  
(identifies healthy)  
Peace of mind



# Impact of Early Prognosis

- Over Diagnosis can lead to over treatment
  - False positives - Diagnosis confirmation
  - Slow burner - Patient stratification/monitoring
- Prognostic applications
  - Mammaprint - Predicts metastatic potential
  - OncoType Dx - Predicts recurrence potential
  - Her2 - Predicts good response - Herceptin
  - BRCA mutation - Predicts elevated risk - PARPi
  - Non responders - Neo adjuvant therapy
    - RA therapy selection



# Epigenetics - Diagnostic Potential

- *“Heritable changes in gene expression without changes in DNA sequence”*
  - Non sequence based changes in phenotype and gene expression
  - Environmentally modulated
  - Reversible
  - Heritable
- *“Structural Adaptation of Chromosomal Regions so as to register, signal or perpetuate altered activity states”*
- *What turns genes on and off and under what circumstances*
  - '09 Silver Jubilee of groundbreaking work by Surani, Solter and Cattanach
  - Global epigenetic market **\$1.7 billion in '09** with **CAGR of 60% to '12**

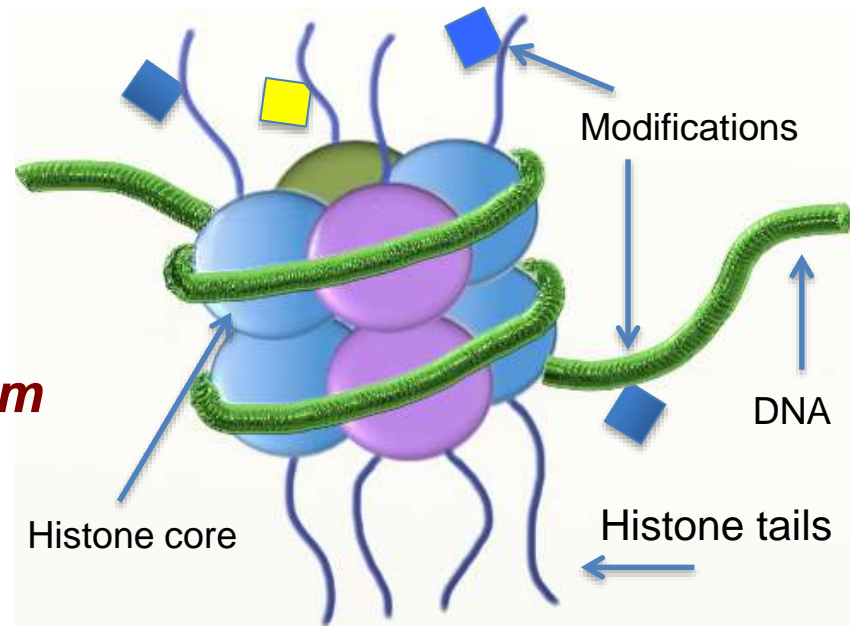
# Epigenetics meets oncology

- Epimutations provide a second hit in two-hit cancer initiation model
- These events can take place **years** before symptoms present\*
- Gradual ramp up to (often) high nucleosome levels on diagnosis
- Histone variants can distinguish nucleosomes of tumour origin
- Altered histone modification profiles in cancer derived nucleosomes
- Applications
  - Low cost screening and early diagnosis
  - Patient stratification e.g. Neoadjuvant therapy selection
  - Prognosis
  - CDx for epigenetic modifiers

