European Commission

Type 1 diabetes research: taking stock and maximising collaboration

European Commission – JDRF workshop

October – 2015

Research and Innovation

EUR KI-04-15-736-EN-N EN

EUROPEAN COMMISSION

Directorate-General for Research and Innovation
Directorate E — Health
Unit *E.4* — Non-communicable diseases and the challenge of healthy ageing

Contact: Dora Navarro Torné

E-mail: RTD-PUBLICATIONS@ec.europa.eu

European Commission
B-1049 Brussels

EUROPEAN COMMISSION

Type 1 diabetes research: taking stock and maximising collaboration

European Commission – JDRF workshop

edited by Dora Navarro Torné

Directorate-General for Research and Innovation
2015 Health, demographic change and well-being EUR KI-04-15-736-EN-N EN

EUROPE DIRECT is a service to help you find answers to your questions about the European Union

Freephone number (*):
00 800 6 7 8 9 10 11

(*) The information given is free, as are most calls (though some operators, phone boxes or hotels may charge you)

LEGAL NOTICE

This document has been prepared for the European Commission however it reflects the views only of the authors, and the Commission cannot be held responsible for any use which may be made of the information contained therein.

More information on the European Union is available on the internet (http://europa.eu).

Luxembourg: Publications Office of the European Union, 2015.

PDF	ISBN 978-92-79-52211-6	doi: 10.2777/239617	KI-04-15-736-EN-N

© European Union, 2015.
Reproduction is authorised provided the source is acknowledged.

Cover images: © Lonely, # 46246900, 2011. © ag visuell #16440826, 2011. © Sean Gladwell #6018533, 2011. © LwRedStorm, #3348265. 2011. © kras99, #43746830, 2012. Source: Fotolia.com

Contents

1. EXECUTIVE SUMMARY 4
2. SCOPE AND PURPOSE 5
   2.1. Objectives 5
3. EXPERT PRESENTATIONS 5
   3.1. Opening speeches 5
   3.2. Presentation summaries 6
   3.2.1. Session 1-Aethiology/Pathophysiology-state of play and perspectives 6
   3.2.2. Session 2- Prevention and Diagnostics-turning progress into every-day solutions 8
   3.2.3. Session 3- Working together for a better treatment and cure 10
   3.2.4. Session 4- Addressing the framework: regulatory aspects, national policy and data-sharing 12
4. PARTICIPANTS' DISCUSSIONS 13
   4.1. Session 1- Aethiology/Pathophysiology-state of play and perspectives 13
   4.2. Session 2- Prevention and Diagnostics-turning progress into every-day solutions 14
   4.3. Session 3- Working together for a better treatment and cure 16
   4.4. Session 4- Addressing the framework: regulatory aspects, national policy and data-sharing 17
5. CONCLUSIONS, RECOMMENDATIONS AND NEXT STEPS 18

1. EXECUTIVE SUMMARY

Diabetes is a chronic disease that constitutes a major cause of morbidity and mortality worldwide. Diabetes rates are alarmingly increasing both in developed and developing countries across the world. It poses a considerable burden to patients and healthcare systems.

The European Commission Directorate General for Research and Innovation (DG RTD) and the JDRF (formerly Juvenile Diabetes Research Foundation))[1] jointly organised a workshop on type 1 diabetes held in Brussels on 23 June 2015 with the ultimate goal of establishing the state-of-art in the field, identifying gaps, and brainstorming about the possibilities offered by personalised medicine approaches in this area.

The programme was divided into four major sections: from aetiology/pathophysiology through prevention and diagnostics to treatment and cure. The regulatory framework for new and complex therapeutic solutions was also introduced together with examples of national policies and challenges in data sharing.

Over 50 participants attended this meeting. Participants included researchers, academics, clinicians, EU project coordinators and partners, representatives from the pharmaceutical industry and biotechnology companies, members of European associations for diabetes, decision makers and European Commission and JDRF representatives.

