A new diabetes patient sub-classification: its application in RHAPSODY

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Aim of RHAPSODY

Improve the *stratification* of people with type 2 diabetes
Clinical variable-based subgroups

N=15,940
- Age
- BMI
- HbA1c
- C-peptide
- HDL-cholesterol

5 clusters

Slieker and Donnelly et al. Diabetologia 2021
Cluster characteristics

Sliker and Donnelly et al. Diabetologia 2021
Comparing the clusters to other data types

Inherited risk
12828 individuals

Metabolites
2945 individuals
17 metabolites

Lipids
2541 individuals
140 lipids

Proteins
1170 individuals
1195 proteins

Slieker and Donnelly et al. Diabetes 2021
Results: metabolites

- Branched-chain amino acids (BCAAs) - leucine and isoleucine
- High BCAAs indicate insulin resistance
Results: lipids

- Diaglycerol is linked to higher insulin resistance
- Phosphatidylcholines with lower insulin resistance
Results: proteins

• Insulin signalling lower in insulin resistant people

• Cytokines, including satiety hormones higher in high BMI group

Insulin-deficient
Insulin-resistant
High BMI
Mild diabetes
Mild with high HDL

High levels
Low levels
Overview

BCAAs  Diacylglycerol  Triacylglycerol  Phosphatidylcholines  Insulin signalling  Cytokines

Insulin-deficient

Insulin-resistant

High BMI

Mild diabetes

Mild with high HDL

High levels
Low levels
Conclusions

• All people have type 2 diabetes, but very distinct molecular signatures

• The insulin resistance- and high HDL groups show opposite effects

• Provides starting points for personalised medicine

• Learn more on the RHAPSODY outcomes webpages: https://imi-rhapsody.eu/outcomes/
Thank you for your attention!

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