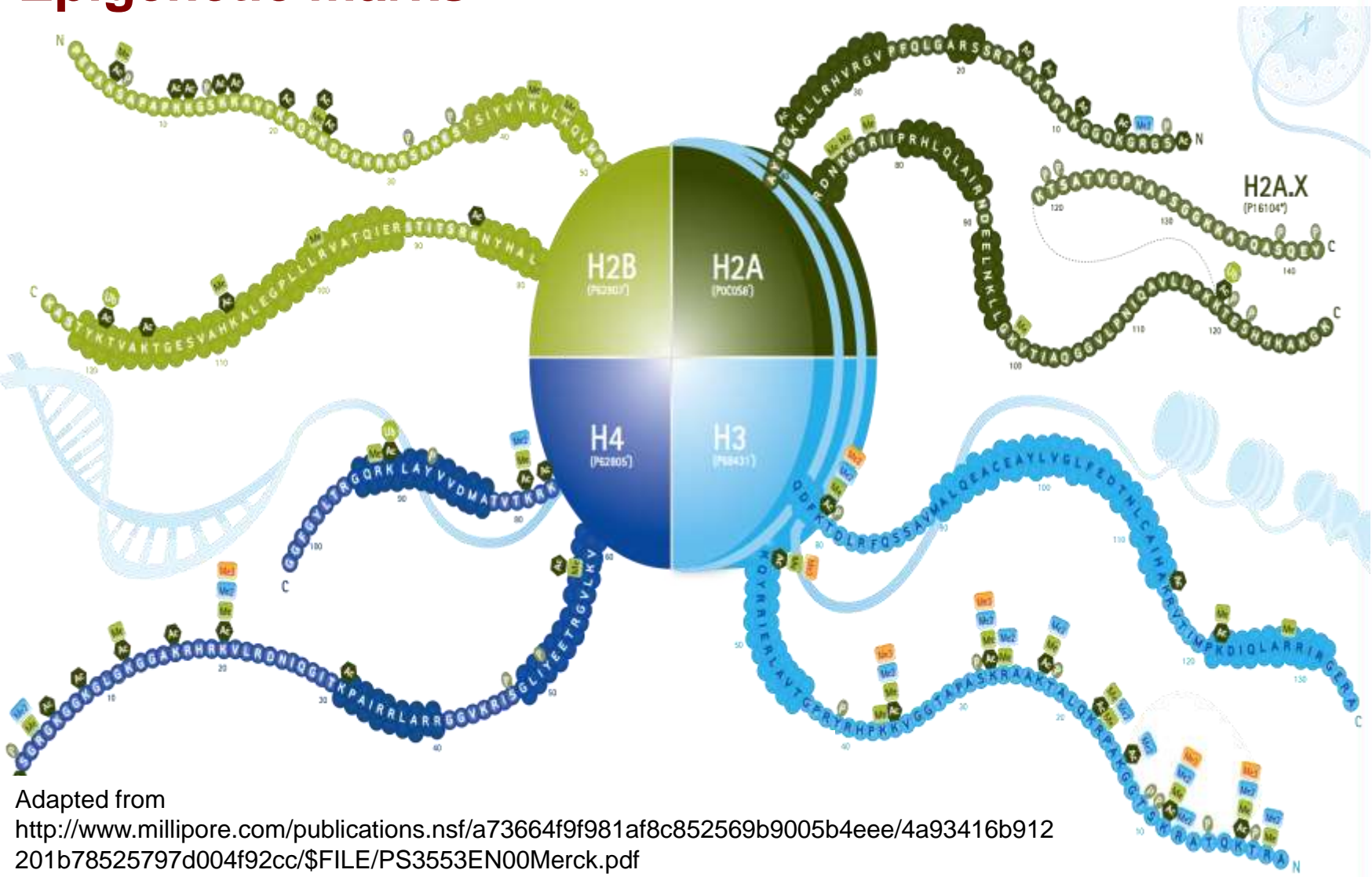
\*Aotake 1999, Holdenrieder 2009

# Nucleosomes - Diagnostic Potential

- Nucleosomes are a basic structural unit for genes
- Elevated cell turnover increases blood nucleosome levels
  - Cancer, heart attack, surgery, severe auto-immune disease
- This has previously limited diagnostic applications
  - Therapy response
  - Relapse
- ***Volition has solved this problem***



# Epigenetic marks - histone code

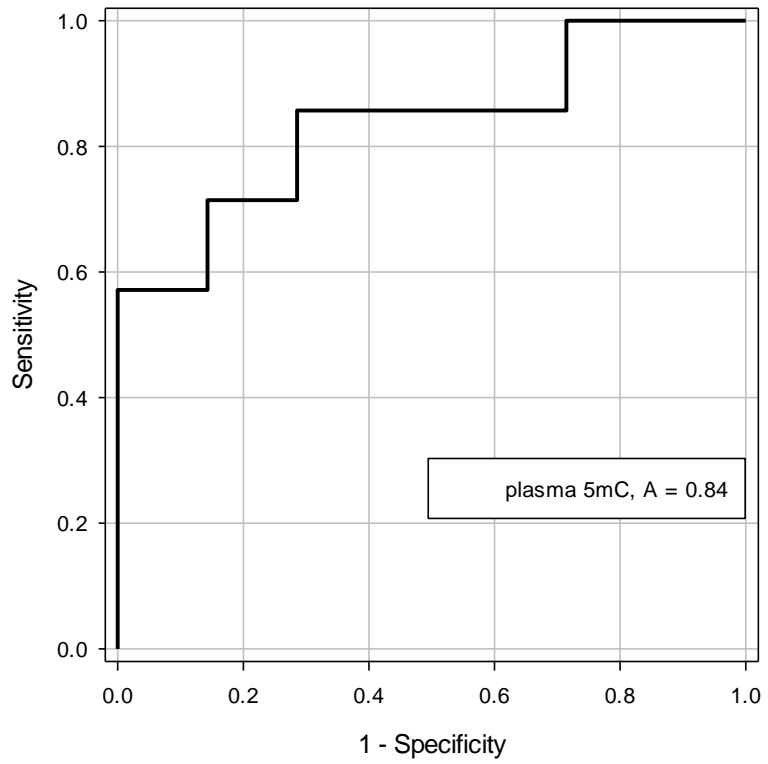
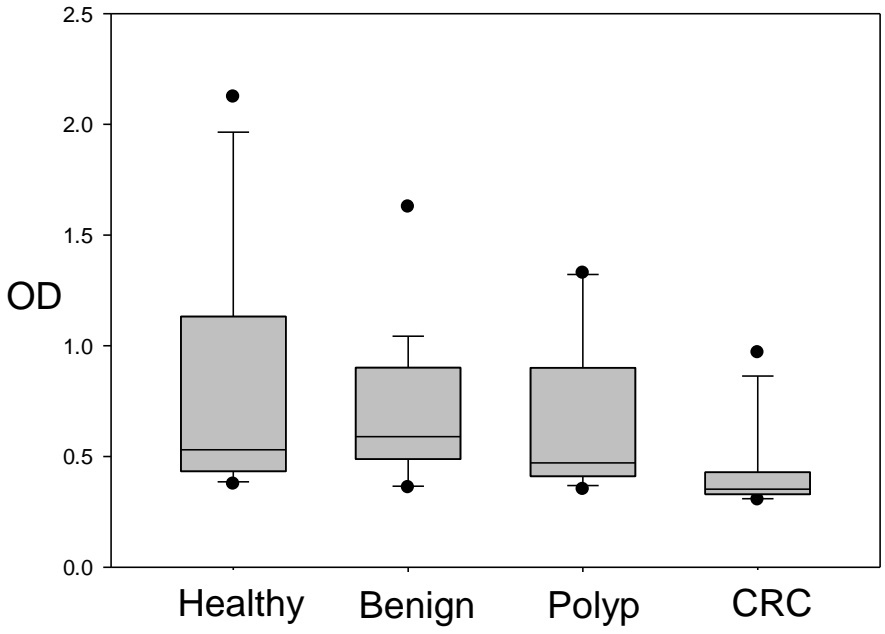


