EDIM Technology – Detecting cancer before it forms

08.02.2018

Made in Germany
1 Cancer

Cancer affects everyone
A global target: Universal cancer blood test

At the forefront of medical research is the dream of a universal cancer blood test.
Cancer can strike anyone

Statistically every second person has cancer in their lifetime
Early detection is key

Early detection of tumors significantly improves the survival rate

5-year relative survival rate in x/10 cancer patients, ages 15-99, by cancer stage at diagnosis

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Stage 1</th>
<th>Stage 2</th>
<th>Stage 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bowel</td>
<td>9.7</td>
<td>8.5</td>
<td>6.3</td>
</tr>
<tr>
<td>Lung</td>
<td>3.5</td>
<td>2.1</td>
<td>0.6</td>
</tr>
<tr>
<td>Skin</td>
<td>10</td>
<td>8.2</td>
<td>5.2</td>
</tr>
<tr>
<td>Prostate</td>
<td>10</td>
<td>9.9</td>
<td>9.3</td>
</tr>
<tr>
<td>Breast</td>
<td>9.9</td>
<td>8.8</td>
<td>5.5</td>
</tr>
<tr>
<td>Cervical</td>
<td>9.6</td>
<td>5.4</td>
<td>3.8</td>
</tr>
<tr>
<td>Ovarian</td>
<td>9.0</td>
<td>4.3</td>
<td>1.9</td>
</tr>
</tbody>
</table>

Cancer screening is highly recommended

But there is no cheap and universal cancer screening technology out there

1. Very expensive
2. Limitation on single or few tumor entities
3. Specificity too low for effective screening
4. Risk of harm through procedure

| Imaging technology     | X-ray  
|                       | CT    
|                       | MRI   
|                       | PET   
| Colonoscopy (bowel)   |
| Mammography           | Breast cancer |
| Tumor markers         | SA (prostate)  
|                       | CEA (gastrointestinal, cervix, lung, ovarian, breast, urinary tract)  
|                       | CA 15-3 (breast)  
|                       | Ca 19-9 (pancreatic, colorectal)  
|                       | CA 125 (ovarian)  
|                       | TTF-1 (thyroid, lung)  
|                       | Tumor M2-PK (colorectal, lung)  
| Liquid Biopsy         | Research ongoing  |
EDIM Technology – universal cancer test

EDIM Technology finds cancer before it forms – universally

First universal cancer test
All cancer types

Cancer screening
EDIM Technology can revolutionize cancer prevention

Biological biopsy
Non-invasive biopsy with excellent scope

99.5% Specificity
97.5% Sensitivity

By means of using the body’s immune system

High
Compared positive predictive value
Ensures suitability as screening test

Easy to establish
Works on BD Canto flow cytometer

New generation flow cytometry
Flow cytometry with automated algorithm-based gating and analysis

Customer retention
Annual testing at affordable prices ensures high customer retention rate
2 EDIM Technology

Biological Biopsy
EDIM – Epitope Detection in Macrophages

TKTL1 and Apo10 represent fundamental biological mechanisms in tumor cells

- TKTL1 protein regulates aerobic glycolysis (fermentation of glucose even in presence of oxygen)
- Accumulates through disrupted cell apoptosis
- Independent of tumor type
- Disrupted apoptosis is root of malignant degeneration
- Indication of proliferative disorder/tumor
Biological Biopsy – Leveraging the immune system

Highest test accuracy achieved by making use of the body’s own immune system

1. Macrophages migrate from blood into tissue

2. Macrophages phagocytose degenerated tumor cells

3. Macrophages with absorbed tumor-specific structures migrate back into the blood

EDIM Technology

The phagocytosed tumor cells are examined

- TKTL1 - positive
- Apo10 - positive
- Macrophages

Schematic display of the basics of EDIM Technology
High sensitivity and specificity

EDIM is the first technology that qualifies as universal cancer screening test

**97.5%**
Sensitivity

- Tumor-specific structures are not diluted but instead conserved within the macrophages

**99.5%**
Specificity

- Use of immune system: Macrophages only phagocytose degenerated or unwanted cells, not healthy ones
EDIM technology can detect all tumor stages

The combination of Apo10 and TKTL1 allows the detection of all tumor stages

Ordinary tissue

- Apo10 - negative
- TKTL1 – negative
- Cum. EDIM – negative

Proliferating disorder

- Apo10 - positive
- TKTL1 – negative
- Cum. EDIM – negative

Carcinoma in situ

- Apo10 - positive
- TKTL1 - negative/positive
- Cum. EDIM – positive

Carcinoma with matrix degeneration

- Apo10 - positive
- TKTL1 – positive
- Cum. EDIM – positive

Metastasizing carcinoma

- Apo10 - positive/negative
- TKTL1 – positive
- Cum. EDIM – positive
Application of EDIM Technology

EDIM Technology can revolutionize cancer prevention
How is EDIM Technology applied?

