Giant Jamboree 2014, Hynes Convention Center, Boston MA
iGEM Team of Ben-Gurion University, Be'er-Sheva, Israel
The Metabolic Syndrome
The Metabolic Syndrome

What is it?

Current treatment

Goals

Strategies

Policy & Practices

High Plasma Triglycerides

Low HDL (good) Cholesterol

High blood pressure

Fatty liver

Insulin resistance

Abdominal Obesity

Diabetes Type 2

Hyperglycemia

Intro

The Metabolic Syndrome
Some Facts

Healthy lifestyle:
- Appropriate dietary
- Routine exercise
- Well sleeping

Lower risk for Metabolic Syndrome
Quick Quiz

- Sweet beverages \(34\%\)
- High-fat food
- Not enough exercising \(60\%\)
The Metabolic Syndrome

What is it?

Current treatment
Current Treatment

- Treating the symptoms rather than the causing factors
- Inefficient overall treatment
- Conflicting side effects
The Vision

Less people suffering from the metabolic syndrome

Goals:

1) Create synergetic multifunctional treatment

2) Raise awareness in population at risk
Among Our Consultants

- Prof. Jacob Bar-Tana, MD
  Metabolic Syndrome expert

- Prof. Assaf Rudich, MD
  Endocrinologist, Diabetes expert
Fatty acid accumulation in the liver

Insulin resistance
Fatty acid accumulation in the liver

Insulin resistance

1. “Aspiration Shift”
2. “Artificial Exercise”
3. “Intelligent Medication”
Fatty Liver

- Non-adipose fat accumulation
- Fatty liver is highly correlated with the Metabolic Syndrome
- We will treat Fatty Liver!
“Artificial Exercise”

- Artificial Exercise
- Aspiration Shift
- Intelligent Medication

- The Metabolic Syndrome
- Goals
- Strategies
- Policy & Practices
“Artificial Exercise”

DNP - 1930’s dietary aid:

- Uncoupling factor
- Increasing oxidative phosphorylation
“Artificial Exercise”

DNP - 1930’s dietary aid:

• Effective for losing weight

• Side effect - heating production
Mechanism

“Artificial Exercise”
Results
“Artificial Exercise”

10 nM TMRM

25 nM TMRM

Normal HepG2

10 nM TMRM

25 nM TMRM

pcDNA3.1 UCP1

HepG2 - Human Hepatocarcinoma cell line
“Aspiration Shift”

Indirectly increasing of fatty acid oxidation

- Encouraging lipid transport
- Mitochondrial biogenesis

Stop storing and start burning!
**Mechanism**

"Aspiration Shift"

![Diagram](image)

- **SREBP**
- **SRE**
- **PGC1-α**
- **PPAR-γ activation**
- **PPAR-γ induced**
- **Repressor**

Fatty acid oxidation

**Artificial Exercise**
**Aspiration Shift**
**Intelligent Medication**
**Goal:**
Validating the personalized behavior of the treatment

**Methods & Tools**

Modeling
"Aspiration Shift"

Artificial Exercise
Aspiration Shift
Intelligent Medication

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Wolfram Mathematica

MATLAB
The model predicts: "Aspiration Shift" is a self-regulating personalized treatment.
Insulin Resistance

Insulin → Glucose absorption

Insulin resistance → Glucose absorption

Insulin resistance in the liver → Hyperglycemia
“Intelligent Medication”

Current treatment:

• High dose injection of insulin

Disadvantages:

• Inefficient
• Uncontrolled
• Non-specific
Targeted Delivery?

Mechanism “Intelligent Medication”

Based on “Conditional Dicer Substrate Formation via Shape and Sequence Transduction with Small Conditional RNAs” (Hochrein, Schwarzkopf, Shahgholi, Yin, & Pierce, 2013)
scRNA Constructor

“Intelligent Medication”

OFF state

ON state

MFE structure at 37.0 C

Free energy of secondary structure: -73.28 kcal/mol

Free energy of secondary structure: -38.50 kcal/mol

Produced by Nupack.org
Proof of Concept
“Intelligent Medication”

Trigger Gene: mRuby2
Silencing Target Gene: eGFP
Our specially designed hairpin reduced the expression of eGFP by 56%!
Multicomplexity Treatment

“Artificial Exercise”
- Evaluation of UCP1 functionality

“Aspiration Shift”
- Mathematical verification of the personalized behavior

“Intelligent Medication”
- scRNA constructor software
- Verification of the scRNA hairpin functionality
Policy & Practices

Research

Policy & Practices

Inner Doctor
Diabetes

Type 2

CEO of the Israeli Diabetes Association
The Bedouins

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The Bedouin Campaign

1) Raise awareness
2) Increase prevention behaviors
3) Spread the vision of synthetic biology treatment

Dr. Younes Abu Rabia, MD
**Metabolic Ambassadors**

**Aims:**
- Raising awareness
- Set the ground for advanced therapy

**Achievements:**
- 40 students participation
- 5 professional speakers supporting the idea
- Participation and honor certificates
Scholarships

- Bedouin student will establish a new branch of the Israeli Diabetes Association in Rahat
- 8 Bedouin students will volunteer in diabetes clinics of their communities

🔗 up to 70% tuition!
**Healthy Cooking Workshop**

**Aims:**

- Impact community’s nutritious habits
- Create a strong link between the Diabetes clinic in Rahat and the Israeli Diabetes Association

**Achievements:**

- 25 Bedouin women participation
- Glucose level monitoring for the participants
- Sharing tips for healthier cooking and consuming
- Established a repeating annual event
Networking

- Israeli Minister of Health, Mrs. Yael German
- Mayor of Be’er-Sheva
- Ben-Gurion University President
- CEO of the Israeli Diabetes Association
- CEO of Trigger Foresight (Deloitte)
- Public figures
- Doctors
- Metabolic Syndrome experts
Inner Doctor Impact

• Inner Doctor video reached over 50,000 impressions

• 3600 likes on our Facebook page

• E-Mails and messages from people all over the world looking forward to use our Inner Doctor technology
Acknowledgements

Prof. Smadar Cohen
Dr. Efrat Forti
Dr. Emil Rubinov
Ms. Dana Neeman
Prof. Assaf Rudich
Prof. Iris Shai
Prof. Emeritus Jacob Bar-Tana
Prof. Ariel Kushmaro
Dr. Ilana Harman
Ms. Karin Yaniv
Prof. Ariel B. Lindner
Dr. Omri Amirav-Drori
Dr. Olga Kryukov
Prof. Varda Shoshan-Barmatz
Mr. Matan Goldshtein
Mr. Alon Szczupak
Mr. Edan Elovic

• All custom DNA was synthesized by GeneScript (HSP70, UCP1, DsbA-L, AdipoQ)
• pcDNA3 mRuby2 was supplied by Addgene
• All custom RNA was synthesized by IDT (scRNA parts A and B)

Want to hear more? come meet us at poster #26
Thank you for listening!