HKG *epi* THERAPEUTICS Ltd.

Harnessing the epigenome

HKG *epi* THERAPEUTICS Ltd.

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CLIA ACCREDITED

CAP ACCREDITED
COLLEGE of AMERICAN PATHOLOGISTS

- **Disclaimer: Forward-Looking Statements**

- The forecasts and projections presented in this business plan are forward-looking statements. Please note that actual results may vary and are subject to inherent uncertainties and risks. We caution readers not to place undue reliance on these forward-looking statements as they are based on current expectations and assumptions. The company undertakes no obligation to update or revise these statements.

Executive Summary: HKG *epi* Therapeutics

❖ **Mission and vision**

Pioneering early disease detection through epigenetics.

❖ **Unique Technology**

Advanced DNA methylation platform for accurate diagnoses.

❖ **Market Strategy**

Targeting key healthcare sectors globally with innovative solutions..

❖ **Expert Team**

Led by epigenetics pioneers committed to healthcare advancement...

❖ **Financial Snapshot**

Leadership committed to healthcare advancement...

Company mission

- Developing a platform for Early Detection of Disease
- Clinical Application of Epigenetics
- Building a global *epi*Health ecosystem; maintaining health and preventing disease through a cloud-driven, global platform of clinical epigenetic labs and one stop shop for epigenetic tests
- Our vision: *improve lives by detecting and preventing illnesses before they become a major health issue.*

OUR COMPANY I

HKG *epi* THERAPEUTICS Ltd.
Harnessing the epigenome

- ✓ Company Name: **HKG *epi*Therapeutics Ltd**
- ✓ Date of Establishment: August 1 2016
- ✓ Employee Number: ~20 in HKG, Montreal and Israel and 14 in Shenzhen.
- ✓ Mission: To develop tools for early detection of cancer and promoting healthy aging
- ✓ Core Competitiveness:
  - ✓ All global IP protected by PCT and exclusively licensed or assigned to company
  - ✓ Low cost
  - ✓ High-throughput by automation (R&D with financially supported by the Innovation and Technology Department of HKG SAR)
  - ✓ Resale agreement for epiAging in Germany, HK, UK, Thailand
  - ✓ Global research collaborations and reach: Canada, USA, Israel, Brazil, Bangladesh, India Hong Kong and China.
  - ✓ CAP accredited and CLIA accredited lab in HK science park which was just audited and reaccredited.
- ✓ Goal: To develop a global world-leading innovative multi-cancer early screening platform

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WORLD CLASS LEADERSHIP

Epigenetic pioneer is leading the company

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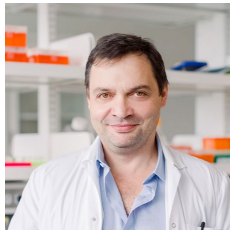
Moshe Szyf, PhD

Glaxo Smith Kline - CIHR chair in pharmacology
James McGill Professor
Department of Pharmacology and Therapeutics at McGill University, Canada

- Fellow of the Royal society of Canada
- Fellow of the Canadian Academy of Health Sciences
- Pioneer in the field of epigenetics
- Inventor of the first patent in the field
- Founder of the field of behavioral and psychiatric epigenetics
- Published ~300 papers in the area
- 2009 Karolinska Research Lectures at Nobel Forum
- Ted Talk: How early life experience is written into DNA
- Distinguished lecture FDA 2010
- NIMH directors Innovation speaker series 2012
- Quebec Scientist of the year 2009
- UK Royal Society of Art lecture 2013



David Cheishvili, Ph.D
Chief Innovation officer

Ye Xiang, Ph.D
Director and member of the board of directors

Levan Cheishvili
Chief Technology officer

Carlos Luiz, MD
Medical Director

Charlie Ban
CEO Epiecho

Sharon Luk, Ph.D
Director of clinical Services

Corporate Structure

香港精准医学技术有限公司
HKG epi THERAPEUTICS Ltd.
Harnessing the epigenome

Board of Directors

HKG epiTherapeutics Hong Kong
(38% Szyf: 62% 8 investors)

MTL Epitherapeutics Ltd.
(90% HKG epitherapeutics, 10% David Cheishvili)

INEX Epitherapeutics Ltd. Singapore
(50% HKG epitherapeutics, 50% Inex)