EDIM Technology allows annual testing to detect cancer before it forms

1. Less than 100€ for patient
2. Only 1 blood sample necessary
3. Suitable for Screening

How EDIM can revolutionize cancer prevention:

- Starting age: +/- 30 years
- Annual testing for best results
- Catch the critical EDIM detection point forms
How can EDIM revolutionize cancer prevention?

EDIM Detect can allow in-time detection of critical tumor turnaround point

<table>
<thead>
<tr>
<th>EDIM Test Result</th>
<th>Ordinary Tissue</th>
<th>Proliferating Disorder</th>
<th>Carcinoma in Situ</th>
<th>Carcinoma with Matrix Degeneration</th>
<th>Metastasizing Carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apo10 – negative</td>
<td>Apo10 – positive</td>
<td>Apo10 – positive</td>
<td>Apo10 – positive</td>
<td>Apo10 – positive/negative</td>
<td>Apo10 – positive/negative</td>
</tr>
<tr>
<td>TKTL1 – negative</td>
<td>TKTL1 – negative</td>
<td>TKTL1 – negative/positive</td>
<td>TKTL1 – positive</td>
<td>TKTL1 – positive</td>
<td>TKTL1 – positive</td>
</tr>
</tbody>
</table>

Tumor: successfully treatable
Cancer: often lethal, rarely treatable

EDIM test result

Cancer: often lethal, rarely treatable

Critical EDIM detection point
Cancer prevention survey results

501 survey participants welcome cancer prevention

- 95% of participants consider **cancer prevention important** or very important
- 95% of participants **would get tested if a simple blood test could detect cancer early**
- 86% of participants would **not** let their decision to get tested be **influenced** by the **risk of a false-positive result**
Why is EDIM interesting to laboratories?

A new business model
Business model: Customer retention

Immense potential for laboratories through high annual customer retention

**Annual** return of the customer
- “Subscription” customer
- New business model for laboratories

**1x a year**

**Interesting Patient profile**
- Healthy individuals
- Age group starting at 30 years
- Interest in disease prevention and prevention
- Ability to pay for diagnostics

**Cross-selling** potential
- High interest in disease prevention
- Potential to cross-sell additional prevention measures

**Future of **EDIM** Technology**
- 200 tests in the next 5 years using EDIM technology
- Rapid progress with Alzheimer/ Dementia, Borrelia, Immune profiling, etc.
## Overview of cancer test sensitivity/specificity

<table>
<thead>
<tr>
<th>Examination</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mammography</td>
<td>77-95%</td>
<td>90-96%</td>
</tr>
<tr>
<td>Mamma-MRT</td>
<td>&gt;95%</td>
<td>81-97%</td>
</tr>
<tr>
<td>Zytological examination</td>
<td>51-53% (median)</td>
<td>96-98%</td>
</tr>
<tr>
<td></td>
<td>Fluctuates from 30 to 87%</td>
<td></td>
</tr>
<tr>
<td>HPV-Testung</td>
<td>95%</td>
<td>95%</td>
</tr>
<tr>
<td>Digital Rectal Examination</td>
<td>53% / 64%</td>
<td>84% / 97%</td>
</tr>
<tr>
<td>PSA</td>
<td>Between 33 and 59%</td>
<td>Between 87 and 95%</td>
</tr>
<tr>
<td></td>
<td>(depending on threshold value)</td>
<td>(depending on threshold value)</td>
</tr>
<tr>
<td>Total endoscopy</td>
<td>87-98% (depending on polyp size)</td>
<td>Up to 100%</td>
</tr>
<tr>
<td>Immunological tests</td>
<td>56-88% (for proof of colorectal carcinoma)</td>
<td>91-98%</td>
</tr>
<tr>
<td>Thorax x-ray</td>
<td>75%</td>
<td>91%</td>
</tr>
<tr>
<td>Thorax CT scan</td>
<td>94%</td>
<td>73%</td>
</tr>
<tr>
<td>Skin examination</td>
<td>42-100% (varies by study)</td>
<td>70-98% (varies by study)</td>
</tr>
</tbody>
</table>
## EDIM vs. liquid biopsy