The presentations addressed the latest advances and challenges concerning type 1 diabetes. They were very interactive and were followed by vivid discussions reflecting the wide range of interests of the participants.

Speakers emphasised that neither the pathogenesis of type 1 diabetes nor the mechanisms of disease progression are known yet. The genetic susceptibility is conferred both by HLA (Human Leukocyte Antigen) and non-HLA genes but the disease process seems to be triggered by an exogenous factor (most likely an infectious agent) and modified by a number of host-related and environmental factors. Autoimmunity plays an important role both for early diagnosis and prevention of overt onset of the disease.

During the workshop it was explained that diagnosis and prevention of major complications of type 1 diabetes such as chronic kidney disease or cardiovascular disease currently focus on developing robust biomarkers and better predictive models for the disease. Apart from –omics studies, the role of electronic medical records, registries and observational data (well phenotyped cohorts and longitudinal studies) was highlighted.

In the realm of treatment, promising new therapeutic solutions such as the development of human beta cells and cell-based therapies, immune-based therapies and artificial pancreas models were featured.

Projects spotlighted throughout the workshop revealed that type 1 diabetes funded research is ground-breaking and state-of-art across areas, either aetiology (DIABIMMUNE[2], NAIMIT[3], IMIDIA[4], BETABAT[5]), prevention and complications (PRIORITY[6], SUMMIT[7]) or treatment and cure

---

[1]JDRF, Juvenile Diabetes Research Foundation, http://jdrf.org/

[2]DIABIMMUNE, Pathogenesis of type 1 diabetes: testing the hygiene hypothesis, http://www.diabimmune.org/

[3]NAIMIT, Natural Immunomodulators as Novel Immunotherapies for Type 1 Diabetes, http://naimit.eu/

[4]IMIDIA, European Combined Excellence in Diabetes Research, http://www.imidia.org/

[5]BETABAT, Development of novel treatment strategies based on knowledge of cellular dysfunction in diabetes, http://betabat.ulb.ac.be/

[6]PRIORITY, Proteomic prediction and renin angiotensin aldosterone system inhibition prevention of early diabetic nephropathy in type 2 diabetic patients with normoalbuminuria, http://www.eu-priority.org/

[7]SUMMIT, Surrogate markers for micro- and macro-vascular hard endpoints for Innovative diabetes tools http://www.summitdiabetes.com/

(AP@home[8], BIOSID[9], PCDIAB[10]). A majority of those studies show complementarities and have created sound basis for potential future collaboration such as the new IMI[11] calls on pathogenesis and novel treatments for T1D and diabetes kidney disease biomarkers.

The relevance of personalised medicine was evident as for instance the search of robust biomarkers to address distinct needs or individualised algorithms for the artificial pancreas. Personalised medicine is particularly relevant for type 1 diabetes and will request dealing with heterogeneity and stratification in clinical research. In this context, it was highlighted that seeking for early regulatory advice was paramount to ensure adaptation of therapeutic solutions to individual biological responses and processes.

The workshop helped to highlight needs and perspectives and to identify potential avenues for future collaboration departing from efforts of existing projects and activities of both organisations.

The speakers laid out that time frame for the next major advances in type 1 diabetes have never been so close for patient access (a matter of few years for Closed Loop system, encapsulation, immunomodulation...) and that efforts and investment have to be pursued to reach the goals.

2. SCOPE AND PURPOSE

The purpose of the workshop was to capitalise on current efforts and assets, integrate existing data, and exploit previous findings to ensure effective use of resources and innovative affordable strategies for the prevention, cure, and management of type 1 diabetes.

It also aimed at taking stock of current state-of-the-art in type 1 diabetes research and up-scaling collaborations by exploring potential areas of common interest.

