IMIDIA

IMPROVING BETA-CELL FUNCTION AND IDENTIFICATION OF DIAGNOSTIC BIOMARKERS FOR TREATMENT MONITORING IN DIABETES

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Diabetes is a metabolic disease characterized by higher than normal blood glucose levels (hyperglycemia) in the fasting state and/or after meals.

Type 1 and type 2 diabetes are the two main types of diabetes.

**Type 1 diabetes**
- 10 à 15 % of diabetic patients
- Destruction of β cells (autoimmune process)
- Onset in young subjects
- Main feature: weight loss, polyphagia, polyuria, asthenia, glycosuria
- Imperatively requires insulin therapy

**Type 2 diabetes**
- 85 à 90 % of diabetic patients
- No destruction of β cells but a decrease in functional β cells mass
- Onset during maturity and in the elderly
- Very progressive
- In theory insulin therapy is not required

Micro (retinopathy, nephropathy)- and macro-angiopathic complications (cardio and cerebro vascular diseases)
Diabetes – a pandemic disease of the 21st century

• Number of patients:
  – 2010: 285 million people worldwide
  – 2030: 439 million people worldwide
  (in particular spreading to the younger population)

• Pancreatic β-cells:
  – A complete or relative decrease in insulin secretion by pancreatic beta-cells underlies the development of, respectively, type 1 and type 2 diabetes.
PATHOPHYSIOLOGY OF TYPE 1 DIABETES
A SCHEMATIC REPRESENTATION

β-cell death

NO INSULIN

Insulin resistance

Glucose utilization

Glucose production

Hyperglycaemia
PATHOPHYSIOLOGY OF TYPE 2 DIABETES
A SCHEMATIC REPRESENTATION

β-cell failure

Insulin response to glucose

Insulin resistance

Glucose utilization

Glucose production

Hyperglycaemia
THE AIMS OF TREATMENT OF TYPE 2 DIABETES

To prevent early death and improve quality of life

To prevent micro- and macro vascular complications

Optimal glycaemic control
MAIN AGENTS USED IN THE TREATMENT OF TYPE 2 DIABETES

7 different approaches. No one prevents the progressive deterioration of glycemic control.
PROGRESSIVE DETERIORATION OF GLYCEMIC CONTROL IN TYPE 2 DIABETES

United Kingdom Prospective Diabetes Study

HbA1c (%) vs Years from randomization

Conventional therapy vs Intensive therapy

6.2% upper limit of normal range
Conventional Therapies Do Not Influence β-Cell Failure

Nonoverweight  Overweight

β-Cell Function* (%)

Years From Randomization

- Conventional
- Sulfonylurea
- Metformin

**β-CELL MASS IN DIABETIC AND NON DIABETIC SUBJECTS**

- Observations made post-mortem
- No information on the time-course of the β cell mass

The requirement of non-invasive methods for the measurement of β cell mass
Relationship between functional β cell mass and glycemic control during the progression of diabetes

Objective
To stop the progression of the disease
A Paradigm Shift in Diabetes Therapy: from symptomatic Treatment to Cure

Current treatment options

β-cell medicines: Regeneration Preservation

Symptomatic treatment

Stop disease progression

Disease prevention

Cure
IMIDIA will address key bottlenecks for the development of these new therapies.

- **Novel tools** for the study of:
  - human beta-cell development, function and survival;
  - human beta-cell functional modulation by potential therapeutic compounds;
  - in vivo beta-cell imaging.
IMIDIA will address key bottlenecks for the development of these new therapies

- **Biomarkers:**
  - for the diagnosis and prognosis of beta-cell failure;
  - for monitoring diabetes progression and treatment.

- **Knowledge:**
  - on novel pathways and sites that control beta-cell proliferation, differentiation and apoptosis,
  - on the role of nutrient-regulated pathways in controlling beta-cell mass and function.
Integrated approach
Expected Outcome – I:

• Disease relevant human islet cell lines:
  - will lead to better models for the development and assessment of diabetes therapies.

• Beta islet cell precursor isolation and purification:
  - will help understanding the birth of beta-cells to help find methods for beta-cell regeneration in diabetes.