EDIM Technology offers clear advantages over liquid biopsy

<table>
<thead>
<tr>
<th>Location of biomarker</th>
<th>EDIM (biological biopsy)</th>
<th>Liquid biopsy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conservation of biomarker</td>
<td>Conserved biomarkers – detection in macrophages that carry tumor material within (activated monocytes = macrophages)</td>
<td>Free-floating biomarkers in the blood/serum</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>Very high sensitivity – leverage of innate immune system – exploits highly accurate detection of tumor cells by the immune system and only degenerated or unwanted cells are phagocytosed by macrophages</td>
<td>Dilution of biomarkers in blood strongly influences sensitivity negatively</td>
</tr>
<tr>
<td>Specificity</td>
<td>3-factor tumor detection – combination of two biomarkers representing fundamental biological processes plus body’s own immune response – very high specificity and avoidance of misdiagnosis</td>
<td>Much lower specificity due to mostly individual biomarkers – results often influenced by inflammations or other factors</td>
</tr>
<tr>
<td>Tumor location</td>
<td>Macrophages reach every region of the human body as part of the innate immune response – even highly isolated organs such as prostate or brain (blood-brain barrier) or locations unreachable by invasive biopsy (brain)</td>
<td>Not all tumors release traces into the bloodstream reliably (e.g. isolated organs such as prostate or the brain)</td>
</tr>
<tr>
<td>Tumor entity</td>
<td>Conservation and concentration of biomarkers in macrophages solve problem of solubility of certain tumor entities</td>
<td>Due to solubility characteristics (not soluble), certain tumor entities are not properly measurable in the blood through liquid biopsy, as they do not release traces into the bloodstream</td>
</tr>
<tr>
<td>Tumor size</td>
<td>Small and benign tumors can be identified as a few macrophages with contained tumor cells suffice for reliable detection</td>
<td>Small/benign tumors cannot be identified in the blood/serum because they release only small amounts of biomarker (diluted in blood volume so no significant increase in concentration of biomarkers is measurable)</td>
</tr>
<tr>
<td>Durability of blood sample</td>
<td>Lower durability of blood sample as room temperature of sample has to be maintained to keep macrophages alive</td>
<td>Higher durability and ability to test retrospectively through ability to freeze blood and therefore conserve it</td>
</tr>
<tr>
<td>Dependencies</td>
<td>Dependent on performance of immune system – unparalleled if healthy but impossible in patients with active cancer treatment (impaired immune system)</td>
<td>Not dependent on immune system but often impaired by presence of other factors such as inflammations</td>
</tr>
</tbody>
</table>
3-factor tumor detection: sensitive and specific

EDIM is the first technology that qualifies as universal cancer screening test

1. Immune system
   - Highly accurate immune response to identify degenerated and unwanted cells
   - Conservation of tumor-specific structures within macrophages

2. Apo10
   - Fundamental biological cancer process of disrupted cell apoptosis

3. TKTL1
   - Fundamental biological cancer process of Invasive growth

97.5% Sensitivity
99.5% Specificity
## EDIM positive predictive values

### Positive predictive values of EDIM Detect by age group

Annual cancer incidence by age group as reported for 2011 by the Robert Koch Institute, Zentrum für Krebsregisterdaten

