Multi-Cancer Early Detection and MRD using AI & Liquid Biopsy

Early detection of 16 common types of cancers via only one tube of blood.

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Rapha Biotechnology Inc.

16 TYPES OF COMMON CANCERS(SOLID TUMORS) COVERED

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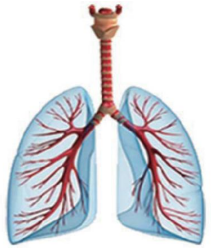
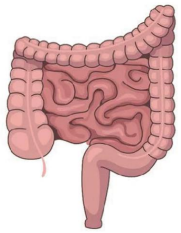
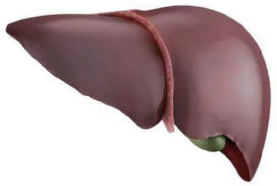


Lung

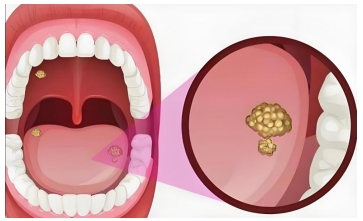


Colorectum



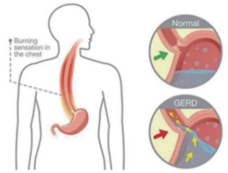
Liver

Stomach



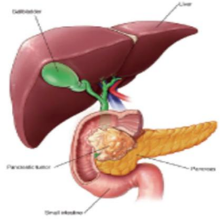
Oral

Breast

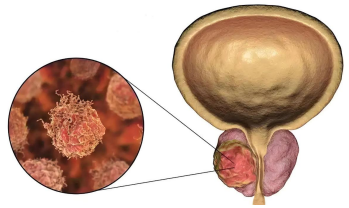


Esophagus

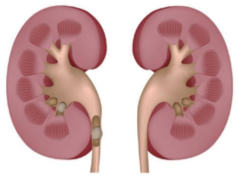
Cervix



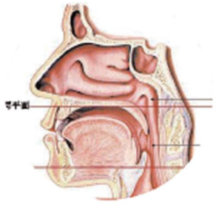
Pancreas



Prostate

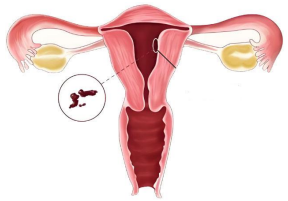


Kidney

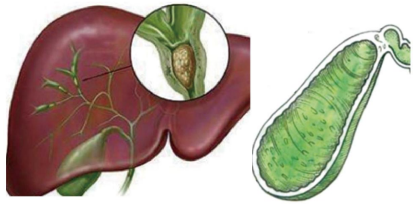


Nasopharynx

Ovary



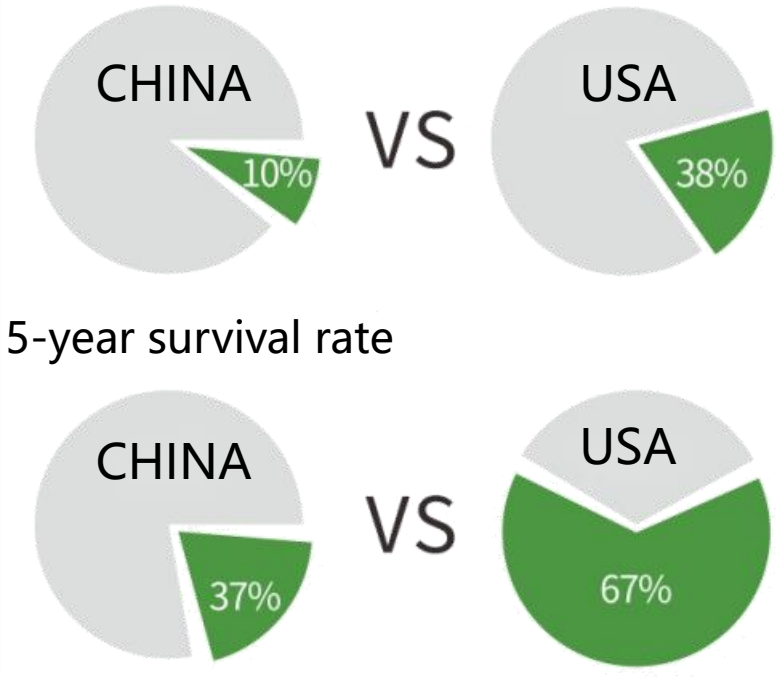
Uterine



Cholangiocarcinoma & Gallbladder

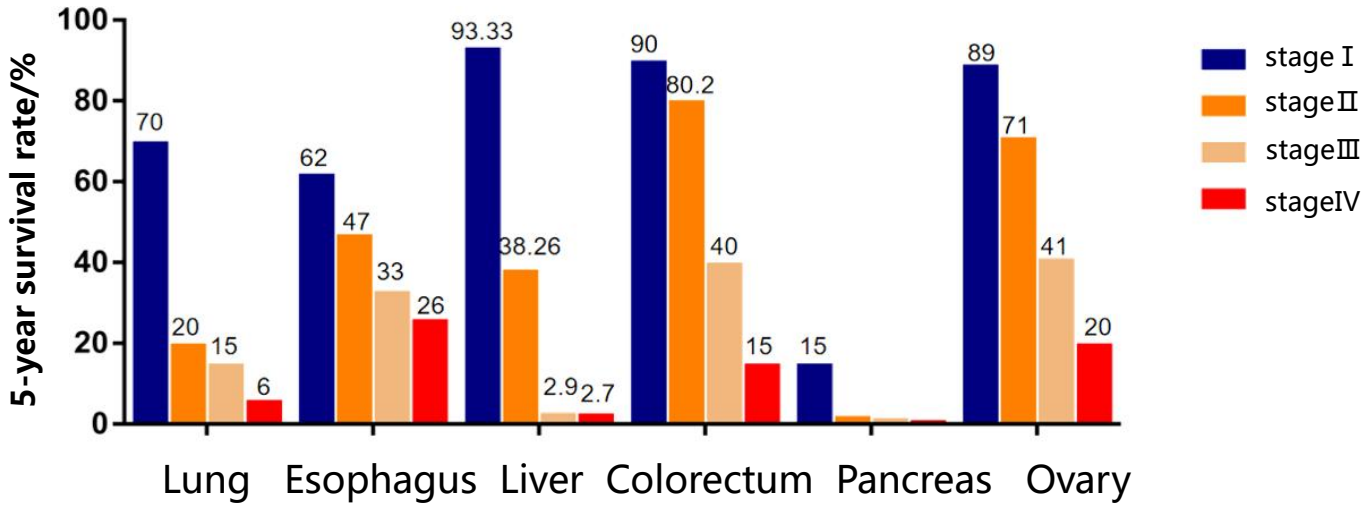
Background- Early screening and prevention are beneficial

The proportion of patients who are still in the early-stage of cancer upon diagnosis.



National Cancer Report, 2019,
National Cancer Center of China.

Health economics study shows investing $1 in screening and prevention can save $15-20 in healthcare expenses.