Adapted from  
[http://www.millipore.com/publications.nsf/a73664f9f981af8c852569b9005b4eee/4a93416b912201b78525797d004f92cc/\\$FILE/PS3553EN00Merck.pdf](http://www.millipore.com/publications.nsf/a73664f9f981af8c852569b9005b4eee/4a93416b912201b78525797d004f92cc/$FILE/PS3553EN00Merck.pdf)

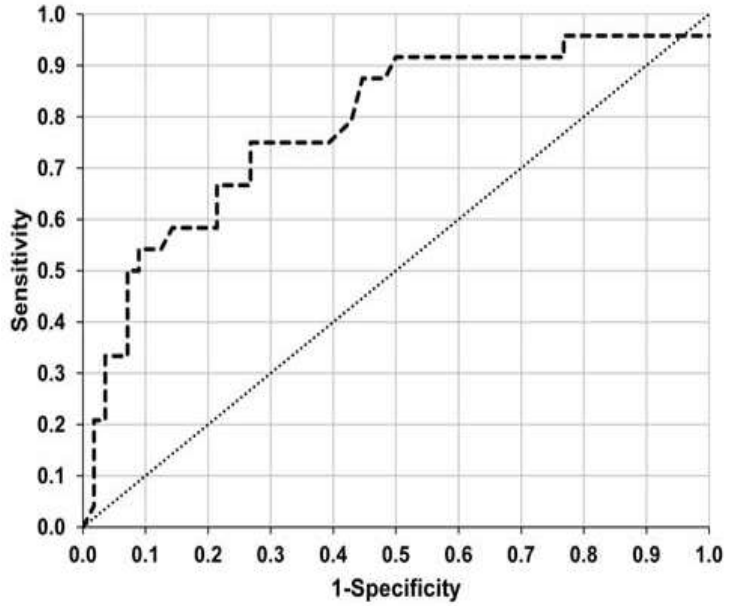
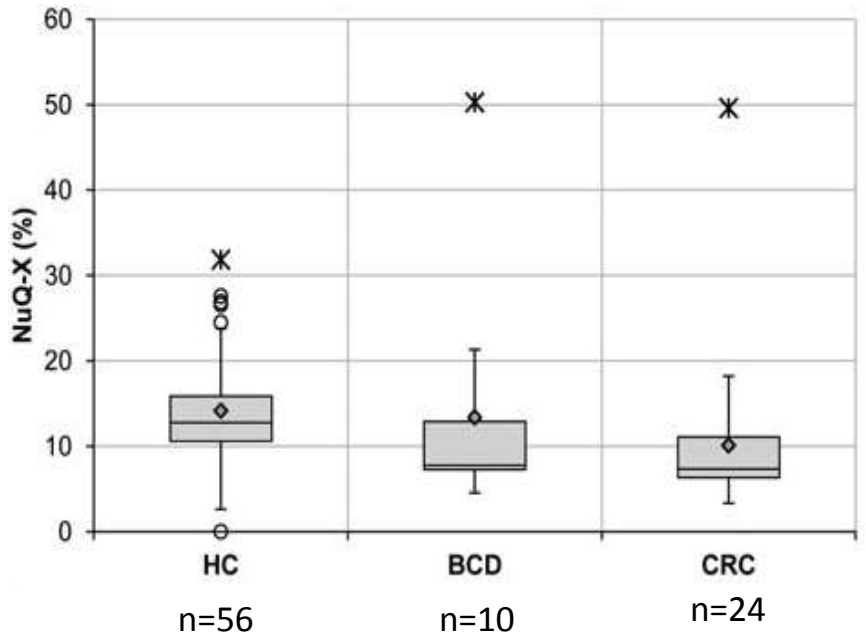