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</tr>
</thead>
<tbody>
<tr>
<td>New cancer patients in sample of 200</td>
<td>1.2</td>
<td>0.1</td>
<td>0.0</td>
<td>0.0</td>
<td>0.1</td>
<td>0.1</td>
<td>0.2</td>
<td>0.3</td>
<td>0.4</td>
<td>0.6</td>
<td>1.0</td>
<td>1.6</td>
<td>2.3</td>
<td>3.1</td>
<td>3.6</td>
<td>4.1</td>
<td>4.5</td>
<td>4.6</td>
<td></td>
</tr>
<tr>
<td>EDIM specificity</td>
<td>99.5%</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
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<tr>
<td>EDIM false positives in sample of 200</td>
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<td></td>
</tr>
<tr>
<td>Total positive results in sample of 200</td>
<td>2.2</td>
<td>1.1</td>
<td>1.0</td>
<td>1.0</td>
<td>1.1</td>
<td>1.1</td>
<td>1.2</td>
<td>1.3</td>
<td>1.4</td>
<td>1.6</td>
<td>2.0</td>
<td>2.6</td>
<td>3.3</td>
<td>4.1</td>
<td>4.6</td>
<td>5.1</td>
<td>5.5</td>
<td>5.6</td>
<td></td>
</tr>
<tr>
<td>Correct diagnosis - positive predictive value</td>
<td>56%</td>
<td>5%</td>
<td>2%</td>
<td>2%</td>
<td>5%</td>
<td>7%</td>
<td>11%</td>
<td>15%</td>
<td>21%</td>
<td>29%</td>
<td>39%</td>
<td>51%</td>
<td>61%</td>
<td>70%</td>
<td>75%</td>
<td>78%</td>
<td>80%</td>
<td>82%</td>
<td>82%</td>
</tr>
</tbody>
</table>
High positive predictive value – example

Calculation example of positive predictive value among 60-64 year olds in 2011

New cancer patients in the **age group 60-64** in Germany in 2011

<table>
<thead>
<tr>
<th>EDIM Technology</th>
<th>Calculation example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specificity</td>
<td>99.5%</td>
</tr>
<tr>
<td>False-positive results</td>
<td>1 in 200</td>
</tr>
<tr>
<td>Total positive results in case of 200 tests</td>
<td>3.3</td>
</tr>
<tr>
<td>Actual cancer patients</td>
<td>2.3</td>
</tr>
<tr>
<td>Correct diagnosis – Positive predictive value</td>
<td>70%</td>
</tr>
</tbody>
</table>

**Suitable** for screening | **Unsuitable** for screening
### Clinical Data 1/2

#### CE-Certificate clinical study (2017)

- **1,011** Patients tested
- **277** Cancer patients
  - Test results:
    - Positive: 270
    - Negative: 7
- **734** Healthy patients
  - Test results:
    - Positive: 7
    - Negative: 727

Combined TKTL1+Apo10 score threshold: 245

#### Grimm et al. study (2013)

- **287** Patients tested
- **213** Cancer patients
  - Test results:
    - Positive: 206
    - Negative: 7
- **74** Healthy patients
  - Test results:
    - Positive: 3
    - Negative: 71

Combined TKTL1+Apo10 score threshold: 228

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1) Assumption of 0.5% incidence in Germany according

### Clinical Data 2/2

**Baum et al. study**

<table>
<thead>
<tr>
<th>Category</th>
<th>Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients tested</td>
<td>362</td>
<td>Lung, breast, colorectal, lymphoma, esophageal, stomach, salivary gland, thyroid, melanoma, renal, non-malignant diseases…</td>
</tr>
<tr>
<td>Cancer patients</td>
<td>240</td>
<td></td>
</tr>
<tr>
<td>Healthy patients</td>
<td>122</td>
<td></td>
</tr>
</tbody>
</table>

**Test results:**

<table>
<thead>
<tr>
<th>Category</th>
<th>Test Results</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer</td>
<td>Positive</td>
<td>XXX</td>
<td>94%</td>
</tr>
<tr>
<td>Healthy</td>
<td>Negative</td>
<td>XXX</td>
<td>81%</td>
</tr>
</tbody>
</table>

**TKTL1 score threshold: 119**

**Ongoing studies**

<table>
<thead>
<tr>
<th>Hospital</th>
<th>Patients tested</th>
</tr>
</thead>
<tbody>
<tr>
<td>University Hospital Tübingen</td>
<td></td>
</tr>
<tr>
<td>GI-Tumors</td>
<td>unknown</td>
</tr>
<tr>
<td>Neuroblastomas in children</td>
<td>40-50 Children tested</td>
</tr>
<tr>
<td>Rhabdomyosarcomas in children</td>
<td>30 Children tested</td>
</tr>
<tr>
<td>Sarcomas in adults</td>
<td>70 Patients tested</td>
</tr>
<tr>
<td>Recently diagnosed tumor patients</td>
<td>80 Patients tested</td>
</tr>
</tbody>
</table>

---

1) Richard P Baum et al.: EDIM-TKTL1 blood test: a noninvasive method to detect upregulated glucose metabolism in patients with malignancies. Future Oncology,