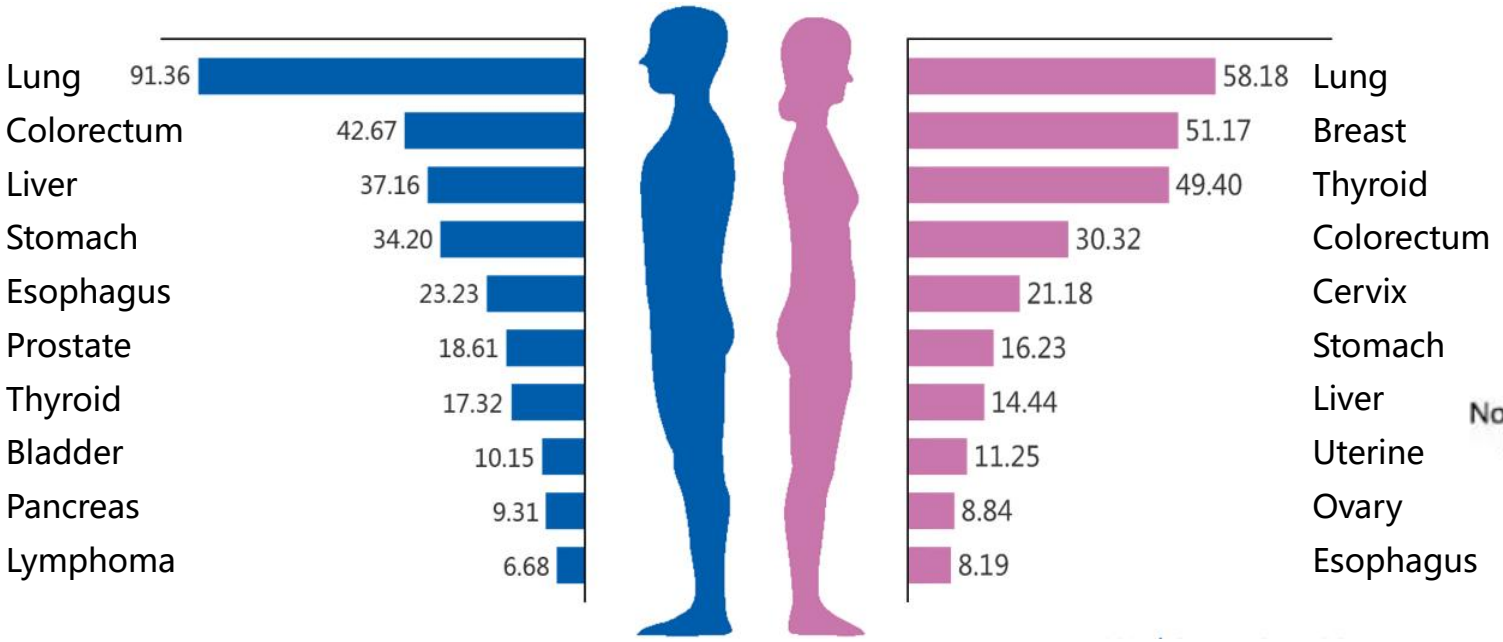


The five-year survival rate of early-stage cancer patients is significantly higher than that of advanced-stage patients.

Background- commonly occured cancers

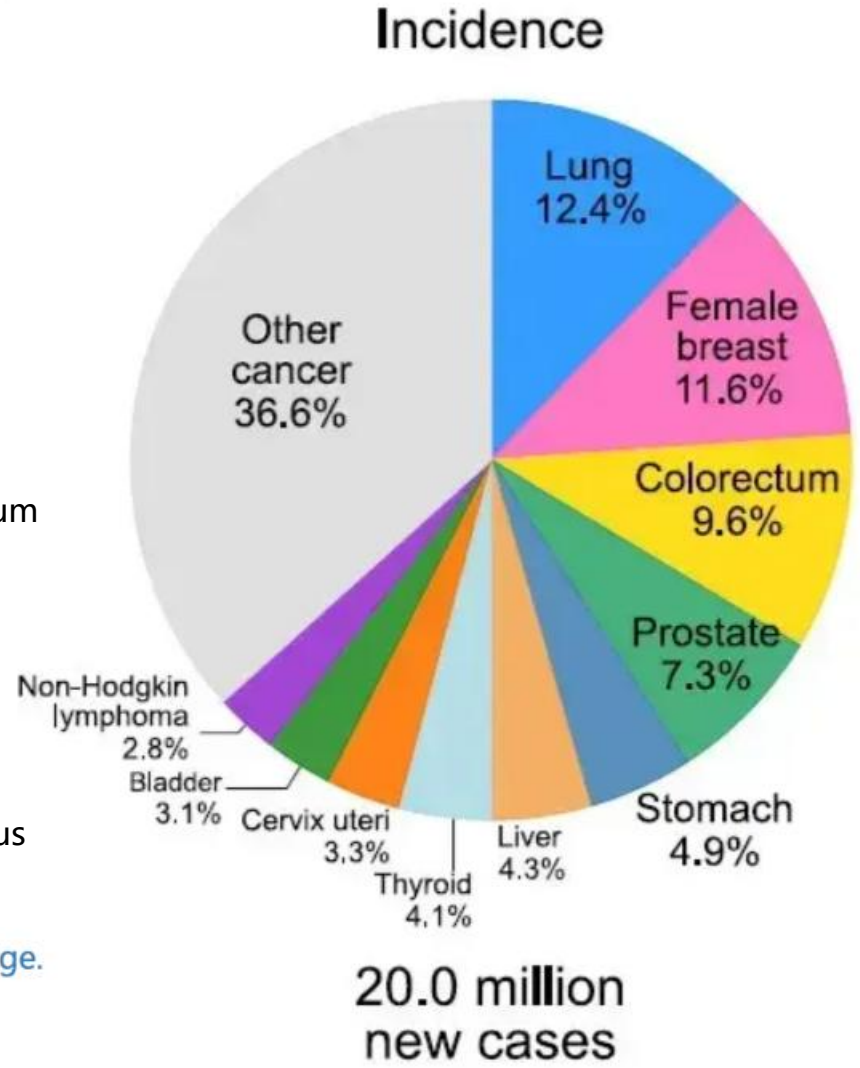
IARC: In 2022, there were an estimated 20 million new cancer cases and 9.7 million deaths globally.

Incidence rate (1/100,000) of male and female in China



J Natl Cancer Cent. 2024,4(1):page.

Cancer incidence focus on around 15 types of common cancers in China.



Global top 10 cancer types by incidence rate

Problems- Routine cancer screening methods have many drawbacks

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Applicable cancer types:
Liver, Prostate, etc

Low sensitivity

Low specificity

Applicable cancer types:
Lung, Breast, etc

Radiation exposure

Low sensitivity

Applicable cancer types:
Colorectum, Stomach, Esophagus, etc

Complicated operation

Painful examination

Low compliance

Applicable cancer types:
multi-cancer

Rely on experience

High cost

Routine tumor screening and diagnostic techniques commonly suffer from problems such as missed detections, false detections, complexed operations, and high costs.