*Multiple histone modifications and variants*

# Nucleosomics<sup>®</sup> - 5MC Single Biomarker



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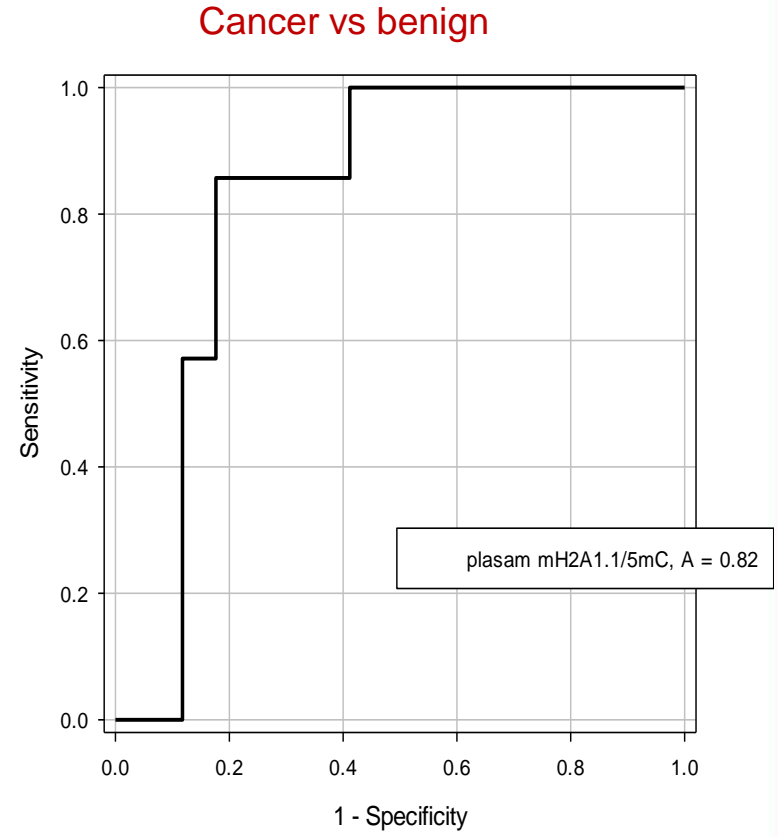
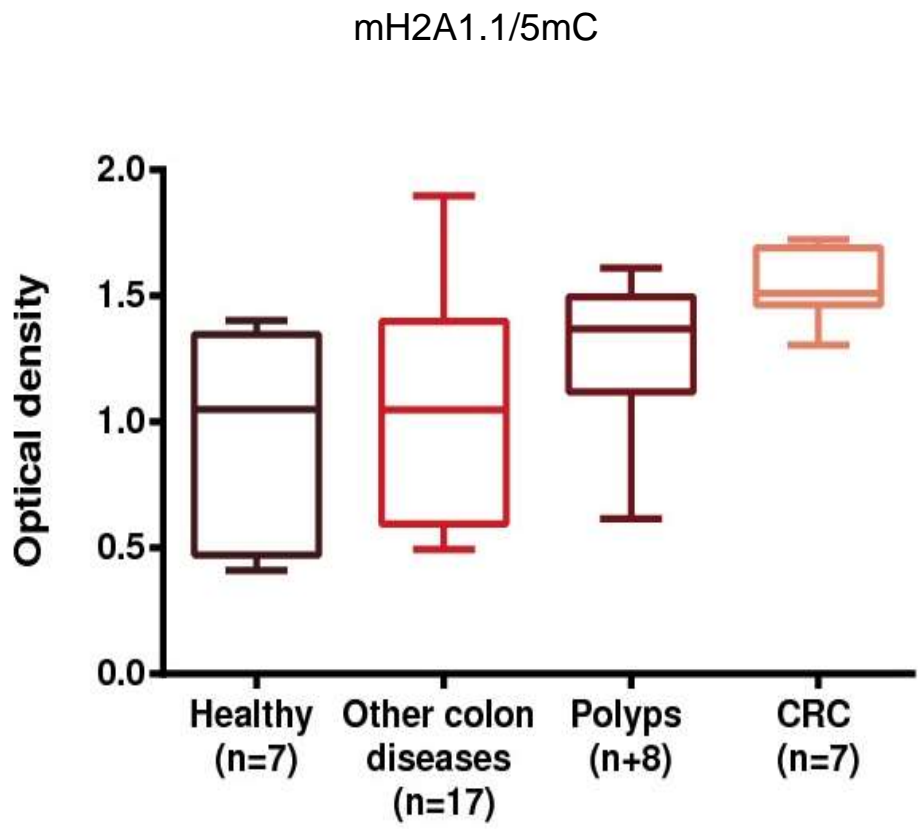


Holdenrieder et. al. ANTICANCER RESEARCH 34: 2357-2362 (2014)



**5MC - 70% Sensitivity / 75% Specificity**

# Nucleosomics<sup>®</sup> - mH2a1.1/ 5MC Dual Biomarker



IFCC worldlab- Istanbul June 2014



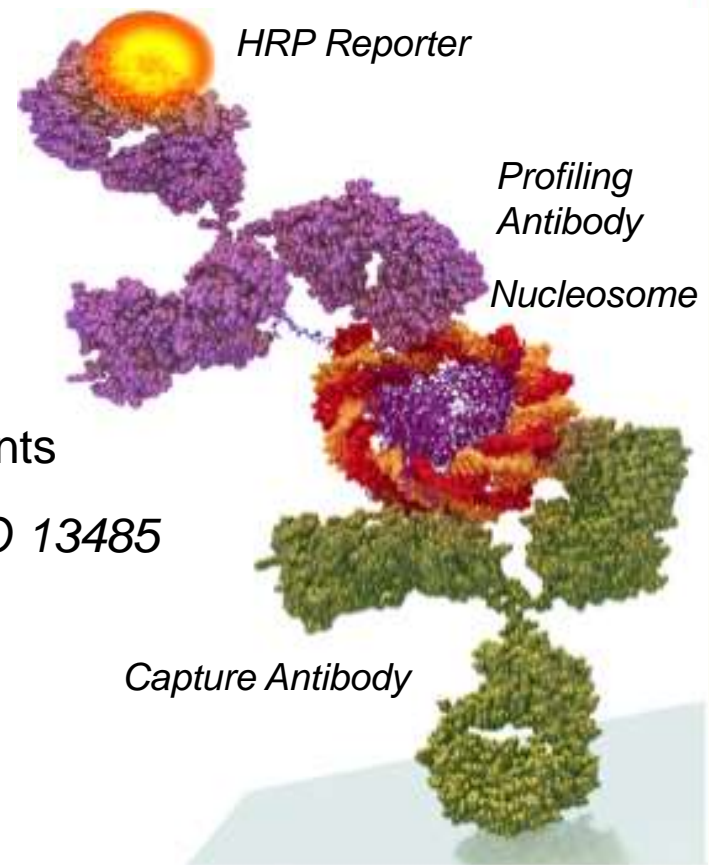
*Multiple markers improve sensitivity/specificity*