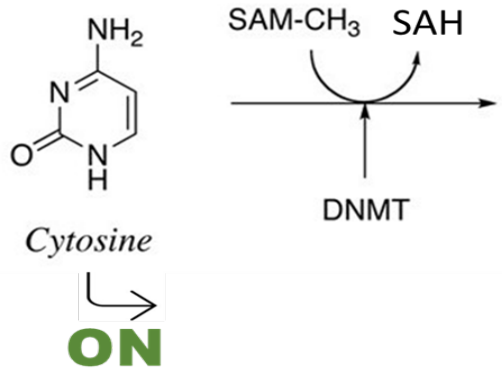
EpiEcho WOFE Beijing China
(100% HKG epitherapeutics)

VIE structure

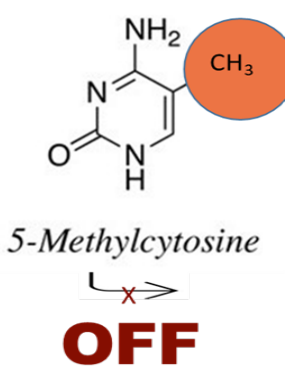
Epishen (Shenzhen)

What is DNA methylation? Why is it the next big thing in medicine?

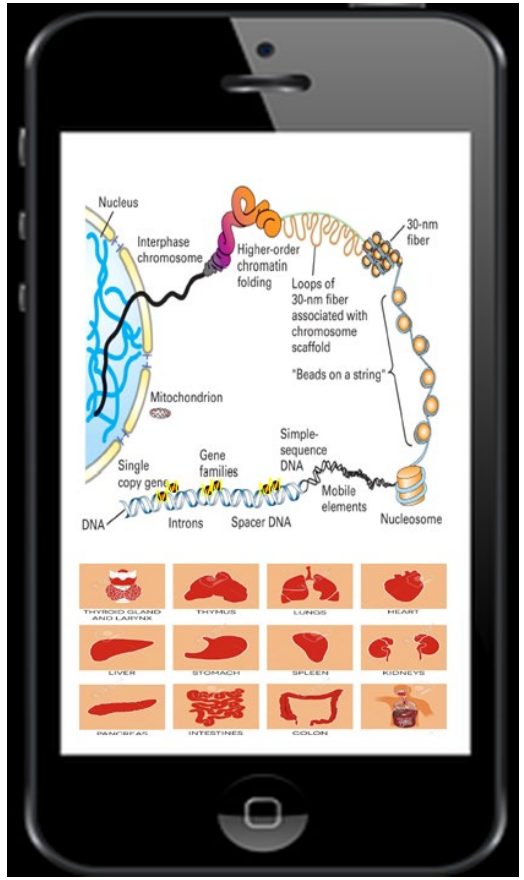
unmethylated



Methylated



DNA methylation is the software of the genome which is written during embryonal development



The DNA methylation software is “bugged” in disease. We can detect these “bugs” using our methods.

Normal	Cancer
Normal	Cardiovascular disease
Normal	Metabolic disorders
Normal	Obesity
Normal	Mental health disorder
Normal aging	Accelerated aging

DNA methylation is the code of our biological state, our exposures and experiences, we know how to read this code and be informed by it.

Huge potential; where is the gap?

- Epigenetic tests are bound to change the way we are performing clinical Lab tests and take over the clinical Laboratory market.
- **However**
- Despite vast advances in epigenetics research and lots of noise very little is translated to clinical practice.
- **Why?**
- There is a huge gap between the vast potential and extremely limited capacity for clinical epigenetic testing globally.

The next big thing

A high throughput, robust global platform for delivery of an evolving landscape of clinical epigenetic tests.

A clinical epigenetic lab blue-print which is the focal node for a heath building and maintenance ecosystem.

A clinical lab for the 22nd century that revolutionizes clinical laboratory medicine.

Our plan

Focus

- Focus not on a test, but on a unified platform for many diverse tests

Translate

- Translate epigenetic discoveries to a panel of clinically validated and accessible tests through a unified platform for, discovery, research and development.

Develop

- Develop a scalable automated cloud-based platform for high throughput-one shop delivery of clinical epigenic tests.