Market Analysis- Highly price-sensitive consumers

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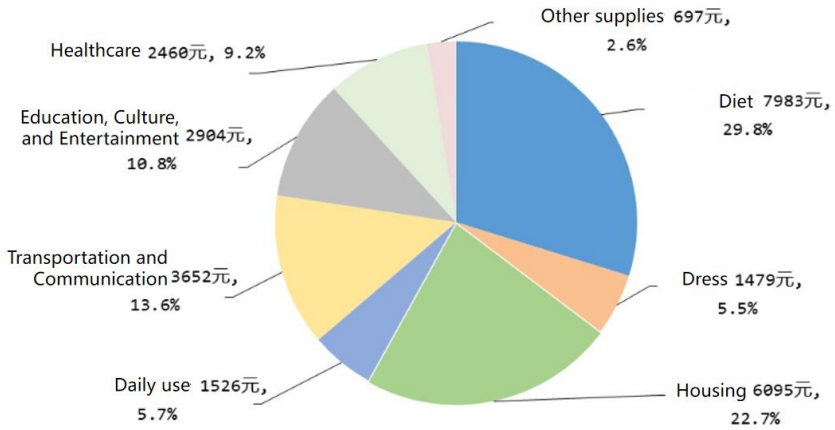
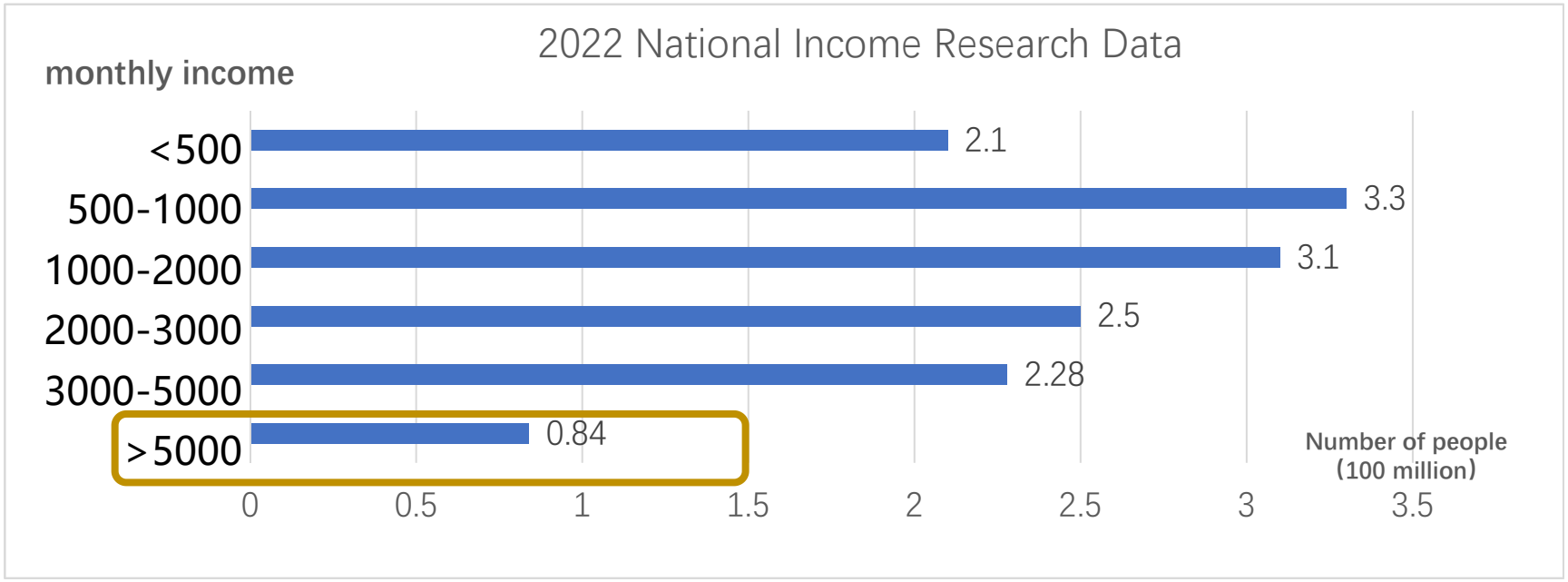
- According to data from the National Bureau of Statistics of China, in 2023：
  - Per capita disposable income of overall residents 39218
  - Per capita disposable income of urban residents 51821
  - Per capita disposable income of rural residents 21691





The average cost of health care in China is **less than 1000 CNY.**

Market Analysis- A product welcomed by the customers

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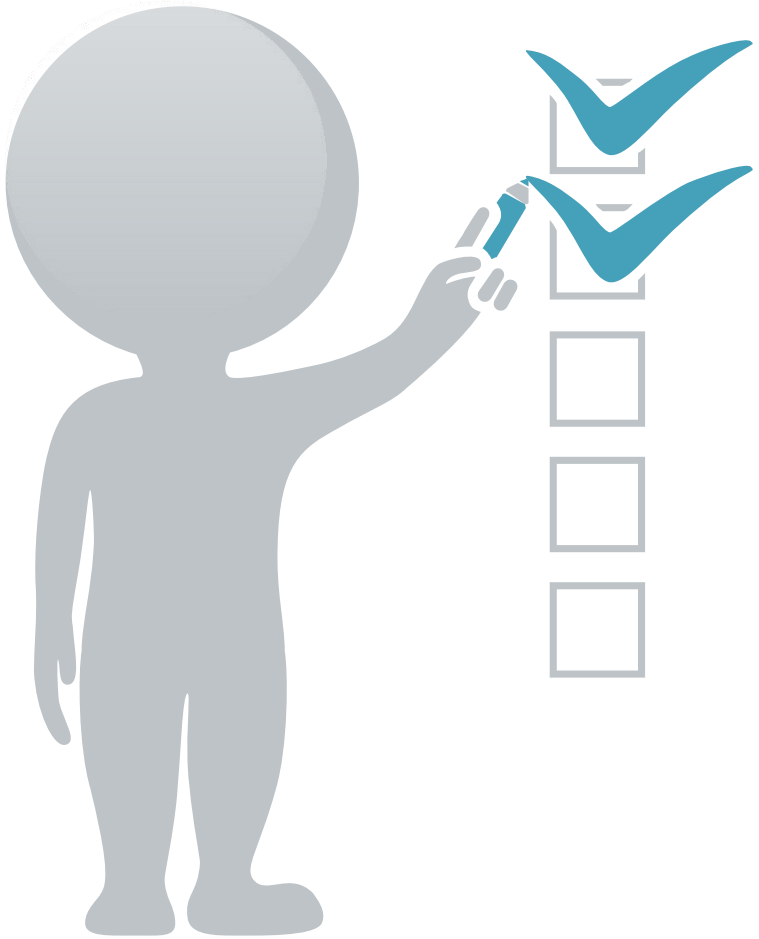

- Reasonable price
- Non-invasive and convenient
- Appropriate biomarkers
- Accuracy
- Validated by large-cohort clinical trials
- Multi-cancer in one assay
- Cancer typing

Solution: Improve quality meanwhile simplify the workflow and strictly control the cost.

TECHNOLOGY

-Method: based on large-scale AI models;
-Biomarker: plasma cell free DNA muti-omics.