2.1.Objectives

The detailed objectives of this workshop were:

- To take stock of knowledge and achievements of existing FP7[12], IMI, and JDRF projects on type 1 diabetes;
- To identify areas of common interest in order to maximise potential opportunities for future collaboration; and
- To identify promising areas for developing personalised medicine in type 1 diabetic patients.

[8]AP@home, Bringing the artificial pancreas home, http://www.apathome.eu/news/aphome-project-successfully-completed/

[9]BIOSID, a bioartificial pancreas, http://biosid-eu.org/project-description/

[10]PCDIAB, Innovative approach to manage diabetes, http://www.pcdiab.eu/

[11]IMI, Innovative Medicines Initiative, http://www.imi.europa.eu/

[12]FP7, 7th Framework Programme for Research and Technological Development, http://ec.europa.eu/research/fp7/index_en.cfm

3. EXPERT PRESENTATIONS

3.1. Opening speeches

The official opening of the workshop included speeches from Dr Ruxandra Draghia-Akli, Director of Health in Directorate General for Research and Innovation, and of Dr Richard Insel, Chief Scientist Officer of JDRF.

Dr Draghia-Akli welcomed the audience and presented the EU contribution to tackle type 1 diabetes through initiatives funded by the Seventh Framework Programme for Research and Technological Development (FP7). She explained that FP7 investment in diabetes amounted to over €376 million supporting 156 projects (excluding obesity and nutrition). She spoke of some bright examples of EU-funded projects on type 1 diabetes. Dr Draghia-Akli's presentation showcased particular features of EU investment (clinical trials, cohort studies, therapeutic approaches) highlighting the intense collaboration between public and private sectors and the opportunities for personalised medicine. Dr Draghia-Akli presented Horizon 2020[13], the Framework Programme for Research and Innovation as a single programme coupling research to innovation with focus on societal challenges and a simplified access providing different opportunities for funding and the new financial instruments including SMEs. Collaborative research on type 1 diabetes, initiatives such as IMI1&2, and EU global health sponsoring as in GACD[14] projects, were some aspects she emphasised. Dr Draghia-Akli outlined the content of the workshop and wished a fruitful outcome.

Dr Richard Insel welcomed the audience and thanked the EC for co-organising the workshop. He drew attention to type 1 diabetes (T1D) as a major and increasing health problem with an important economic impact**.** He stated that the incidence of childhood-onset T1D has been increasing worldwide (~3-4% per year) with predictions that the incidence of childhood-onset type 1 Diabetes in 2020 in Europe will be twice that of the year 2000. In the developed world, particularly in USA, Canada, Australia, even in Eastern Europe, diabetes rates are on the rise. Furthermore, he said that the age of onset is decreasing in Europe and that the disease penetrance has been extended to what heretofore were considered lower genetic risk groups. He argued that despite insulin discovery more than one hundred years ago, the management of type 1 diabetes remains challenging. Dr Insel referred to the participation of JDRF in FP7, IMI1 &2 and Horizon 2020 projects. JDRF is also partnering with the Food and Drug Administration (FDA) and the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)[15] in the USA, and with private companies in Europe for better treatments, prevention and a cure. He highlighted that JDRF represents families and patients affected by type 1 diabetes with projects in 17 countries and that the global investment of JDRF in Europe amounts to approximately $ 20 million. He expected the workshop to be a pathway that contributed to accelerate on the delivery of more efficacious healthcare and prevention and a cure of type 1 diabetes.

3.2. Presentation summaries

3.2.1. Session 1-Aethiology/Pathophysiology-state of play and perspectives

- **Professor Mikael Knip**

Professor Knip presented his findings (some belonging to DIABIMMUNE) about the aetiology/pathophysiology of type 1 diabetes through studies mainly performed in Finland.