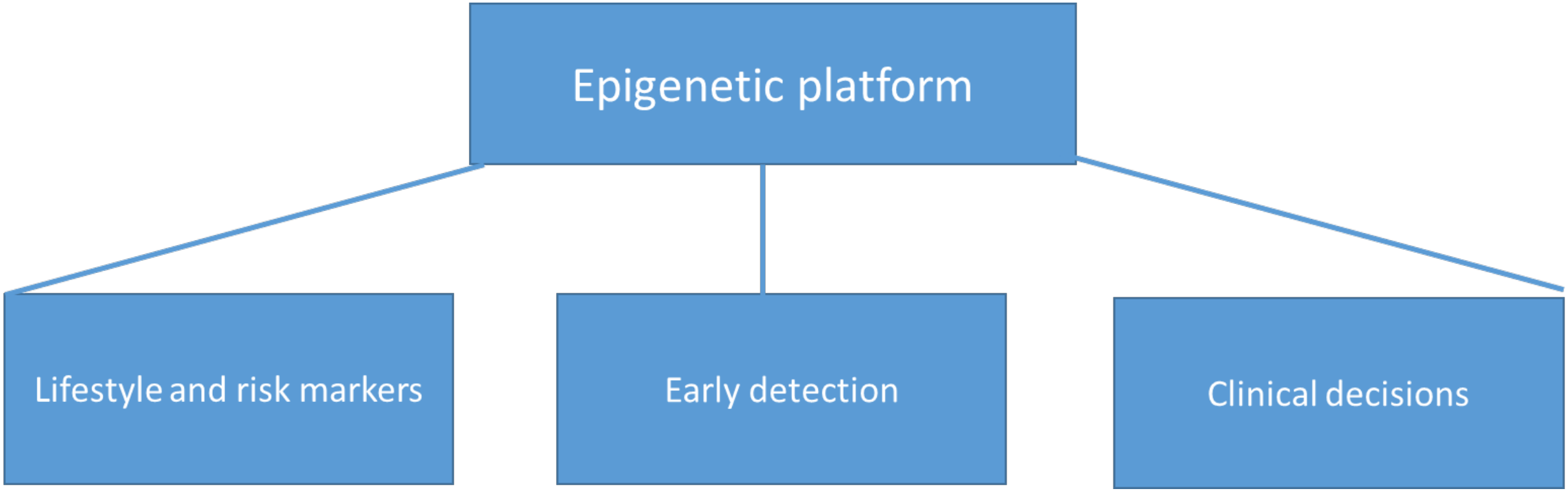
Create

- Create a blueprint of the clinical epigenetic lab of the 22nd century that would be implemented globally

Integrate

- Integrate epigenetic testing into a platform of a multitiered epihealth ecosystem. .

Epigenetic markers portfolio



Products and Production Laboratory Overview

Global Operations and Expertise in Epigenetic Testing: HKG epiTHERAPEUTICS Ltd

Innovation and Data Analysis

(Montreal, Canada)

Clinical Management and Regulatory Oversight

Sanford, FL. USA

Computation and Cloud Management

(Israel)

Test Production and R & D

(Hong Kong science park)

China Test Production Lab

Shenzhen

Products : Ready to market test Production system and lab launched in 2021

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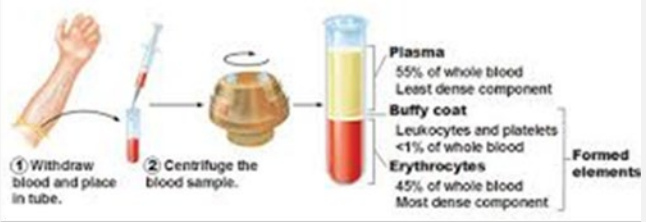
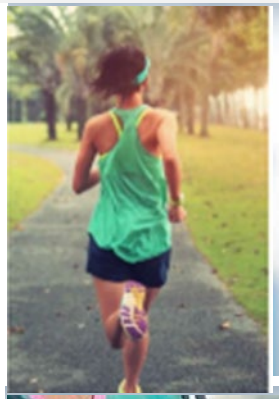
*epi*Liver

Early Detection of Liver Cancer



Early detection product pipeline including panCancer product.