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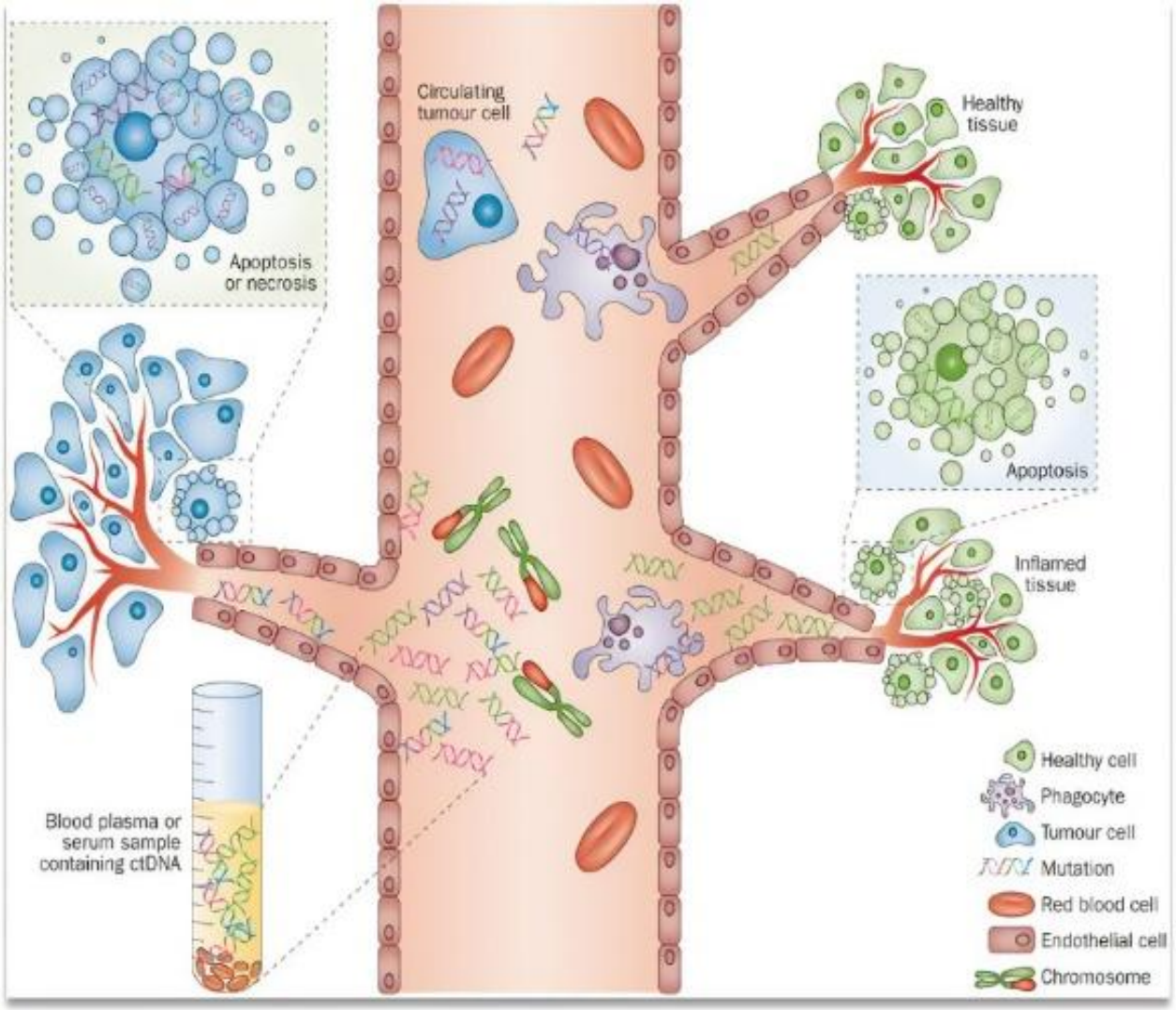

Crowley, E. et al. Nat. Rev. Clin. Oncol. 2013

What is plasma cell free DNA?

- DNA fragments that freely circulate in the human blood and are released into the bloodstream after apoptosis or necrosis of surrounding tissue cells (including healthy cells, inflammatory cells, and tumor cells).
- A portion of cfDNA that originates from tumor cells is also known as circulating tumor DNA (ctDNA)
- ctDNA contains tumor specific molecular features and can be used as tumor/cancer biomarker.

Technology- ctDNA Epigenomic Biomarkers

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High-profile SCI journals (Cell, Nature, Science) have published articles on this topic.
The **epigenetic modifications** such as **ctDNA methylation** and **fragmentation patterns** have been extensively proved to be the most effective biomarkers for cancer early detection.

Internationally recognized biomarkers for Multi-cancer Early Detection(MCED)

Epigenetic modifications of DNA provide another source of early detection biomarkers. These include cancer-specific DNA methylation profiles (*68*), noncoding RNAs (*69*), small regulatory RNAs, and the DNA modification 5-hydroxymethylcytosine (*70*). One promising approach analyzes methylation patterns of cfDNA in blood (*71*) and is now entering large-scale prospective clinical trials in the UK (NCT03934866) and the US (NCT04241796). Another emerging technique is based on the observation that fragmentation patterns in

Science

REVIEW SUMMARY

CANCER

Early detection of cancer

David Crosby*, Sangeeta Bhatia, Kevin M. Brindle, Lisa M. Coussens, Caroline Dive, Mark Emberton, Sadik Esener, Rebecca C. Fitzgerald, Sanjiv S. Gambhir, Peter Kuhn, Timothy R. Rebbeck, Shankar Balasubramanian*

nature medicine

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Review Article | Published: 19 April 2022

The future of early cancer detection

Rebecca C. Fitzgerald, Antonis C. Antoniou, Ljiljana Fruk & Nitzan Rosenfeld

Nature Medicine **28**, 666–677 (2022) | Cite this article

8855 Accesses | **171** Altmetric | Metrics

医世象

Review

Cell

Circulating cell-free DNA for cancer early detection

Qiang Gao,[1,2,6] Qiang Zeng,[3,6] Zhijie Wang,[4,6] Chengcheng Li,[5,6] Yu Xu,[5] Peng Cui,[5] Xin Zhu,[5] Huafei Lu,[5] Guoqiang Wang,[5] Shangli Cai,[5,*] Jie Wang,[4,*] and Jia Fan[1,2,*]

*Correspondence: shangli.cai@brbiotech.com (S.C.); zlhuxi@163.com (J.W.); fan.jia@zs-hospital.sh.cn (J.F.)

Received: February 14, 2022; Accepted: May 2, 2022; Published Online: May 6, 2022; https://doi.org/10.1016/j.xinn.2022.100259

AI Guided Multi-Cancer Risk Detection

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Artificial Intelligence Algorithms

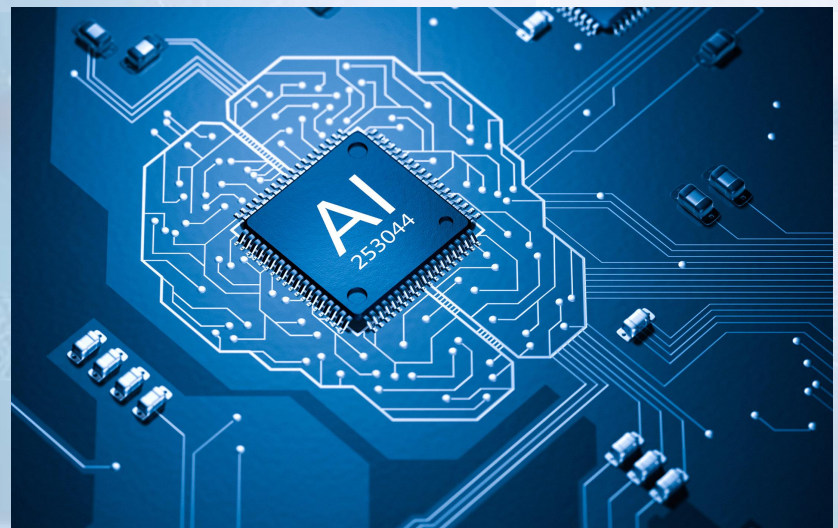
- Data Integration
- Deep Learning
- Visualization
- Function Analysis
- …