---

[13] Horizon 2020, the Framework Programme for Research and Innovation (2014 – 2020), http://ec.europa.eu/programmes/horizon2020/

[14] GACD, Global Alliance for Chronic Diseases, http://www.gacd.org/

[15] NIDDK, National Institute of Diabetes and Digestive and Kidney Diseases, http://www.niddk.nih.gov/Pages/default.aspx

Finland has the highest incidence of diabetes in the world. In 2006 it was 65 per 100.000 among children below 15 years of age and it has increased sixfold over a time period of less than 60 years. He stated that type 1 diabetes is an immune-mediated disease. The asymptomatic period is variable and depends on personal variability. He drew attention to a number of statements in relation to type 1 diabetes:

3. the genetic susceptibility is conferred by HLA (Human Leukocyte Antigen) and non-HLA genes;
4. the disease process is triggered by an exogenous factor, most likely an infectious agent;
5. driven by an exogenous antigen, potentially a dietary antigen;
6. modified by a series of host-related and exogenous factors; and
7. affected by gene-gene and gene-environmental interactions in each phase of the process.

Overall, association with type 1 diabetes has been established for 52 genes, of which the complex HLA, *INS, PTPN22 and IL2RA drive the highest risk. There has been a temporal shift in the distribution of HLA genotypes in patients with newly diagnosed diabetes in Finland. HLA genotypes DR3-DQ2/DR4-DQ8 (OR 15.1) and DR4-DQ8/DR4-DQ8 (OR 8.1) show the highest association with type 1 diabetes in Finland.

Professor Knip referred to the development of autoantibodies. These autoantibodies are mainly ICA (islet-cell autoantibodies), IAA (insulin autoantibodies), GADA (glutamic acid decarboxylase autoantibodies), IA-2A (insulinoma-2-associated autoantibodies) and ZnT8A (zinc transporter 8 antibodies). They can appear during the first period of life, as early as 3 to 6 first months of life and they develop sequentially. Testing positive to two or more autoantibodies is associated with 80% of probability to progress to overt disease within the following 15 years.

He also discussed the role of some pathogens in the development of diabetes, particularly enteroviruses (mainly coxsackie B1 with susceptibility and B3 and B6 with protection). CBV1 is associated with increased risk for seroconversion (autoantibody positivity). He said that the highest risk lies in the window of 6 months before seroconversion.

Glycated haemoglobin (HbA1c) is also a marker of progression and predictor of clinical disease and increases before overt disease.

Professor Knip also spoke about lipidome showing that progressors to overt disease had decreased phospholipids compared to non-progressors. Therefore decreased specific phospholipid concentration predicts rapid progression to overt disease. He spoke of other predictive markers and/or biomarkers such as proteomics, transcriptomics (supporting the role of enteroviruses as triggers of beta cell autoimmunity), and proteomics. Nevertheless, he stated that there is a need for further studies and appropriate integration of the great amount of -omics data that will be generated.

Finally, Professor Knip referred to the relation of autoantibodies and the gut microbiome. He pointed out that there is a decrease in the diversity of intestinal flora after seroconversion to antibodies associated with progression to symptomatic disease. He set some open questions that need further investigation:

-Is there a possibility to modify the intestinal flora? The role of intestinal microbiome in the development of the disease needs to be further elucidated.

-Prospective studies are needed.

-Maternal effects on type 1 diabetes need to be further investigated.

-Addressing heterogeneity of T1D.

- **Dr Raphael Scharfmann**

Dr Scharfmann spoke about new therapeutic strategies targeting beta cells in type 1 diabetes in human. He admitted that we have a great knowledge about beta cells in mice: residual beta cell mass and differentiation, beta cell protection, beta cell regeneration, different rodent beta cell lines and mice models, efficient islet preparations etc. However, similar knowledge is lacking about human beta cells due to the scarce availability of these cells. Major supplies come from islets from cadaveric donors that constitute an excellent source but limited in quantity, purity and reproducibility; beta cells from hESC-iPSC are being developed for the last fifteen years but the final goal has not been reached yet. Human beta cell lines are also suitable.

