Universal Genomic Screening

RNA Screening and AI for CVD

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The future of disease detection and prevention is digital

- **Artificial Intelligence** - Data transformation and analysis
- **Genomic Sequencing** - Provides us with more data than ever before
- **Data management, processing and integration** - A vast amount of different sources of information providing insight on health and disease
The scaling up of Artificial Intelligence

Source: https://cmte.ieee.org/futuredirections/2023/04/18/ai-flanking-business-consultants/
Genomic sequencing is exploding

Source: NCBI
Cost of genomic sequencing

Cost per Raw Megabase of DNA Sequence

Moore’s Law

Source: NIH

genome.gov/sequencingcosts
The Virtuous Circle of AI Genomics

1. Costs
   Less than U$100 whole genome sequencing

2. Computational Power
   U$0.01/GFLOPS

3. Data availability
   2,631,493,489 WGS uploaded to NCBI (Aug/2023)
Adoption of AI in the healthcare industry

Rate of generative AI adoption in the workplace in the United States 2023, by industry

- Marketing and advertising: 37%
- Technology: 35%
- Consulting: 30%
- Teaching: 19%
- Accounting: 16%
- Healthcare: 15%

Source: statista.com
MultiplAI empowers anyone and their doctors to safely, privately, and accurately assess disease risk exceptionally early to proactively manage long-term health outcomes.

Next-gen genomic sequencing  | Proprietary data transformation  | AI neural networks
Digitizing the blood

DNA mainly offers insights into hereditary conditions.
RNA also reflects environmental factors.

We express the complexity of RNA in a format ideal for algorithmic analysis.
MultiplAI: Current Results

More than 1,000 samples sequenced
~100m reads
30-40k out of 65k genes detected
120k transcripts
7000 circRNAs
350k exons
The complex landscape of AI and Genomics
Cardiovascular disease (CVD) is the #1 cause of mortality globally.

Almost 1 in 3 annual deaths globally are caused by CVDs.

- 18m deaths / year
- 15x more women die of it than breast cancer
- #1 reason for waste in healthcare spending
Traditional risk stratification does not accurately detect vascular disease early enough.

Died of stroke at 91

Heart Attack at 35

Millions of people are at risk without knowing it.
80% of CVD early deaths worldwide could be prevented with improved screening tools.
Presence of **coronary calcium** according to **risk score category**

- **CVD Event Rates by CAC Category**

  - MESA, n=6814, FU=7.6y, AER=1.21
  - HNR, n=4487, FU=8.6y, AER=1.37
  - Rotterdam, n=2063, FU=3.3y, AER=2.18
  - Framingham, n=3238, FU=7.0y, AER=1.19
Gold standard of diagnosis has its challenges

CT Scans not recommended in low risk classification

Only 30% of countries have at least one CT scanner per million people
CAC by Risk score (Framingham)
Prevalence of CAC>0 → 45%

- Risk equations are not reliable for determining the presence or absence of coronary artery calcification (CAC)
- Misclassification rate = 33%

CAC by Risk score (Framingham)
Most patients were classified as low risk (mainly due to Age)

- Failure to identify patients who would benefit from early prevention
Determination of the presence and extent of coronary calcifications by transcriptomic analysis of whole blood assisted by artificial intelligence: pilot study

The CCT-1 study
The CCT-1 Study: Study design & Data collection

<table>
<thead>
<tr>
<th>Participants</th>
<th>Chest CT Comparator</th>
<th>Whole blood RNA</th>
<th>Clinical data</th>
<th>Incident events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non prior CVD</td>
<td>CT-Baseline/Outcomes</td>
<td></td>
<td></td>
<td>Death from any cause</td>
</tr>
<tr>
<td>Men 40-70 years</td>
<td>Coronary artery calcium (CAC)</td>
<td></td>
<td>Sex-Age</td>
<td></td>
</tr>
<tr>
<td>Women 50-70 years</td>
<td>Aortic calcium</td>
<td>Drug treatments</td>
<td>Blood Pressure</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Steatosis</td>
<td></td>
<td>Body weight/ Height</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Epicardial fat</td>
<td></td>
<td>Cancer</td>
<td></td>
</tr>
</tbody>
</table>

Baseline: Diagnostic results
Precision for CAC detection

5 Year follow up: Prognostic results
Precision for predicting incident events
CCT1 study results. Area Under the Curve (AUC)

Prediction of coronary calcium compared to the traditional approach

Source: https://doi.org/10.5694/mja2.50702
CCT1 study results. Area Under the Curve (AUC)

Prediction of ANY coronary calcium compared to the traditional approach

<table>
<thead>
<tr>
<th>Method</th>
<th>AUC</th>
</tr>
</thead>
<tbody>
<tr>
<td>CardioRisk WHO</td>
<td>0.63</td>
</tr>
<tr>
<td>Clinical Variable</td>
<td>0.72</td>
</tr>
<tr>
<td>Transcriptomics</td>
<td>0.76</td>
</tr>
<tr>
<td>Clinical Variables + Transcriptomics</td>
<td>0.80</td>
</tr>
</tbody>
</table>

Outcome: Presence of coronary atherosclerosis (CT- Coronary Agatston units > 0)
Covariates: sex, age, smoker status, BMI
CCT1 study results. Area Under the Curve (AUC)

Prediction of ANY coronary calcium compared to the traditional approach

Variables Included in the model:

- Age and Sex
- Linear RNA
- transcripts
- circRNA
- Blood microbiome.

Outcome: Presence of coronary atherosclerosis (CT- Coronary Agatston units > 0)
Covariates: sex, age, smoker status, BMI
Early detection of subclinical CAC in asymptomatic individuals

The CAC-TRAIT study
clinicaltrials.gov ID NCT05619042
Whole Blood Transcriptome Patterns according to the Coronary Atherosclerotic Plaque Burden determined by CT Angiography

The CORPLAQ-TRAIT pilot study
CT Scan

CT Scan versus angioCT Scan
Universal Genomic Screening for multiple pathologies

Artificial Intelligence and Genomic Sequencing allows us to face the challenges of complex diseases like CVD and make them available to anyone on the planet.

Universal Accessibility

Today

Universal Affordability

Universal

Universal Sustainability

Anywhere

Scalable

Anytime

$1000

$10,000

$10M

$10

$1B

$10

Low carbon blood collection

Virtual medicine

Sustainable Sequencing

Unit Price

Volume

Revenue

100,000,000

10,000

100,000,000

10,000

1B

$10
"The future of cardiology is personalized medicine, and AI is essential to making that happen."

– Eric Topol
Thank You

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