Medical big data

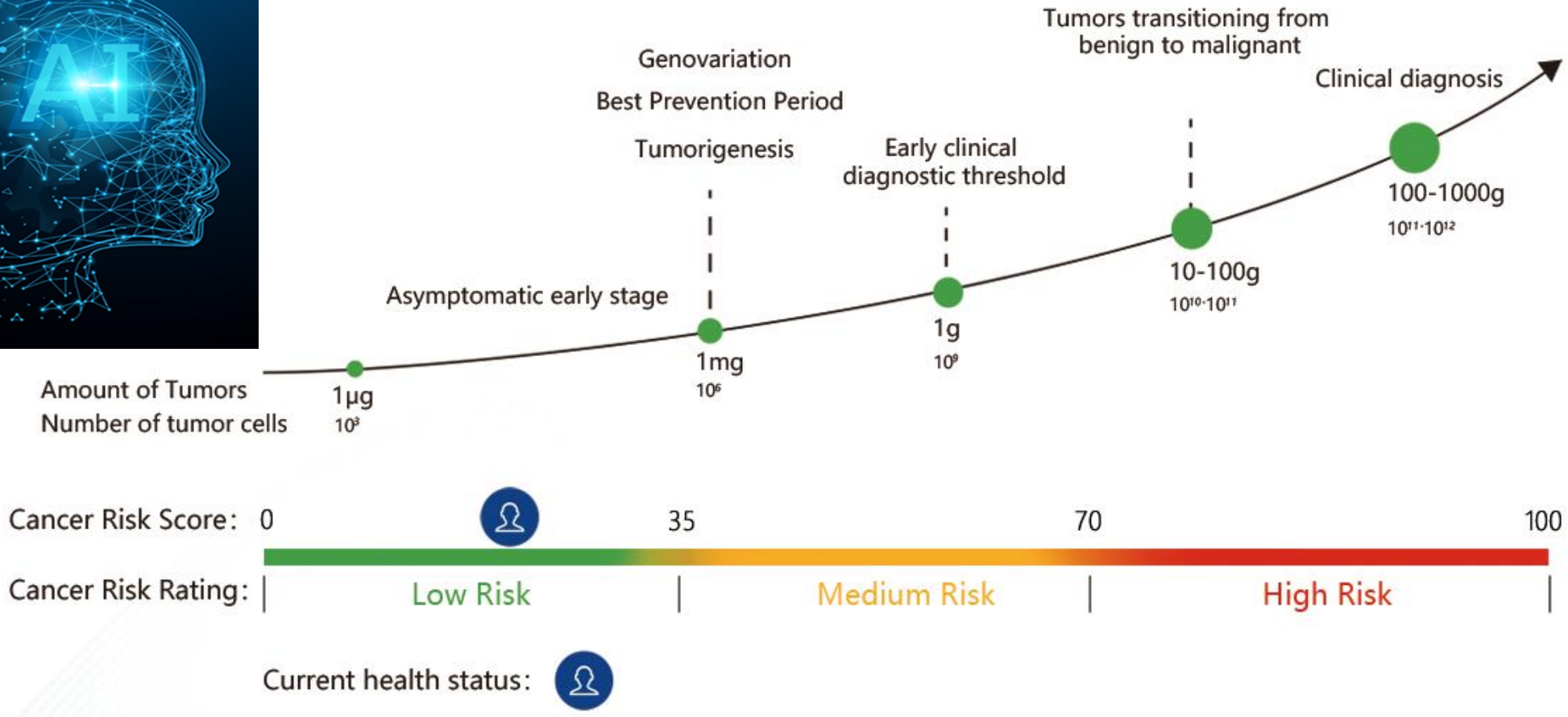
- Patient data
- Clinical data
- Gene data
- Epigenetic data
- …

Multi-modal Big date assessment

- Multi-cancer early detection
- Cancer tracing & localization
- Benign & malignant discrimination
- Surveillance & monitoring
- Molecular typing & prognosis
- Medication Guide
- MRD
- …



AI Guided Pan-Cancer Risk Assessment and Classification



Note: The risk score range is 0-100. The higher the score, the higher the predicted risk for cancer.

Products- AI empowered products & Quality guarantted by Top Insurance

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PICC 中国人民健康保险公司 PICC HEALTH INSURANCE COMPANY

CancerScanner®
(Validated by 6000+ clinical cases)

Pan-cancer screening

- Purpose: Pan-cancer risk assessment
- Sampling: 5 to 10 mL of peripheral blood
- **Accuracy**: sensitivity 88%, specificity 94%
- Lead time： 2 working days
- **Technology: ctDNA fragmentomics + AI**
- Benchmarking: Freenome, a leading American early screening company, has a sensitivity of 82% and a specificity of 85% for its products, FDA Breakthrough Medical Device Certification.

Primary Screening

High Risk

Precise Cancer Localization

中国人寿 CHINA LIFE

CancerSeer®
(Validated by 3000+ clinical cases)

Multi-Cancer Localization

- Purpose: Multi-cancer risk assessment+localization
- Sampling: 10 mL of peripheral blood
- **Accuracy**: sensitivity 92%, specificity 95%
- **Accuracy of localization：88%**
- Lead time： 9 working days
- **Technology: ctDNA multi-omics + AI**
- Benchmarking: Grail, with an localization accuracy of 88.7%, FDA Breakthrough Medical Device Certification.

High profile collaboration institutions

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First Affiliated Hospital of Sun Yat-sen University

Second affiliated hospital of Guangzhou Medical College

Beijing Chest Hospital

Peking University Shenzhen Hospital

Xiangya Hospital of Central South University

Shenzhen Traditional Chinese Medicine Hospital

Chinese PLA General Hospital

Shenzhen Second People's Hospital

Cancer Hospital of Hunan Province

The Central Hospital of Wuhan

West China Hospital, Sichuan University

The Third People's Hospital of Shenzhen

Clinical Study-Over 9000 clinical cases completed

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2021 H1 | 2021 H2 | 2022 H1 | 2022 H2 | 2023 H1 | 2023 H2 | 2024 H1 | 2024 H2 | 2025 H1 | 2025 H2 | 2026 H1 | 2026 H2

Retrospective clinical study

Liver, Lung

Stomach, Colorectum

Esophagus, Pancreas

Breast, Cervix, Prostate, Ovary, Kidney, Endometrium, Nasopharynx, cholangiocarcinoma, Gallbladder, oral

Prospective cohort (50000 cases)

Large population follow-up cohort (500000 cases)

Assess the accuracy of pan-cancer screening and publish 20 SCI papers with IF>10

To be approved by NMPA (single-cancer) by 2027

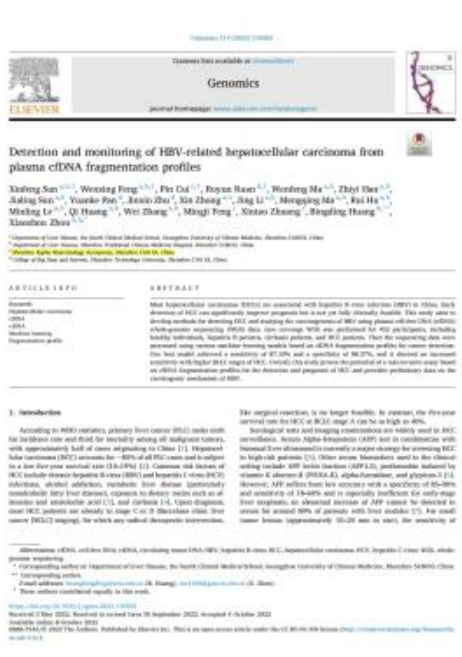
qPCR platform Auxiliary diagnosis Class Ⅲ-certificates application