A number of human beta cell sources have been published in the scientific literature. Dr Scharfmann highlighted that his group in INSERM[16] and CNRS[17] developed their own protocol and created the spin-off ENDOCELLS[18] to produce human beta cell lines.

They developed a genetically engineered human pancreatic beta cell line secreting glucose-inducible insulin. The first generation was delivered in 2011 and the second generation in 2014. They work in close collaboration with IMI and Sanofi-Aventis within the IMIDIA programme and other biotech and pharma companies. Currently they are providers of their beta cell line for more than 60 laboratories across the world.

At present Dr Scharfmann's group is aiming at reproducing human beta cell destruction. These investigations will be used to discover molecules to prevent beta cell demise.

- **Professor Decio L. Eizirik**

Professor Eizirik presented findings (some of them from the projects NAIMIT and BETABAT) highlighting that the pathogenesis of type 1 diabetes is not yet fully understood. He emphasised that further basic research is needed. He presented novel data indicating the "dialog" between beta cells and the innate/adaptive immune system in the triggering of diabetes. Pancreatic beta cell apoptosis as well as local inflammatory responses (chemokines and cytokines) are involved. Over 80% of type 1 diabetes candidate genes are expressed at the beta level, besides their role at the immune system level. These candidate genes are involved in signaling recognition of viral infection and triggering of cellular defenses against pathogens. Pro-inflammatory cytokines trigger a similar beta cell autonomous immune response. His team studied the response of islet cells to viral stimuli and they found that there are important differences between pancreatic beta and alpha cells. Whereas alpha cells mainly survived a CVB5 challenge and neutralised the virus, CVB5 induced apoptosis in beta cells. These different cellular responses may explain why beta cells, but not alpha cells, are destroyed in type 1 diabetes. Therefore, the early innate immune response may play an important role in the subsequent development of autoimmunity and the disease, but we do not fully understand either the pathogenesis or the mechanisms of disease progression.

Conclusions

The session ended with some conclusions made by the moderator Professor Miriam Cnop:

- There has been a substantial increase in the incidence of type 1 diabetes in which changes in environmental factors might have had a role;

8. We have a significant body of knowledge about diabetes in mice but this knowledge is not yet sufficient in humans to enable targeted therapeutic interventions;
9. Transcription factors' networks in response to viral infection have helped identify the role of innate and autoimmune response in the destruction of beta cells.

3.2.2. Session 2- Prevention and Diagnostics-turning progress into every-day solutions

- **Professor Peter Rossing**

Professor Rossing spoke about diabetes complications particularly diabetes kidney disease. He presented his findings (some of them from research on FP7 projects SYSKID[19] and PRIORITY). Diabetes progression causes micro and macrovascular complications overtime. In the Helsinky study complications due to type 2 diabetes are associated to a 24-fold excess cost compared to diabetes without complications. This excess cost is 12-fold for type 1 diabetes. Professor Rossing

[16] INSERM, Institut National de la Santé et de la Recherche Médicale, http://www.inserm.fr/

[17] CNRS, Centre National de la Recherche Scientifique, http://www.cnrs.fr/index.php

[18] ENDOCELLS, http://www.endocells.com/

[19] SYSKID, Systems Biology towards Novel Chronic Kidney Disease Diagnosis and Treatment, http://www.syskid.eu/

spoke about prognostic and predictive biomarkers in chronic kidney disease (CKD). He explained that currently the detection of microalbuminuria is used in clinic as a surrogate marker of renal damage. Nevertheless, it is not approved by the regulatory agencies (FDA). Glomerular filtration rate (GFR) is another marker utilised in clinical practice. These two markers are included in updated CKD guidelines and correlate with renal and cardiovascular prognosis. They are relatively cheap and allow for therapeutic interventions that improve outcomes. He emphasised though that these markers have some flaws. Not all patients with albuminuria progress to end-stage renal disease and some patients without albuminuria progress to CKD. Some studies have unveiled that high uric acid might be a risk factor for renal disease in type 1 diabetes. Dr Rossing referred to the PERL[20] study in which uric acid is inhibited and GFR is monitored for 3 years to detect if the intervention confers protection against renal disease.

