Addressing the challenges of diabetes and its complications:
The IMI Diabetes Platform

EACPT 2013 Congress – 29 August – CICG Geneva

Bernd Jablonka
Sanofi
Challenges of Diabetes Treatment

• Novel targets / therapeutic approaches
  – Identification of novel genes or cellular pathways that are involved in:
    • Pancreatic beta-cell regeneration / degeneration, proliferation / apoptosis and demise
    • Glucose uptake of insulin target cells
  – Transplantation of human pancreatic beta-cells

• Tools for accelerated access to novel therapies
  – Validated biomarkers to predict
    • Onset of diabetes and / or diabetic complications and disease progression
    • Response to therapeutic intervention
    • Prevention or reduction of diabetes and / or diabetic complications
  – Validated non-invasive imaging probes / techniques for clinical use
    • To assess in vivo beta-cell function and mass
    • To monitor disease progression and treatment response
  – Novel models adequately reproducing diabetes & diabetic complications in men
    • Characterization of existing and development of novel animal models to better investigate key pathogenic mechanisms and predict outcomes of therapeutic interventions in the clinical setting
The IMI Diabetes Platform

- Lack of understanding disease development and heterogeneity
- Lack of tools for disease monitoring
- Lack of biomarkers predictive for disease development and progression, treatment response and disease complications
- Lack of novel therapeutic targets / therapies

No company or academic institute or traditional scientific network can solve hurdles of such complexity alone

IMIDIA – DIRECT – SUMMIT:
Bringing together experts from academia, industry and biotech to generate novel approaches for diabetes research and treatment in a unique collaborative European Public-Private-Partnership (PPP)

Ultimate goal of faster development of better medicines for diabetes care
The IMIDIA consortium is working towards developing innovative approaches to shift the management of diabetes from symptomatic to beta-cell focused treatment

- **Innovative tools to**
  - study human pancreatic beta-cells development, function, survival and modulation by potential therapeutic compounds
  - perform *in vivo* beta-cell imaging

- **Biomarkers to**
  - assess diagnosis and prognosis of beta-cells failure
  - monitor diabetes progression and treatment success

- **Information regarding**
  - novel pathways that control beta-cells proliferation, differentiation and apoptosis
  - the role of nutrient-regulated pathways that control beta-cells mass and function

- **The overall goal is:**
  - to develop new approaches to assess, predict or prevent pancreatic beta-cells demise
  - to restore normal beta-cells mass and function for the treatment of diabetes patients

For further information see: www.imidia.org
The IMIDIA consortium is organized into five interacting work packages as described below:

- **WP1**: Human cell lines
- **WP2A&B**: Novel pathways and sites
- **WP3**: Nutrient regulated pathways
- **WP4**: Imaging
- **WP5**: Data repository and analysis

These packages interact with each other, as indicated by the diagram.
The DIRECT consortium is working towards developing a personalized medicines approach for the treatment of type 2 diabetes with existing or novel therapies

- **Complete phenotyping of**
  - patients with rapid or slow glycaemic deterioration (extremes)
  - extreme glycaemic response vs. non-responders to therapeutic intervention in already well-characterized subjects from large cohorts available throughout Europe

- **Identification of**
  - biomarker for subtypes with rapid diabetes development and progression
  - biomarkers for altered response to diabetes treatments
  - surrogate response biomarkers that reflect the underlying disease progression based on transcriptional and functional genomics, proteomics, lipidomics and metabolomics

- **Validation of biomarker candidates as surrogate markers in**
  - a large intervention trial for the delay progression of diabetes or pre-diabetes
  - smaller trials for therapeutic response
The DIRECT consortium is organized into seven interacting work packages as described below:

- **WP1**
- **WP2**
- **WP3**
- **WP4**
- **WP5**
- **WP6**
- **WP7**
- **WP8**

**Part 1**
- WP3: Cohort investigations
  - Therapeutic response in type 2 diabetes
- WP4: Omics
  - Genetic and genomic analysis
- WP5: Data repository and integrative biology

**Part 2**
- WP2: Cohort investigations
  - Glycaemic deterioration
- WP6: Assay development and validation of biomarkers
- WP7: Validation of biomarkers for drug response in small clinical trials
- WP8: Validation of biomarkers for glycaemic deterioration in a larger clinical trial
The SUMMIT consortium is working towards developing innovative approaches to make clinical trial testing of novel medications in diabetic vascular complications shorter and more efficient. The major focus is on diabetic nephropathy, diabetic retinopathy and cardio-vascular disease in type 2 diabetes patients.