Select cancer type
Establish GMP, quality system
Registration

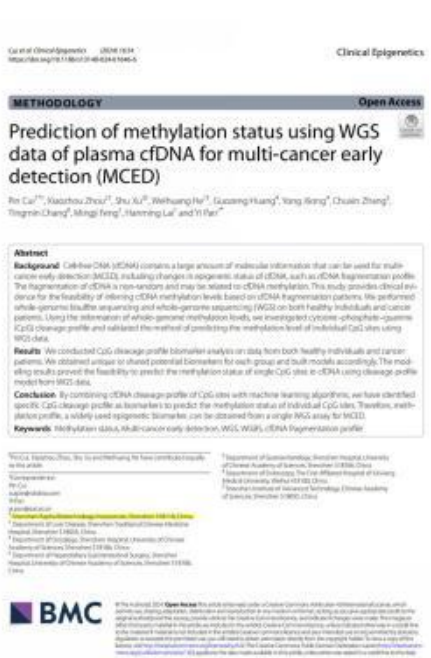
GMP maintenance
Complete clinical trials
Prepare registration

Pending approval

Publications of Clinical Study- ctDNA multi-omics data + AI large models


Genomics

Detection and monitoring of HBV-related hepatocellular carcinoma from plasma cfDNA fragmentation profiles


Clinical Epigenetics

METHODOLOGY Open Access

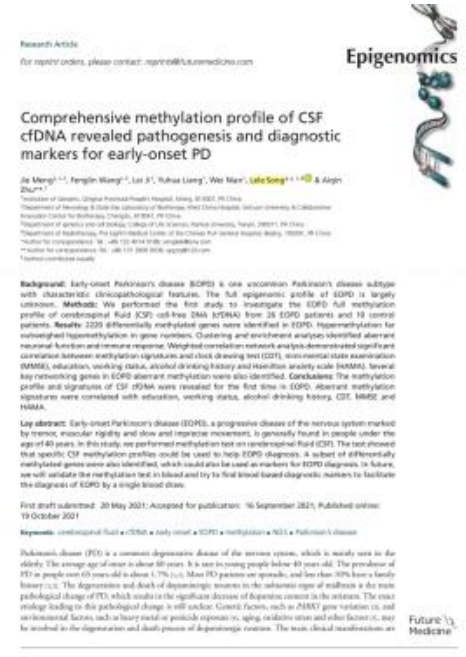
Prediction of methylation status using WGS data of plasma cfDNA for multi-cancer early detection (MCED)

BMC


Genomics

Early detection and stratification of colorectal cancer using plasma cell-free DNA fragmentomic profiling


Early Detection and Stratification of Nasopharyngeal carcinoma using Plasma Cell-free DNA Fragmentomic Profiling


Epigenomics

Comprehensive methylation profile of CSF cfDNA revealed pathogenesis and diagnostic markers for early-onset PD

Future Medicine

- HCC cfDNA fragmentomics, in collaboration with the Hepatology Department of Shenzhen TCM Hospital(2022, Genomics);
- Independent research and development of pan-cancer early screening technology(2024, Clinical Epigenetics);
- CRC cfDNA fragmentomics, in collaboration with the Second affiliated hospital of Guangzhou Medical College and the Peking University Shenzhen Hospital(2024, Genomics);
- NPC cfDNA fragmentomics, in collaboration with Shenzhen Guangming District People's Hospital(2025, HEAD NECK-J SCI SPEC);
- In collaboration with Beijing Chest Hospital for fragmentomic study of lung cancer(submitted to Cancer Res., in peer review);
- Multi-omics study of gastric cancer(2025, BMC Cancer);
- Cerebrospinal fluid cfDNA project research based on our technology in collaboration with West China Hospital.

Intellectual property- Patents and Software copyrights(AI & Medical Big Data)

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As of Feb. 2025

Inventions

9 authorized
15 pending

Utility models

12 authorized
9 pending

Software copyright

7 authorized
2 pending

Appearance

4 authorized
3 pending

Intellectual property- Trademarks (AI & Medical Big Data)

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As of Feb. 2025

Trademarks

52 authorized
14 pending

ABOUT US- AI + Big Data + Health Care = Rapha Biotech

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Our Vision

AI leads precision health in the aging society.

01

Our Goal

The Mutli-Cancer Early Detection and Monitoring of Choice for All.

02

Expertise

- **AI & Medical big data**.
- Multi-cancer early screening and early recurrence monitoring.
- Translation of latest technology

Team- The Founder and CTO

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Pin Cui

Ph.D., Senior Engineer

◆ **Research Experience**

- Ph.D. in Genomics, **Max Planck Society**, Germany
  (Supervisor **Svante Paabo,** **2022 Nobel Laureate in Physiology or Medicine**)
- Postdoctoral fellow in Single Cell Genomics, **Harvard University**, MA, U.S.
  (Supervisor **Xiaoliang Sunney Xie,** **Member of U.S. Natl Academy of Sciences**)

◆ **Honors & Awards**

- 2019 Shenzhen Overseas High Talent. 2022 ZAODX Emerging Entrepreneur.
- 2023 ZAODX Outstanding CTO Award. 2024 ZAODX Breakthrough Innovation Award.
- 2023 Guangdong-Hong Kong-Macau Greater Bay Area Enterprise Innovation Award.

◆ **Industry Experience**

- Senior Scientist for Novel NGS technology development, Novogene Inc.
- Vice Director of Research and Development, BGI Genomics Co., Ltd.
- Director of Clinical Laboratory, Apostle Inc.

◆ **Achievements in Translational Research**

- Director for several translational research projects of Guangdong Province.
- Developed multiple genetic test products for tumor diagnosis and monitoring.
- Approved 30+Patents and Software copyright, published 20+SCI papers.

Team- Scientific Advisory Committee

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Prof. Yi Pan
Chief Scientific Adviser

- Dean, Chair Prof.,Faculty of Computer Sciences, Shenzhen University of Advanced Technology.
- National Distinguished Expert, Changjiang Scholars;
- Fellow, American Institute for Medical and Biological Engineering, Royal Society for Public Health of UK, Institution of Engineering and Technology of UK, European Academy of Sciences and Arts;
- Have been cited 20000+ times, H-index>102;
- Chief editor of Big Data Mining and Analytics-Top 4% of magazines in the world. Associate editor of Journal of Computer Science and Technology (JCST).
- Associate editor of Chin. J. of Electronics Top 2% scientists, top 1k computer scientists

Prof. Youming Zhang
Chief Technology Advisor

- Member, National Academy of Engineering of Germany, European Academy of Sciences.
- National Key Talent Project Expert
- Chair Professor, Faculty of Synthetic Biology, Shenzhen Univ. of Advanced Technology.
- Director of the State Key Laboratory of Microbiological Technology, Shandong University
- Natural Science Second Prize in 2020
- Director of Center for Reorganization Engineering and Genome Manipulation, Shenzhen Institute of Advanced Technology, Chinese Academy of Sciences

Prof. Bingding Huang
Co-founder, Chief Bioinformatics Advisor

- Ph.D. in Computer Science, TU Dresden.
- Director, Department of Big Data Science, Shenzhen Technology University
- Staff scientist, German Cancer Research Center(DKFZ), International Cancer Genome Consortium (ICGC),.
- Developed bioinformatics algorithms for cancer companion diagnostic products
- Expert reviewer of Shenzhen Science and Technology Innovation Commission.
- Published 60+ high-profile SCI articles, cited >3200 times. Approved 20+ software copyrights and multiple invention patents.