# Nucleosomics<sup>®</sup> - Accessing the Epigenome

## Four patent-protected NuQ<sup>®</sup> suites of products:

1. **NuQ<sup>®</sup>-X** specific DNA modifications
2. **NuQ<sup>®</sup>-V** histone variants
3. **NuQ<sup>®</sup>-M** histone modifications
4. **NuQ<sup>®</sup>-A** nucleosome-protein adducts

- Antibody supply and development agreements
- In house manufacturing and outsourced *ISO 13485*
- Research use only kits launched Q1 2014
- 6 assays (retail €795-€995) and growing
- Global distribution agreement



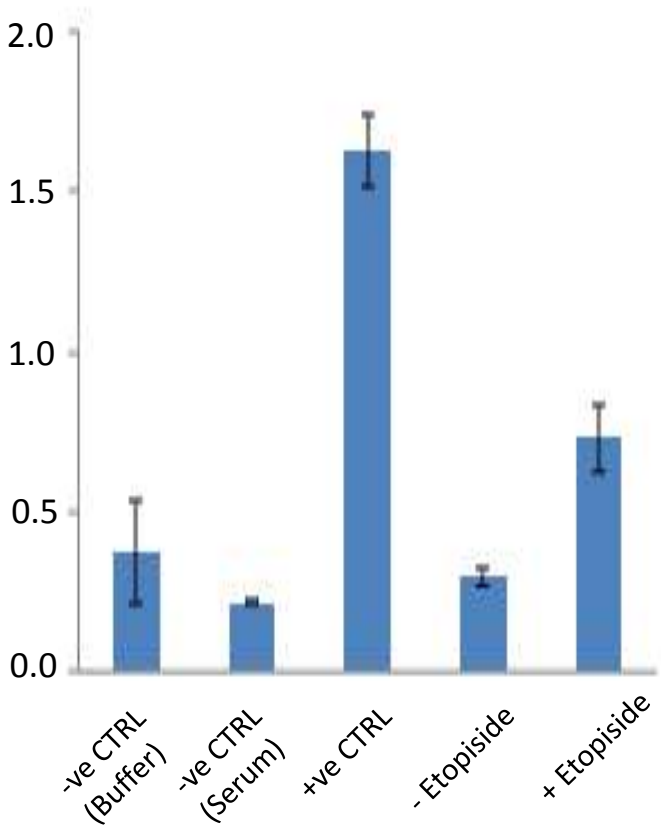


# Opportunities for biomarker integration - Discovery

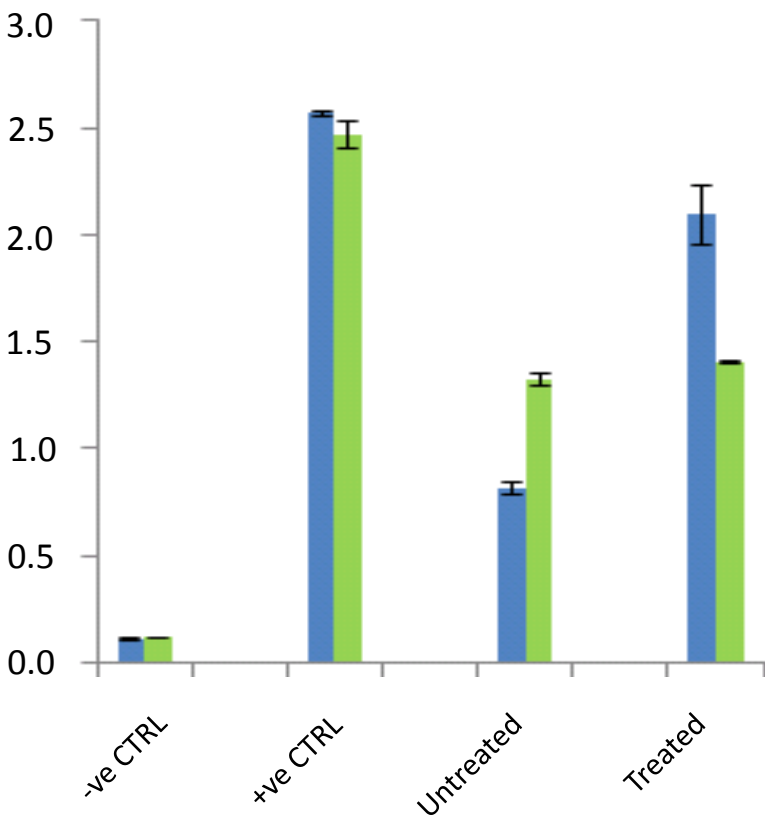
- Epigenetic Target qualification
- HDACi, DMTi, HDMi, HMTi - Candidate validation
- Exploitation
  - Research kits
  - Academia
  - CRO tie ups
  - Platform providers
  - Pharma

# Nucleosomics<sup>®</sup>- In-vitro tissue culture

Healthy and Apoptotic HepG2 cells



HepG2 cells treated with HDACi (TSA)



