DIRECT
Diabetes Treatment Gets Personal

*IMI and personalised medicine – 20 March 2013 – Dublin, Ireland*

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Challenges of Diabetes Treatment

• Novel therapeutic approaches
  – Novel targets for the treatment of diabetes
    • Identification of novel genes or cellular pathways that are involved in pancreatic beat-cell regeneration / degeneration, proliferation / apoptosis and demise
  – Reliable probes for in vivo imaging of beta-cells
    • Assessment of beta-cell function, mass and disease progression, treatment response

• Individual therapy of diabetes patients (personalized medicines approach)
  – Prediction of disease progression and treatment response
    • Identification of biomarkers that are predictive for progression of glycaemic deterioration in pre-diabetes patients or patients with early onset of diabetes
    • Identification of biomarkers that are predictive of treatment response to current standard therapies
  – Prediction of cardio-vascular risk of diabetes patients
    • Identification of biomarkers that are predictive for the development of diabetic macro- and micro-vascular complications
IMIDI – DIRECT – SUMMIT:

3 DIABETES PROJECTS

bringing together experts from academia, industry and biotech
to generate novel approaches for diabetes research and treatment

in a unique European Public-Private-Partnership (PPP)

*Innovative Medicines Initiative – Joint Undertaking: a Public-Private-Partnership between the European Commission (EC) and the European Federation of Pharmaceutical Industries and Associations (EFPIA)
Novel Treatment Strategies in Diabetes

Current treatment of diabetes

- No estimation of diabetes onset is possible in high-risk pre-diabetes patients
- No prediction of disease progression is applicable in patients with early onset of diabetes
- First line therapy for Type 2 Diabetes (T2D) patients is metformin or sulfonylureas for all
- Substitution therapy with insulins
- Second line therapy with GLP-1 receptor agonists

Need for novel prediction and treatment strategies to

- classify high-risk pre-diabetes patients, who will develop diabetes as early as possible
- improve control of diabetes development and disease progression
- identify individual therapy options immediately after onset of diabetes
- avoid non-response to diabetes therapy or treatment intolerance
Scientific contributions of DIRECT participants to the consortium

- Availability of large cohorts of T2D patients from academic partners
- Use of improved risk prediction models for high-risk pre-diabetes patients and patients with early onset of diabetes
- Access to “omics” labs of leading European academic experts for the analysis of patient samples
- Development of joint database and installation of analysis server accessible to all participants
- Provision of Pharma expertise in the preparation and conduct of clinical validation studies

Unique opportunities of the consortium

- to elucidate mechanisms of glycaemic deterioration and treatment response to current standard therapies in T2D patients
- to identify novel biomarkers predictive for disease progression and treatment response
- to validate biomarker candidates in clinical study(ies)
- to develop selective treatment options of T2D in a personalized medicines approach
- to establish diabetes network among scientists and between Academia and Pharma across Europe

Rationale for the implementation of DIRECT as PPP

- Each single participant cannot undertake this holistic approach alone
- Close collaboration between expert institutes for diabetes research and clinical development is required to achieve the ambitious goals of the consortium
The DIRECT consortium is working towards developing a personalized medicines approach for the treatment of type 2 diabetes with existing or novel therapies

- The scientific program of the consortium aims at delivering:

**Part 1 of the project (years 1-4)**

- Complete phenotyping of
  - extreme phenotypes of patients with rapid and slow glycaemic deterioration
  - extreme glycaemic response 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
    - based on transcriptional and functional genomics, proteomics, lipidomics and metabolomics analyses of patient plasma samples
  - surrogate response biomarkers that reflect the underlying disease progression
Part 2 of the project (years 5-7)

- Validation of biomarker candidates as surrogate response markers in
  - a large intervention trial for the delay progression of diabetes or pre-diabetes

Or

- smaller trials for therapeutic response

For further information see: www.direct-diabetes.org
The DIRECT consortium is organized as a highly integrative and synergistic structure dividing the project into seven interacting work packages as described below:

**Part 1**
- **WP3** Cohort investigations
  - Therapeutic response in type 2 diabetes
- **WP4** Omics
  - Genetic and genomic analysis
- **WP5** Data repository and integrative biology
- **WP6** Assay development and validation of biomarkers

**WP2** Cohort investigations
- Glycaemic deterioration

**Part 2**
- **WP7** Validation of biomarkers for drug response in small clinical trials
- **WP8** Validation of biomarkers for glycaemic deterioration in a larger clinical trial

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The IMI diabetes project DIRECT was launched on February 01, 2012
Deliverable Timelines

Part 1

- Start of patient recruitment: PY1 (2012)
- Availability of baseline data: PY3 (2014)
- Selection of “extremes” for follow-up: PY3 (2014)
- Availability of follow-up data: PY4 (2015)
- Selection of biomarker candidates predictive for glycaemic deterioration and treatment response: PY5 (2016)

Part 2

- Start of clinical validation study(ies): PY5 (2016)
- Completion of biomarker assay development and up-scaling: PY6 (2017)
- Availability of clinical validation data: PY7 (2018)
Budget and Funding

No. of participants: 25
- 21 Academia and 4 EFPIA participants

- Dedicated resources from EFPIA partners: 16.5 mio. €
- Dedicated resources from public and SME* partners: 26.6 mio. €

- Total project budget: 43.1 mio. €
- IMI funding to public and SME partners: 21.5 mio. €

Project duration: 7 years

* Small to Medium Enterprises
Benefit of personalized medicines for the T2D patient

- **Early classification** of high-risk, pre-diabetes patients for development of T2D
- **Improved prognosis** of glycaemic deterioration after onset of T2D
- **Individual therapy** after T2D diagnosis
- **Better control** of blood glucose levels
- **Less side effects**
- **Less cost** for society

→ Can only be achieved through large collaboration among public and private partners across borders and institutions
On behalf of the DIRECT Consortium

Thank you for your attention!