Team- Medical Advisory Committee

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Prof. Shubin Wang

• Chief physician, M.D.
• Chairman of Oncology Committee, the 5th Shenzhen Medical Association
• Head of the Shenzhen Branch of the National Cancer Clinical Medical Research Center.
• Head of the Oncology Professional Group of the Drug Clinical Trial Institution.
• **Director, Departmentof Oncology, Peking University Shenzhen Hospital.**
• Director of Oncology Teaching and Research Office, Peking University Shenzhen Hospital
• Executive Deputy Director of the Institute of Oncology at the Hong Kong University of Science and Technology Medical Center, Peking University, Shenzhen

Prof. Xiaozhou Zhou

- Professor at Guangzhou University of Traditional Chinese Medicine, M.D., Doctoral Supervisor
- Chief Physician
- **Director of the Hepatology Department and Head of the Liver Disease National Key Discipline Ward at Shenzhen Traditional Chinese Medicine Hospital**
- Responsible for major national science and technology projects during the 11th and 12th Five Year Plans
- Member of Guangdong Provincial Committee for Integrative Traditional Chinese and Western Medicine Liver Disease
- Hosted over 10 scientific research projects
- Edited a book, published 30+ SCI papers

Prof. Hui Yang

- **Vice President of the Second Affiliated Hospital of Guangzhou Medical University**
- Professor of Gastroenterology, Doctoral Supervisor, M.D.
- Obtained the Guangdong Provincial Natural Science Outstanding Youth Fund.
- Obtained multiple scientific research projects such as the National Natural Science Foundation.
- Experience in the field of diseases in digestive system and early diagnosis of gastrointestinal tumors, minimally invasive surgical treatment, and molecular targeted treatment of HCC
- Hosted over 20 research projects and published 30+ papers

Team- Closely Collaborated Clinical Experts

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Prof. Zhengzhi Wu
（Pan-solid tumors）

- Foreign Member of the Ukrainian National Academy of Engineering, postdoctoral fellow at UCLA, Senior Visiting Scholar in UCSD
- **Director of the National Proteomics Level III Laboratory, Shenzhen.**
- **Director of the National Key Research Laboratory of Traditional Chinese Medicine, Shenzhen.**
- Published 300+ , cited 3000+ ; ~300 patents.

Prof. Zhiming Xu
（Pan-solid tumors）

- Engaged in liver and kidney transplantation, oncology expert, medical doctor, chief physician
- Professor and doctoral supervisor of University of Chinese Academy of Sciences
- **President of Shenzhen Hospital (Guangming), University of Chinese Academy of Sciences**
- Chief Scientist, Genetic Resources Research and Development Center(South), CAS.

Prof. Xiaohua Tan
（Pan-solid tumors）

- **Director, Departmentof Oncology , Shenzhen Third People's Hospital**
- Doctor of Medicine from the First Military Medical University of the PLA
- Postdoctoral Fellow in McMaster University
- Associate editor of Global Journal of Microbiology. Chinese Journal of Cancer Research, Journal of Translational Medicine

Dr. Yadong Zhang
（Health management）

- **Deputy Director of the Health Management Center of the First Affiliated Hospital of Sun Yat sen University**
- **Executive Director of Nansha Campus Health Management Center**
- Associate Professor, Associate Chief Physician
- Supervisor for Master
- Shenzhen Emerging Industry Project Evaluation Expert.

Prof. Zhidong Liu
（Lung cancer）

- **Director of the Second Department of Thoracic Surgery at the Affiliated Chest Hospital of Capital Medical University** Chief Physician, Ph.D., M.D.
- Experience in thoracic surgery for 30+ years, dedicated to the diagnosis and surgical treatment of chest tumors including lung cancer, esophageal cancer
- Published 30+ SCI papers with total impact factor 70+

Prof. Shu Xu
（CRC, GC）

- Doctor of integrated traditional and western medicine oncology, Southern Medical University
- **Chief physician, director of oncology department of Shenzhen Hospital of University of CAS**
- Clinical experience in the integrated traditional Chinese and Western medicine for 20 years, familiar with comprehensive treatment of common tumors.

Honors & Qualifications

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Developed by Rapha Biotech & Released by Xiangya Medical Lab

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Compliance & Qualification

国家卫生计生委司(局)便函

国卫医 医护便函〔2013〕103号

国家卫生计生委医政医管局关于同意开展个体化医学检测试点的函

中国医科大学附属第一医院、中南大学湘雅医学检验所、北京博奥医学检验所:

你单位关于申请作为个体化医学检测试点单位的请示收悉。经研究，现函复如下：

根据《卫生部办公厅关于同意开展个体化医学检测规范化管理工作的函》（卫办医政函〔2013〕195号），以及卫生部个体化医学检测技术专家委员会意见，同意你单位作为个体化医学检测试点单位。