*In-vitro Research Use Only assays*

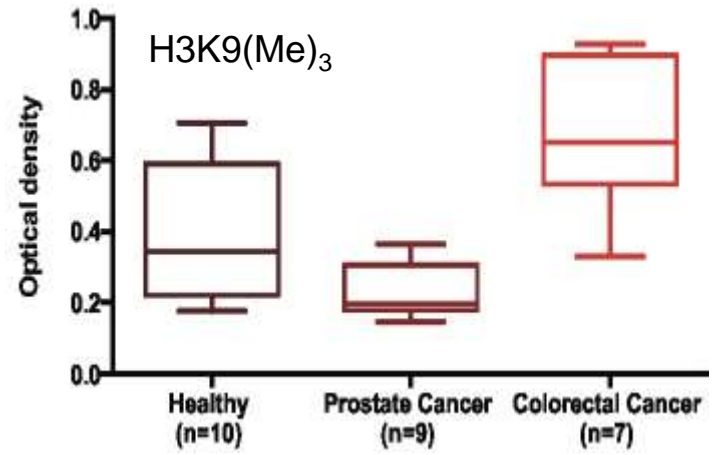
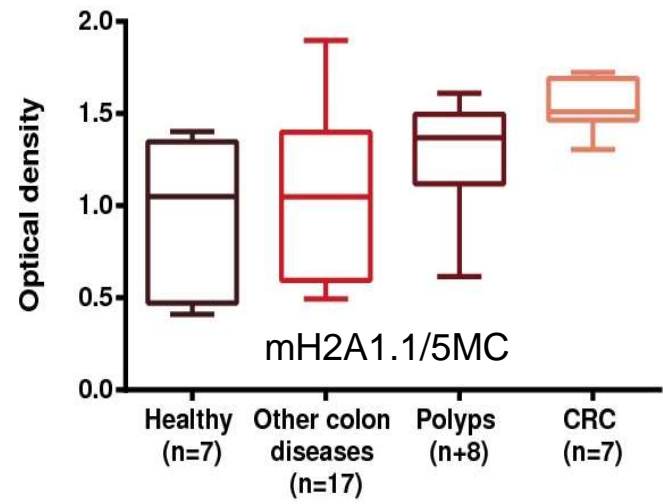
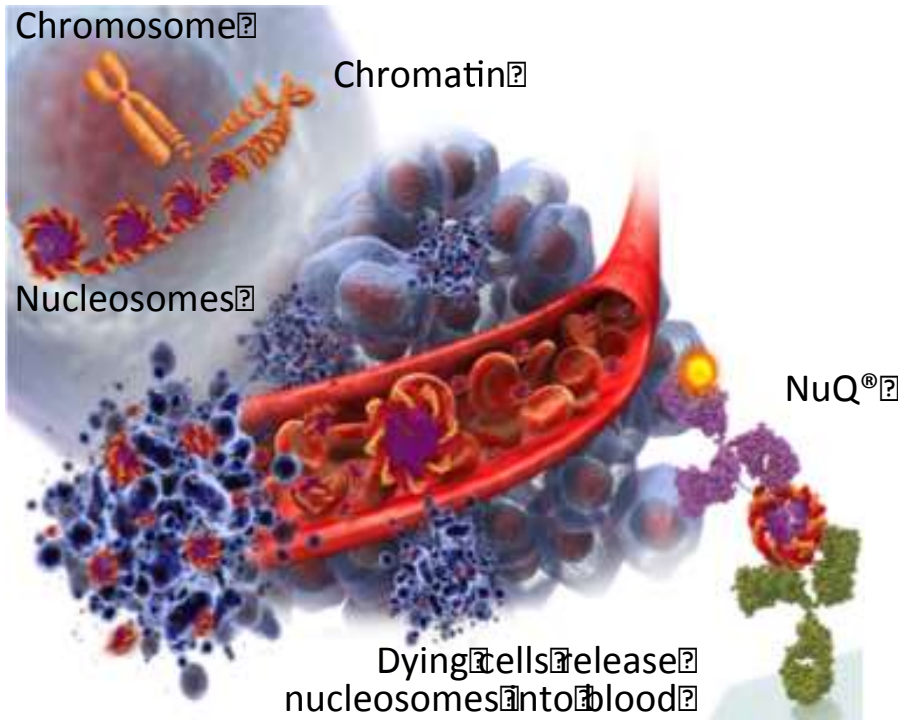
# Opportunities for biomarker integration - Preclinical

- In-vivo therapeutic efficacy monitoring
- Safety/tox - off target effects
- Correlate tissue and liquid biopsy
- Exploitation
  - CROs
  - Pharma (Validation)
- Clinical biomarker potential
- Animal health applications