Detection of Biological Age

*epi*Smoke

*epi*Age (Saliva)

Early Detection of Cervical Cancer

*epi*Cervix (Pap smears)

Our regulatory strategy is via LDT path; The lab in HKSTP is CLIA and CAP accredited and CLIA registered; our plan is to copy this platform in strategic global locations

CENTERS FOR MEDICARE & MEDICAID SERVICES
CLINICAL LABORATORY IMPROVEMENT AMENDMENTS
CERTIFICATE OF ACCREDITATION

LABORATORY NAME AND ADDRESS
HKG EPITHERAPEUTICS LTD
UNIT 313-515, 3/F BIOTECH CENTRE 2,
11 SCIENCE PARK WEST AVE HONG KONG SCIENCE PARK
hong kong, SAR
HONG KONG

CLIA ID NUMBER
99D2281144

EFFECTIVE DATE
06/21/2023

LABORATORY DIRECTOR
CARLOS J RUIZ M.D.

EXPIRATION DATE
06/20/2025

Pursuant to Section 353 of the Public Health Services Act (42 U.S.C. 263a) as revised by the Clinical Laboratory Improvement Amendments (CLIA), the above named laboratory located at the address shown hereon (and other approved locations) may accept human specimens for the purposes of performing laboratory examinations or procedures.

This certificate shall be valid until the expiration date above, but is subject to revocation, suspension, limitation, or other sanctions for violation of the Act or the regulations promulgated thereunder.

CMS
CENTERS FOR MEDICARE & MEDICAID SERVICES

Monique Spruill, Director
Division of Clinical Laboratory Improvement & Quality
Quality & Safety Oversight Group
Center for Clinical Standards and Quality

COLLEGE of AMERICAN PATHOLOGISTS

CERTIFICATE OF ACCREDITATION

HKG epiTherapeutics Ltd
Laboratory
Hong Kong, China
Carlos J. Ruiz, MD

CAP Number: 9143982
AU-ID: 2142729

The organization named above meets all applicable standards for accreditation and is hereby accredited by the College of American Pathologists' Laboratory Accreditation Program. Reinspection should occur prior to **December 27, 2023** to maintain accreditation.

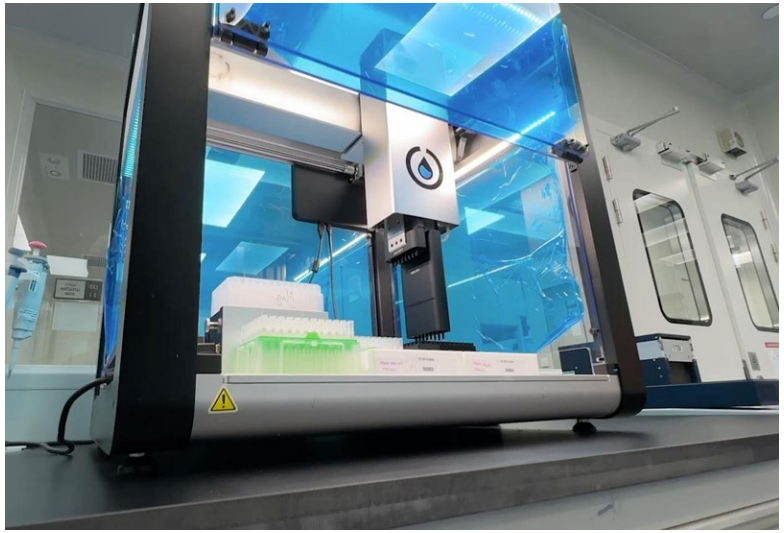
Accreditation does not automatically survive a change in director, ownership, or location and assumes that all interim requirements are met.

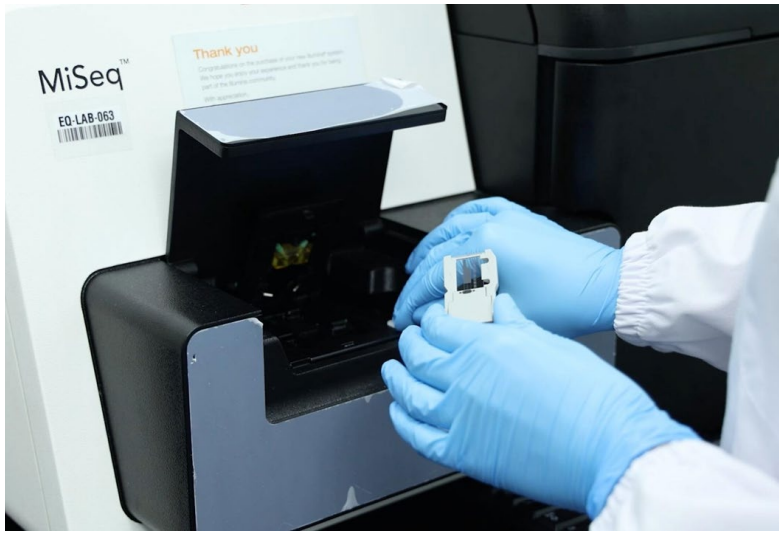
Michael Bradley Datto, MD, PhD, FCAP
Chair, Accreditation Committee