请你单位在卫生部个体化医学检测技术专家委员会的指导下，在医疗机构开展个体化医学检测试点工作，主要内容包括：

一、对个体化医学检测相关管理办法及技术指南进行验证，并提出建议。

二、对本单位实验室开发的个体化医学检测项目进行验证、评价及先期试行。

三、在项目、技术或产品的准入、审批、收费、物价审批及推广应用等方面的相关部门沟通，为制定相关政策提供依据。

四、接受卫生部临床检验中心及其他相关机构的能力验证计划，保证检测结果准确可靠。

试点进展情况请及时报我局。

联系人：医疗与护理处　王曼莉

联系电话：010-68792733

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国家卫生计生委医政医管局

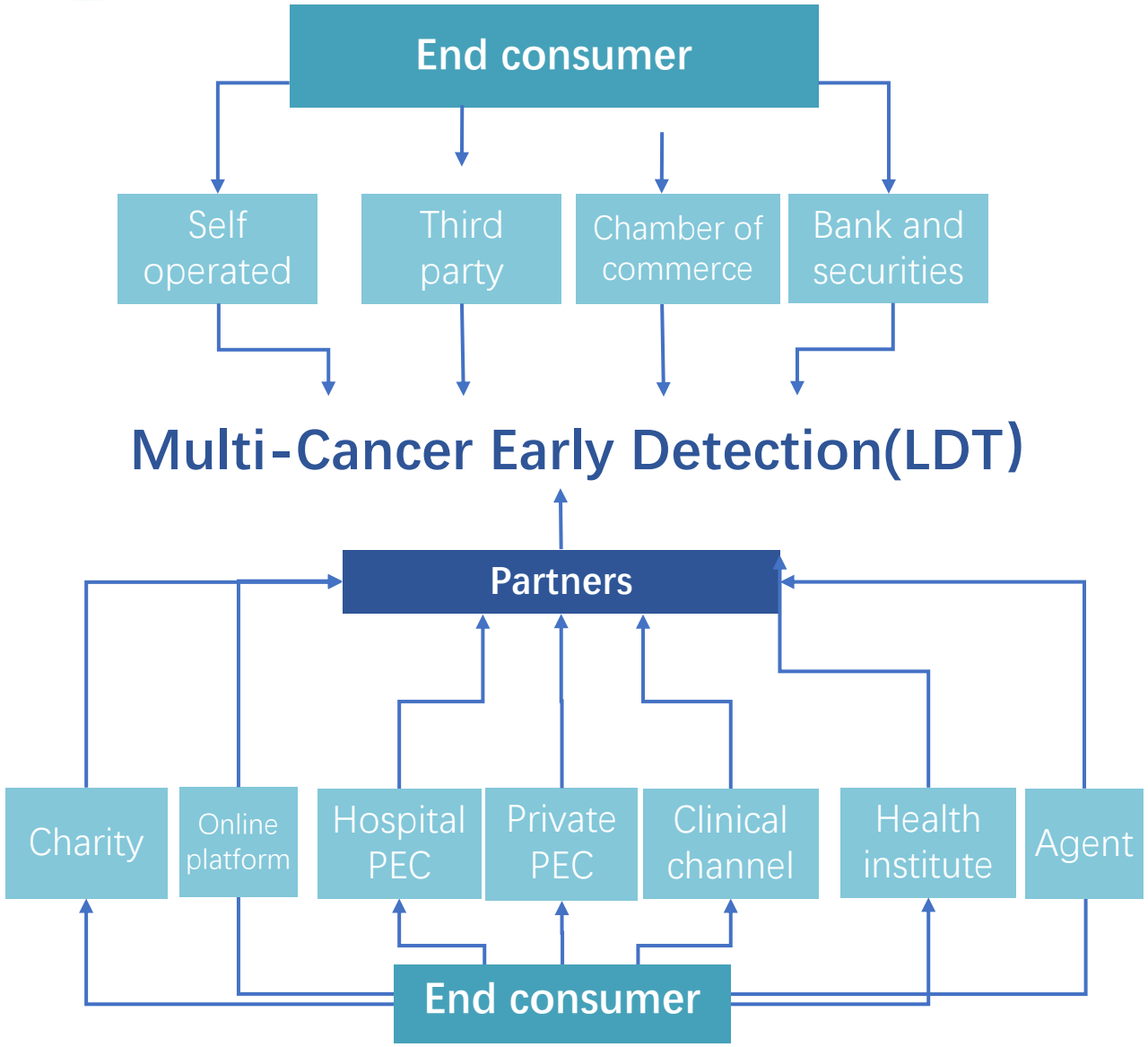
2013年9月17日

（信息公开形式：依申请公开）

中南大学湘雅医学检验所 XYML 2010 Xiangya Medical Laboratory

Xiangya-Academic Reputation of 110+ Years
State Approved & Industry Benchmark & KOL Lead

Marketing- Multi-channel promotion, covering 16 provinces of China.



PEC Physical Examination Center

Qualified for transportation of blood in tubes at room temperature all over China.

No need for fasting before blood draw, and the blood in the tube can be stored at room temperature for 14 days.

Goals- Serve the aging society with AI and precision medicine

睿法生物
RAPHA BIOTECH

R&D

- R&D Center construction
- **Patents & Trademarks application**
- **MCED product development**
- MRD product development
- R&D team set up

Phase 1
(2020-2022)

Registration and Marketing

- Medication guidance and **monitoring** (Targeted drugs)
- Adjuvant immunotherapy
- Gene Big Databank set up
- **Application for National High-tech enterprise**
- **Registration of Class Ⅲ certificates**

Phase 2
(2023-2026)

To-B/To-C marketing

- **Production and Service Center**
- Personalized and intelligent medical technology comprehensive service
- Cloud to terminal smart healthcare
- R&D of diagnosis and treatment for aging related diseases
- **Collaboration in drug development**
- **Participate in making rules of the industry**

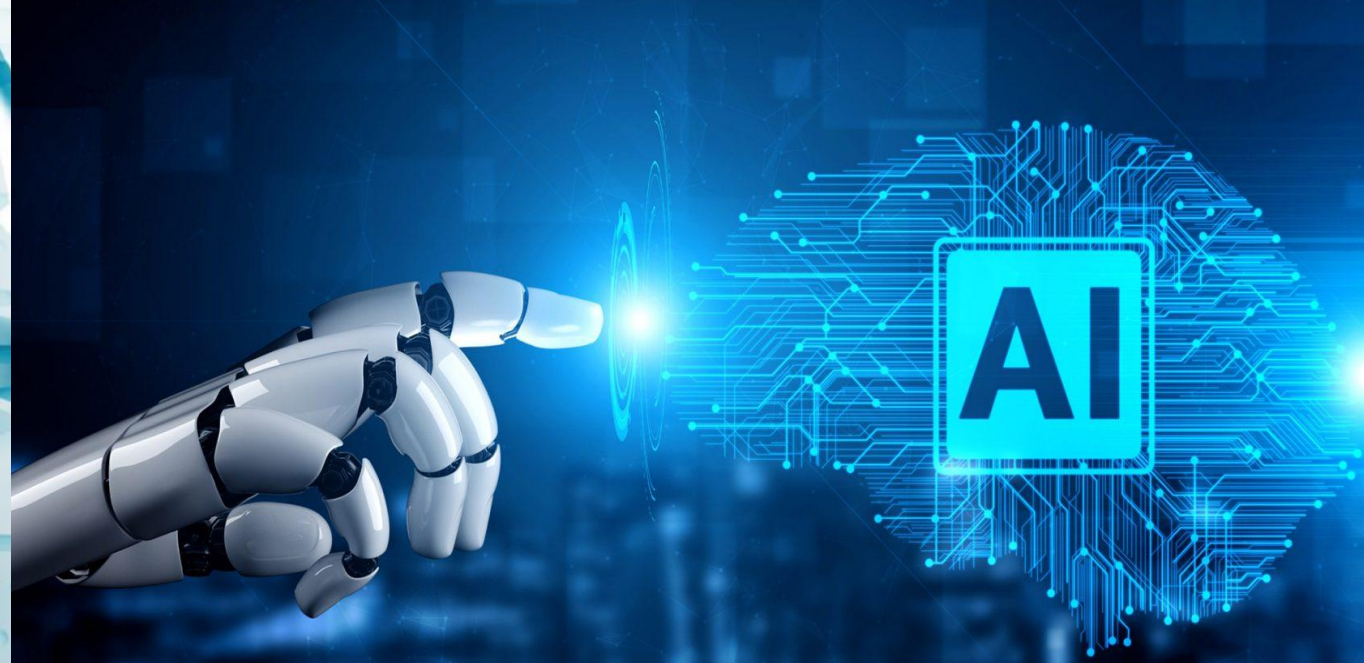
Phase 3
(2027-2028)

IPO& Global BD

- **Tumor full course service**
- **Diagnosis&treatment for other aging related diseases**
- AI guided healthcare
- Big Datebank of Gene and Clinics
- Unicorn and **IPO**
- Production and finance integration, value reconstruction
- **Global BD**

Phase 4
(2029- 2031)

The Mutli-Cancer Early Detection and Monitoring of Choice for All.



Explore infinite possibilities with AI

睿法商城
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睿法生物
RAPHA BIOTECH

睿法生物科技 Rapha Biotech Inc.

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