# Opportunities for biomarker integration - Clinical

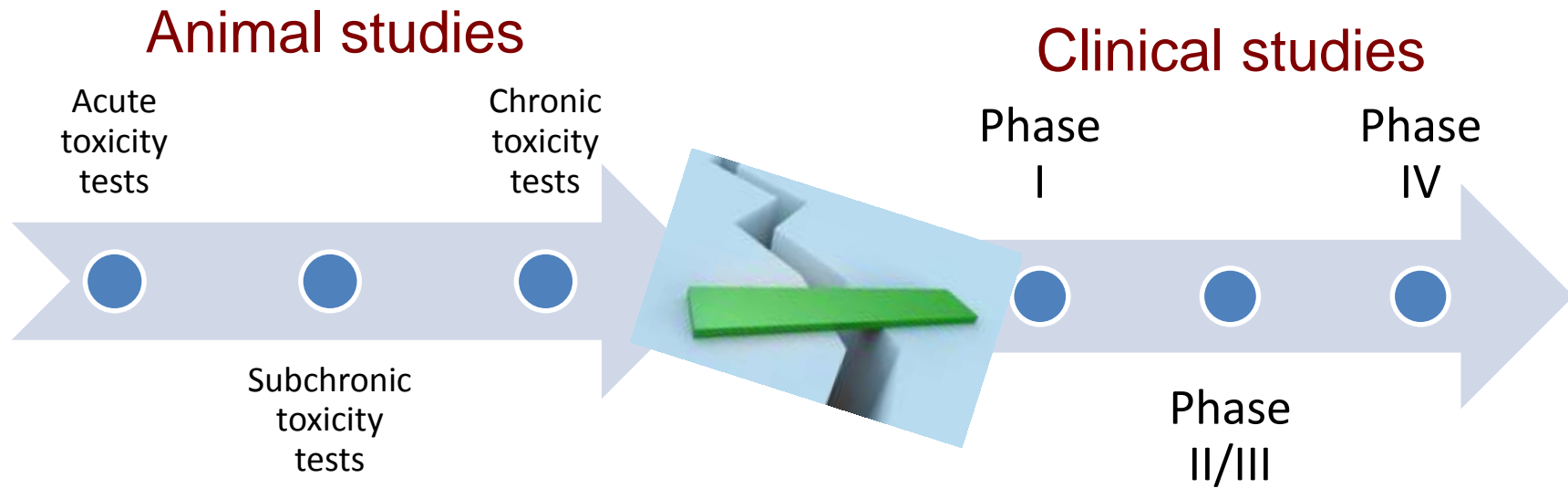
- Patient selection
- In-vivo therapeutic efficacy monitoring
- Safety/tox - off target effects
- Exploitation
  - CROs
  - Veterinary
  - Pharma

# Nucleosomics<sup>®</sup>- Companion Diagnostic potential



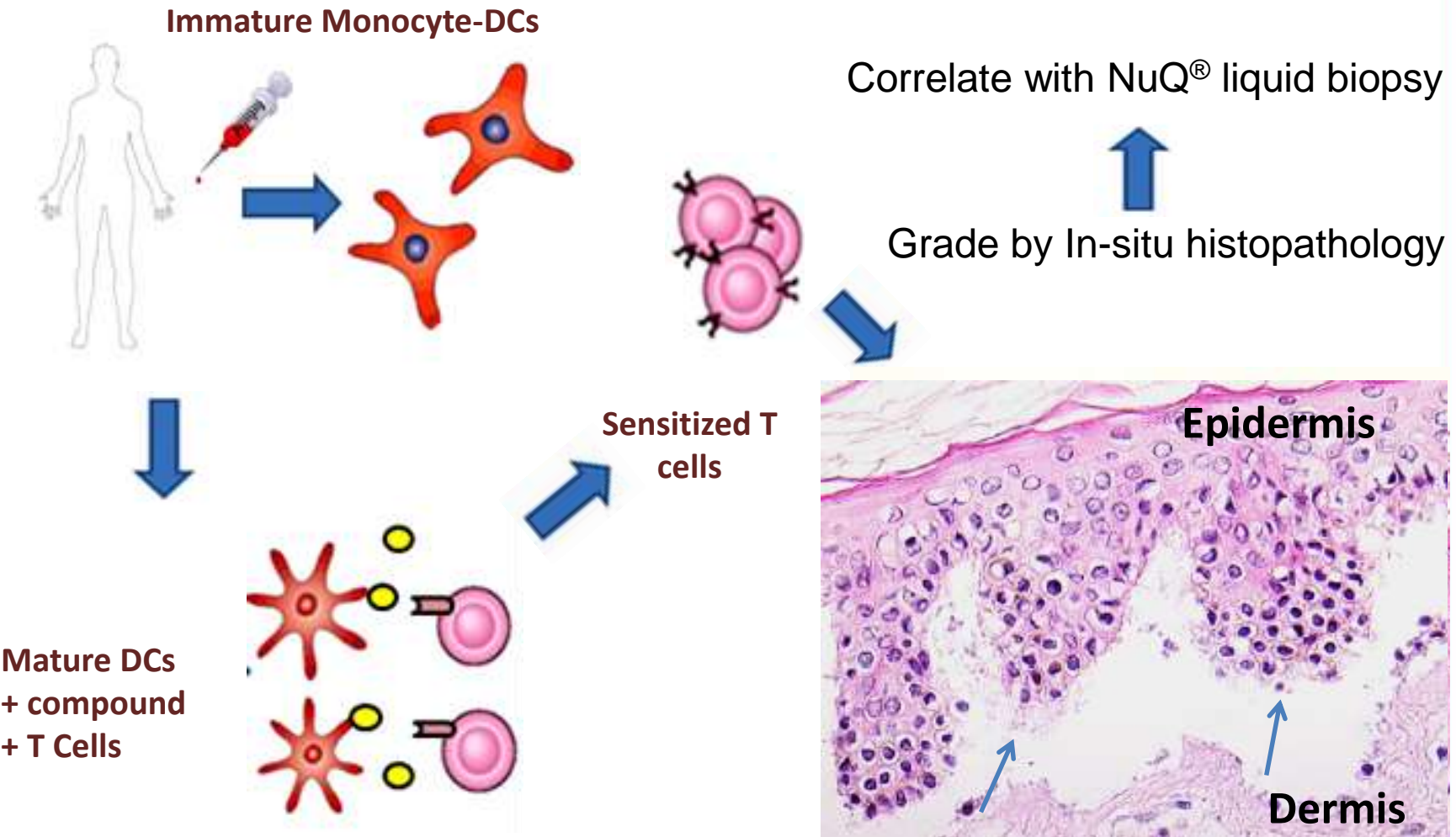
- Clinical trials colon and prostate cancer
- CE mark application for lead indication
- Expand to US and pilot new indications

