DIABESITY - novel molecular drug targets for obesity and type 2 diabetes

Novel molecular targets for obesity and type 2 diabetes

A European Union Framework Programme VI Integrated Project
(LSH-CT2003-503041)
Introduction

DIABESITY is a European Union Framework Programme VI Integrated Project involving a consortium of 27 partners from 24 European Institutions, coordinated by The University of Gothenburg, Sweden.

DIABESITY aims to identify new genes implicated in obesity and type 2 diabetes (diabesity) and to develop strategies for validating these genes as targets for future pharmacological manipulation. We will study how these genes interact with hypothalamic pathways that regulate appetite and metabolism using multiple approaches to establish the functional role of genes in regulating metabolism, body weight and composition. Using this approach we aim to identify several new drug targets for the treatment and prevention of diabesity.

Why Diabesity?

- Obesity and type-2 diabetes (diabesity) are a major global health problem
- In the European Union type 2 diabetes costs 15 b Euros per year
- By 2010, approximately 33 million Europeans will suffer from diabetes
- Obesity, which is a major recognised risk factor for type 2 diabetes, is rapidly increasing in prevalence, resulting in a diabesity epidemic
- For most people, neither dieting nor current pharmacological interventions are effective in achieving long-term weight reduction
- To treat diabesity, we must develop approaches to modulate the ways in which the brain controls metabolism, body weight and composition
Members

DIABEITY is a “virtual research institute” of 27 basic and clinical scientists from 10 European countries, coordinated by The University of Gothenburg, Sweden.

The DIABEITY consortium unites 11 European Universities, 9 research institutes and four biotechnology companies in an integrated project encompassing research activity in molecular genetics, bioinformatics, proteomics, transgenics, functional genomics, cell biology, neuroscience, neuroendocrinology, integrative physiology and human physiology.
Research Programme

DIABESITY aims to combine neurophysiological, neuroanatomical and systems physiological approaches to establish the functional role of genes in regulating body composition, in order to understand how manipulation of gene activity impacts upon whole body physiology, endocrinology and phenotype. We will identify novel genes and processes linked to the pathogenesis of diabesity and thereby find potential molecular drug targets. Characterisation of those drug targets, in particular by using molecular physiological studies and integrative human biology, will be followed by target validation resulting in the identification of several novel drug targets for the treatment and prevention of diabesity.

The DIABESITY research programme consists of four workblocks focussing on different aspects of obesity and type 2 diabetes research.

Workblocks

1: Human genetics and human physiology
   leader: Steve O’Rahilly

2: Mouse and invertebrate genetics
   leader: Sven Enerbäck

3: Neuroanatomy and neuroendocrinology
   leader: Matthias Tschöp

4: Peripheral regulation: endocrinology and cell biology
   leader: John-Olov Jansson

The DIABESITY research programme has three distinct phases:

  target identification
  target validation
  target characterisation
Target Identification

Aim
To identify genes and processes linked to the pathogenesis of diabesity and obesity and discover novel molecular drug targets

Invertebrate Genetics

Mouse Genetics

Bioinformatics

Human Genetics

New targets

Expected results

Identification of novel genes implicated in diabesity

Validation of selected genes involved in diabesity
Target Characterisation

Aim
To characterise potential drug targets using molecular physiological studies and integrative human biology

New targets
Known targets

Neuroanatomy & Neurophysiology
Afferent Pathways

Gene Targetting

Systems Physiology
Adipose Regulation

Expected results
Clinical physiological studies of potential targets and their effects on metabolism, body weight and composition
Target Validation

Aim
To validate targets using molecular genetic approaches in conjunction with phenotypic analyses

Monogenic Disease  Case Control Studies

Clinical Investigation

Human Physiology

diabetes drug targets

Expected results
Identification of 4 - 5 novel validated molecular drug targets
Summary

- Obesity and type 2 diabetes (diabetes) are a major global health problem.
- Dieting and current drug treatments do not work for most people.
- There is a need to identify new ways of preventing and treating diabetes.
- The DIABESITY consortium brings together basic and clinical researchers forming a “virtual research institute”, enabling the available resources in Europe to be used optimally.
- Using this approach the DIABESITY consortium will discover, characterise and validate several novel drug targets for the treatment of diabetes.
Disclaimer

This research was supported by EU FP6 funding (contract no. LSHM-CT-2003-503041). This publication reflects the authors’ views and not necessarily those of the European Union. The information in this document is provided as is, and no guarantee or warranty is given that the information is fit for any particular purpose. The user thereof uses the information at its sole risk and liability.