• A Systems Biology approach of beta-cell demise in type 2 diabetes:
  - will provide better understanding of the beta-cell pathogenesis;
  - will deliver biomarker candidates for diagnosis, prognosis and assessment of therapeutic efficacy.
Expected Outcome – II:

- A network and technology allowing the isolation of human islet cells from surgical specimen of diabetic and non-diabetic patients.

- Unraveling key pathways and sites that control GLP-1 trophic actions on beta-cells.

- New and unique imaging technologies and novel probes for earlier and better monitoring of beta cell function and mass in humans.
Benefit to the patient:

To monitor specific disease progression and enable improved disease management.

To pave the way for the development of β cell focused therapies via:
- Better biomarkers to monitor therapy benefit in patients
- Better disease centric in-vitro and in-vivo models
- Better understanding to enable focused therapeutic approaches
IMIDIA: Collaboration
(Sustainable win-win)

IMIDIA - Collaboration

Data / Results Sharing

Innovation Focus academia

Application Focus industry

In-vitro Models:
Generation of models
Assessment Drug Discovery

Imaging Biomarkers:
In-vitro Assessment Clinical Assessment
Results/achievements so far: 4 months into the project

Tools:
- Evaluation of first version of in-vitro models
- Data acquisition process for Systems Biology established
- Biorepository Harmonization Initiated
- Synthesis of first Imaging Molecules Candidates initiated

Biomarker:
- Human assessment study in preparation
Time and money

Financing

- IMI funding: € 7,074,760
- EFPIA contribution, mainly in kind: € 15,081,800
- Other contributions (e.g. unfunded act., act. in the USA): € 3,750,920
- Total project cost: € 25,907,480

Timing:

- Starting date: 01. Feb. 2010
- Duration: 5 years
imidia
European combined excellence in diabetes research

Leadership team
- Sanofi-Aventis Deutschland
- Servier
- University of Lausanne
- W. Kramer
- A. Ktorza
- B. Thorens

Participants
- AstraZeneca Pharmaceuticals
- Boehringer Ingelheim Pharma
- CEA Institut d’imagerie Biomédicale
- CNRS UMR 7091
- CNRS-University Paris Diderot
- Dresden University of Technology
- F. Hoffmann-La Roche
- Hannover Medical School (MHH)
- Imperial College London
- INSERM U845
- Lilly Deutschland
- Novo Nordisk A/S
- Novartis Institutes
- SARL ENDOCCELLS
- Swiss Institute of Bioinformatics
- University of Geneva
- University of Pisa
- Vrije Universiteit Brussel

*Location of key scientific contacts in Europe*
Launch of IMIDIA

An Innovative Medicines Initiative Project for Diabetes

Academia, biotech and the pharmaceutical industry have joined forces to fight diabetes.

Frankfurt, Germany / Lausanne, Switzerland / Paris, France - June 14, 2010.
Further information

- www.imidia.org
- Email: info [AT] imidia.org

www.imi.europa.eu
Type 1 and type 2 diabetes impose a huge burden to welfare systems

Relative or complete decrease in insulin secretion underlies the development of type 1 and type 2 diabetes

Limited therapeutic options

Limited knowledge β-cell biology (function, survival, pathophysiology)

Lack of biomarkers for prognostic of β-cell failure

The IMIDIA project

New tools for the study of human β-cell development, function and survival

Biomarkers

Knowledge of novel pathways and sites that control β-cell development, function and survival

Non-Invasive Imaging of the Human Endocrine Pancreas
CONTROL OF BETA-CELL MASS

- **Neogenesis**
  - Cluster of new β-cells
  - Probably increased in type 2 diabetes

- **Apoptosis**
  - Apoptotic nuclei
  - Probably deficient in type 2 diabetes

- **Replication**

- **Hypertrophy**

- **Potential therapeutic target**

- **Duct cells**

- **Mitosis**
EXPECTED MAIN COMPETITIVE ADVANTAGE

Close interaction between academic teams, pharmaceutical companies and SMEs

Unique conjunction of expertise and will form a strong basis for a successful enterprise

Improvement of industrial competitiveness and Public Health in Europe

• **Content advantage**
  – All results transparent to all project participants during the project
  – “Validation” of new technologies / tools from academia during the project by participating industry

• **Time advantage**
  Access to generated IP within the project “foreground” for “research use”
The Path to innovative Diabetes Therapies: enhancing functional β-Cell Mass

Scientific key questions
Tools & Technologies

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