Diabetes Research on Patient Stratification (DIRECT) addresses the personalized medicines approach in Type 2 diabetes patients. The focus of the consortium is the identification of novel surrogate markers that can be used for patient stratification according to glycemic deterioration and treatment response by

- Completing phenotyping of already well-characterized subjects from large cohorts in Europe
- Establishing a high-quality European databank with phenotypical datasets
- Developing a systems biology platform by integrating clinical and biological data, transcriptional and functional genomics, proteomics, metabolomics, and other relevant data
- Developing novel data-mining tools and algorithms to generate stratification biomarker candidates
- Identifying novel biomarkers for Type 2 diabetes subtypes with (a) rapid development and progression of diabetes and (b) altered response to diabetes treatment
Validating the novel biomarker candidates in a large intervention trial to delay diabetes or pre-diabetes or in smaller trials of treatment response

Mission

DIRECT’s focus is patient stratification, which involves identifying different subgroups of patients. The project will develop and validate tests to predict who will get diabetes, whose condition will deteriorate rapidly after diagnosis, and who will respond well or badly to certain drugs. The tests will then allow the DIRECT project to determine which existing drugs are effective for different varieties of Type 2 diabetes.

Specific DIRECT objectives are divided into Work Packages (WPs). Two key phenotyping work packages will focus on glycemic deterioration (WP2) and therapeutic response (WP3). For each, DIRECT brings considerable existing resources, which will be augmented by large-scale prospective cohort collection with intensive physiological and imaging phenotyping.

To maximize the likelihood of finding biomarkers suitable for patient stratification DIRECT will concentrate its phenotyping and multi-level genomic analysis (WP4) on the extreme phenotype of rapid and slow glycemic deterioration and extreme glycemic response to therapeutic intervention. Additional data will be added, such as existing studies on acute response to intravenous beta-cell secretagogues, and functional genomics on human islets, liver, muscle, and adipose tissue, to maximize the power and utility of an innovative integrated biology approach (WP5). To enable a computational multi-level integration across phenotypes and data types, a robust and secure data repository will be developed.

To facilitate rapid deployment of biomarkers into drug development and clinical trials, high-throughput assays for biomarkers that arise from the discovery phase of DIRECT will be developed and validated (WP6).

Because the ultimate aim of DIRECT is patient stratification, biomarkers arising from the discovery phase will be used to design one or more prospective clinical trial (WPs 7 and 8).

Results of the DIRECT consortium will be communicated to its target audience (WP1) such as the
scientific community, lay public, patient organizations, and agencies.

Consortium History

Jan. 1, 2012: Start date
Dec. 31, 2018: End Date

Structure & Governance

DIRECT is organized in a highly integrative and synergistic framework, dividing the project in two consecutive parts with contributions of seven strongly interrelated scientific WPs. In this seven-year program of work, there are a total of nine WPs.

WPs 1 and 9 are management WPs, with WP9 specifically designed to address the ethical and legal requirements of a large data repository of pan-European data, and the specific issues related to treatment stratification. WP1 addresses the aspects of project management and administration.

The seven interrelated research WPs can be broadly split into phenotype generation and provision (WPs 2 and 3), data generation and analysis (WPs 4 and 5), validation and assay development (WP6), and validation through prospective clinical trials (WPs 7 and 8).

Financing

The research is being funded by the European Union, with funding from some leading pharmaceutical companies. The Innovative Medicines Initiative (IMI) contributed €21.4 million, the European Federation of Pharmaceutical Industries and Associations contributed €16.5 million in kind, and other sources contributed €5.1 million, for a total cost of €43.0 million.

Impact/Accomplishment
IMI’s three diabetes projects — IMIDIA, SUMMIT and DIRECT — are set to deepen their cooperation following the signature of a new Memorandum of Understanding (MoU) that formally creates the IMI Diabetes Platform. “With a combined budget of €100 million and the involvement of over 300 leading experts in diabetes, this is one of the world’s leading initiatives in this area focusing on overcoming key bottlenecks for novel therapies and improved disease management,” the projects write in a press release announcing the MoU. “The importance of the findings of the IMI diabetes projects will be strongly increased by the multiple opportunities for information exchange now enabled by the implementation of a formal collaboration framework for the IMI Diabetes Platform.” The projects have already been collaborating informally for some time. For example, they jointly organized a symposium to present their results at the recent annual meeting of the European Association for the Study of Diabetes (EASD) in Barcelona.

Links/Social Media Feed

Homepage  http://www.direct-diabetes.org/index.php
Twitter  https://twitter.com/DIRECTdiabetes
Facebook  https://www.facebook.com/pages/Direct-Project/580539302017263

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