# Pinpointing opportunities for biomarker integration



- Predicts immune response in *ex-vivo* human skin model
- Discriminates between sensitizers and non-sensitizers
- Safety and efficacy assessment of novel compounds

# Alcyomics - Skimune™ case study

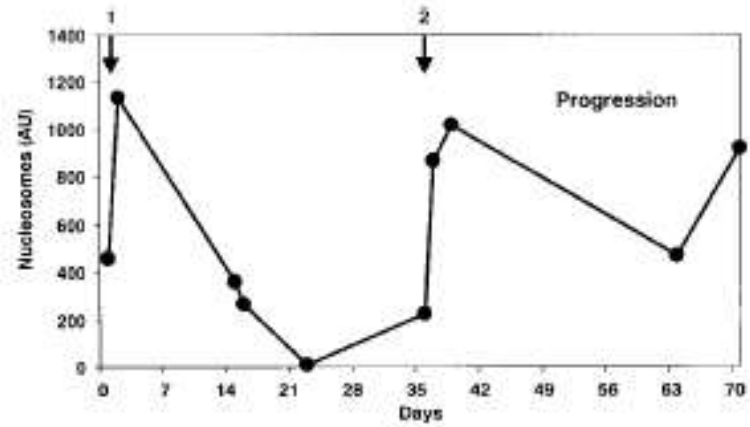


# CDx can open up markets

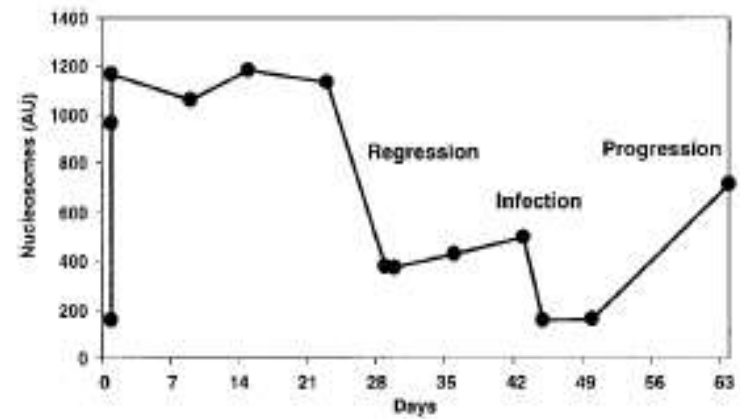
- Multi niche buster
  - CDx stratify patients - Target group confirmation
  - CDx increase costs - Reduce failures
    - Enable reimbursement
- Cancer as a molecular disease
  - MDx for rationale stratify cancer classification
  - Target the disease not the organ
- Epigenetic therapeutics beyond oncology
  - HDACi in neurological disease
  - HDACi in inflammatory disease



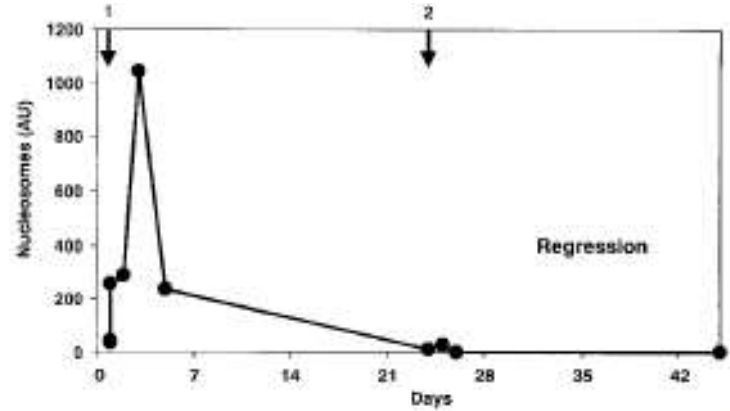
# Cell free nucleosomes for disease monitoring



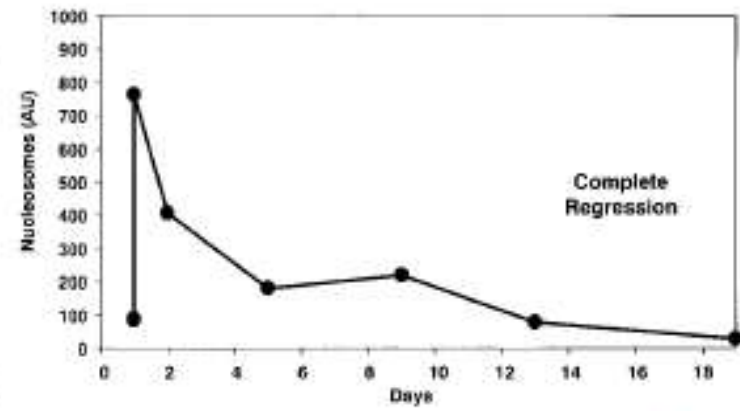
Pancreatic Cancer – Chemo progression



Lung Cancer – Chemo progression



Lung Cancer – Chemo regression



Head and neck Cancer – Radio regression

Holdenrieder et al, Nucleosomes in serum of patients with benign and malignant diseases. Int. J. Cancer (Pred. Oncol.): 95, 114–120, 2001

# VolitionRx - Partnering opportunities

*Volition is seeking collaborators with well-annotated blood or urine samples from various stages of disease as well as suitable control materials for further clinical studies particularly from therapeutic trials for patient stratification*

Hardware platform providers – research and diagnostic

CROs - epigenetic assays and generic efficacy/toxicity biomarkers

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[www.VolitionRX.com](http://www.VolitionRX.com)

[www.Nucleosomics.com](http://www.Nucleosomics.com)



***Seeking additional development partners***