Susceptibility markers predicting diabetic micro- and macro-vascular complications

- Identification of genetic markers / biomarkers / non-invasive markers that can be used to:
  - Identify diabetes patients at risk of vascular complications
  - Monitor progression, reduction or prevention of vascular complications and / or response to therapy
  - Serve as useful surrogate endpoints in clinical trials, which are accepted by regulatory agencies

- Develop animal models better reproducing diabetic complications in men, novel cardio-vascular imaging technologies and *in-silico* modeling tools for preclinical research
The SUMMIT consortium is organized into five interacting work packages as described below:

- **WP1:** Genetic marker
- **WP2:** Bio-marker
- **WP3:** Non-invasive marker
- **WP4:** New animal models
- **WP5:** Data mining & *In silico* modeling

**Organisation of Project Activities**

Patient overlap

strongly integrated - **INDICATION** centered – across WP approach

**DR**

**DN**

**CVD**

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## The IMI Diabetes Platform: Facts

<table>
<thead>
<tr>
<th>IMPROVING BETA-CELL FUNCTION AND IDENTIFICATION OF DIAGNOSTIC BIOMARKERS FOR BETTER TREATMENT</th>
<th>DIABETES RESEARCH ON PATIENT STRATIFICATION</th>
<th>SURROGATE MARKERS FOR MICRO- AND MACROVASCULAR HARD ENDPOINTS FOR INNOVATIVE DIABETES TOOLS</th>
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<tr>
<td><strong>START DATE</strong></td>
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<td>01/02/2012</td>
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<td><strong>DURATION</strong></td>
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<td><strong>RES. EFPIA</strong></td>
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<td><strong>FUNDING IMI</strong></td>
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<td>21.4 Mio</td>
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<td><strong>RES. ACADEMIA</strong></td>
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<td><strong>TOTAL BUDGET</strong></td>
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* Academia / Pharma / Small and Medium-sized Enterprises

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Benefit for the Diabetes Patient

- **Disease heterogeneity**
  - Early classification of pre-diabetes patients at high risk for T2D development
  - Improved prognosis of glycaemic deterioration after onset of T2D
  - Early identification of diabetes patients at risk for micro- and macro-vascular complications

- **Therapeutic implications**
  - Early therapeutic intervention in pre-diabetes patients and individual therapy after diagnosis of diabetes
  - Better control of blood glucose levels
  - Faster access to novel treatments for diabetes and/or diabetic vascular complications beyond glucose lowering therapy
  - Reliable monitoring of disease progression using novel biomarkers and improved imaging probes/technologies

- **Future treatment opportunities**
  - Novel therapeutic targets through extended pathway knowledge
  - Novel biomarkers for diagnosis and prognosis of beta-cell failure
  - Reliable monitoring of disease progression using novel biomarkers and improved imaging technologies
  - Novel therapies to slow down disease progression
  - Vision to ultimately find a cure for diabetes

Can only be achieved through large collaborations among public and private partners across borders and institutions
Results from IMI Diabetes Projects

- Generation of human pancreatic beta-cell lines
- Unique bio-repository of human pancreatic beta-cell samples
- Novel biomarker modules corresponding to diabetic phenotypes
- Visualization of insulin turnover in the pancreatic beta-cell

- Biomarkers evaluation of retrospective samples of type 2 diabetes patients

- Biological insight and translational opportunities from genetic and non-genetic analysis of samples from type 1 and 2 diabetes patient with nephropathy
- Novel findings in genetics and ...omics of type 2 diabetes patients with cardiovascular disease
- Improved animal models for replicating diabetes vascular complications
- Imaging of vascular complications
Thank you for your attention!
Backups
The IMI diabetes project IMIDIA was launched on February 01, 2010.
Participants and EU Countries

Sanofi-Aventis Deutschland GmbH (Coordinator)
Eli Lilly (Co-coordinator)
University of Dundee (Academic Lead)

University of Bath
Consiglio Nazionale delle Ricerche
Technical University of Denmark
Eberhard Karls Universitaet Tuebingen
Helmholtz Zentrum München – Deutsches Forschungszentrum für Gesundheit u. Umwelt GmbH
Consorti Institut D'Investigacions Biomediques
August Pi i Sunyer
Imperial College London
Kungliga Tekniska Högskolan
University of Lille- CNRS
Leiden University Medical Center
University of Copenhagen
University of Eastern Finland
Lunds Universitet
University of Newcastle upon Tyne
University of Exeter
Université de Genève
University of Oxford
Universitaet Ulm
VU University Medical Center
Novo Nordisk A/S
Servier
Lille University Hospital

The IMI diabetes project DIRECT was launched on February 01, 2012
The IMI diabetes project SUMMIT was launched on November 01, 2009

Participants and EU Countries

Boehringer Ingelheim (Coordinator)
Eli Lilly (Co-Coordinator)
Lund University (Academic Lead)
University of Dundee (Academic Co-Lead)

AstraZeneca
Biocomputing Platforms Ltd
F. Hoffmann-La Roche Ltd
Folkhälsan, Helsinki
Helmholtz Zentrum Muenchen
Instituto di Ricerche Farmacologiche “Mario Negri”
Karolinska Institute
Pfizer
Sanofi-Aventis Deutschland GmbH
University of Cambridge
University of Dundee
University of Exeter
University of Gothenburg
National Institute for Health and Welfare, Finland
University of Eastern Finland
University of Oxford
Università degli Studi di Padova
Università degli Studi di Pavia
Università di Pisa
Università Cattolica del Sacro Cuore, Rome
University of Turku
University of Edinburgh
Università di Firenze