Emily Volk, MD, FCAP
President, College of American Pathologists

CAP ACCREDITED COLLEGE of AMERICAN PATHOLOGISTS

HKG Epigenetic Test "Production" Laboratory at HKSTP





- Laboratory Construction Tailored for Biochemical Testing Procedures.
- Segregated Spaces for Each Testing Step.
- Automated Testing Process with Cloud-Based Management, Analysis and Reporting.

Recent peer reviewed clinical validations of our tests

nature communications

Article

https://doi.org/10.1038/s41467-023-39055-7

A high-throughput test enables specific detection of hepatocellular carcinoma

Received: 24 September 2022

Accepted: 25 May 2023

Published online: 07 June 2023

Check for updates

David Cheishvili[1,2], Chifat Wong[1], Mohammad Mahbubul Karim[3], Mohammad Golam Kibria[3], Nusrat Jahan[3], Pappu Chandra Das[3], Md. Abul Khair Yousuf[4], Md. Atikul Islam[4], Dulal Chandra Das[4], Sheikh Mohammad Noor-E-Alam[4], Moshe Szyf[5], Sarwar Alam[6], Wasif A. Khan[3] & Mamun Al Mahtab[4]

High-throughput tests for early cancer detection can revolutionize public health and reduce cancer morbidity and mortality. Here we show a DNA methylation signature for hepatocellular carcinoma (HCC) detection in liquid biopsies, distinct from normal tissues and blood profiles. We developed a classifier using four CpG sites, validated in TCGA HCC data. A single F12 gene CpG site effectively differentiates HCC samples from other blood samples, normal tissues, and non-HCC tumors in TCGA and GEO data repositories. The markers were validated in a separate plasma sample dataset from HCC patients and controls. We designed a high-throughput assay using next-generation sequencing and multiplexing techniques, analyzing plasma samples from 554 clinical study participants, including HCC patients, non-HCC cancers, chronic hepatitis B, and healthy controls. HCC detection sensitivity was 84.5% at 95% specificity and 0.94 AUC. Implementing this assay for high-risk individuals could significantly decrease HCC morbidity and mortality.

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Received: 27 January 2023 | Revised: 17 July 2023 | Accepted: 21 July 2023

DOI: 10.1002/ijc.34686

IJC INTERNATIONAL JOURNAL of CANCER

RESEARCH ARTICLE

Cancer Genetics and Epigenetics

Validation of novel DNA methylation markers in cervical precancer and cancer

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[3]HKG Epitherapeutics, Hong Kong

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Email: mariam.elzein@mcgill.ca

Funding information
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Abstract

We have recently identified, using a genome-wide approach, new methylation markers which were evaluated among various cervical intraepithelial neoplasia (CIN) grades and cervical cancer. We herein validate the methylated state of these genes in independent study populations, based on histology ascertained outcomes regardless of human papillomavirus status. *CA10*, *DPP10*, *FMN2* and *HAS1* (discovery set: 54 normal, 50 CIN1, 40 CIN2, 42 CIN3) were evaluated by targeted bisulfite next generation sequencing (NGS) (Illumina MiSeq platform) in 258 (training set: 100 normal, 50 CIN1, 50 CIN2, 50 CIN3, 8 cancers) and 373 (validation set: 100 normal, 57 CIN1, 61 CIN2, 53 CIN3, 102 cancers) physician-collected samples (PreservCyt). Using targeted amplification NGS data from the training set for 94 normal and eight cancer samples, we calculated for each gene the median methylation value. These were summed and normalized to compute a four-gene Marker Polygenic Score (MPS). We compared the relationship between MPS and progression from normal through CIN grades and cancer, separately in the training and validation sets, and tested its clinical performance via receiver-operating characteristic curves. MPS increased with increasing CIN grade, and accurately predicted cervical cancer in the

- For more info: https://www.hkgepitherapeutics.com/
- https://www.epi-age.com/