Therefore a shift in the paradigm is needed from these biomarkers to personalised treatments. New approaches such as the hypothesis driven search, the capillary electrophoresis-mass spectrometry (CE-MS) technique and the applications of system biology (SYSKID) have contributed to the discovery of biomarkers for CKD. However, the road to the final implementation of biomarkers into clinical practice is a long one (validation, evaluation, reimbursement) and can take over 14 years. Professor Rossing stated that studies for new markers (-omics) are needed. These can encompass clinical trials for high-risk profiles but also observational studies in low-risk profiles. There is also a need to develop appropriate means for -omics data integration and to better understand their best use. To conclude he said that diabetic nephropathy is a major problem and that new treatment modalities are needed.

- **Professor Helen Colhoun**

Professor Colhoun presented results from her research in IMI-funded SUMMIT and other projects. In her studies she found a major loss of life expectancy due to diabetes complications, in particular cardiovascular diseases. Moreover, there are differences between men and women which may pose health inequalities. The risk of cardiovascular disease increases sharply with GFR decrease. Even if the renal function is conserved in diabetic patients, there is still risk for cardiovascular disease. She highlighted that in the SUMMIT project, an important number of markers showed association to progression of CKD. However, she asked how useful these biomarkers were and in comparison to what clinical covariates. She emphasised the role of electronic medical record systems as a wealth of knowledge and the need to better exploit them for the definition of predictive models. She stated that clinical covariates are very useful and relatively cheap to obtain and contribute to the usefulness of biomarkers.

Professor Colhoun drew attention to the fact that type 1 diabetes cohorts are scarce and therefore validation of biomarkers in replication cohorts are a major challenge. Another important issue is the decision between the use of single or several platforms for detection of biomarkers. She called for the evaluation of biomarkers in multiplatform collaborative studies.

She showcased the role of the Scottish Diabetes Research Network T1 Diabetes Bioresource[21] (SDRNT1 BIO). It includes data and samples from a Scottish cohort of 6152 adults with type 1 diabetes. Professor Colhoun said that there is a need for more investment in creating sample banks and that industry (not just academia) needs to ensure that clinical trial sample banks are made available too. In the Scottish cohort, samples are endowed of a unique healthcare identifier linked to healthcare data. She stated that there is a need for better predictive models on cardiovascular disease in type 1 diabetes.

Concerning the genetic studies her team has identified kidney-related candidate genes that will be validated with exome chip data and the support of JDRF. DKD GWAS, kidney phenotypes, common and rare variants have been covered.

To conclude she pointed to the need of investment to prevent complications, optimisation of prediction using clinical data, -omics studies that are robust and reputable, larger sample sizes and the need of large well phenotyped representative cohorts which constitutes a major challenge.

- **Professor Åke Lernmark**

Professor Lernmark spoke about staging type 1 diabetes into primary, secondary prevention or clinical diagnosis (intervention). He presented the TEDDY project that has studied 420.000 newborns of which 21.000 have resulted eligible for the protocol. For primary prevention, the

[20]PERL study, Preventing Early Renal Loss in Diabetes, http://www.perl-study.org/

[21]SDRNT1 BIO, http://www.diabetes-healthnet.ac.uk/Default.aspx?pageid=413

genetic susceptibility, the presence of islet autoantibodies and the progression to clinical diabetes is being studied in a cohort of 8.676 individuals. Barely 10% of newly diagnosed children have a parent with the disease. Therefore there might be other factors with major effect on the development of the disease.

He said that the first autoantibody appears within the first 1-2 years of life. There is an association between different genetic HLA variants and age of appearance of autoantibodies. In DQ8/8, IAA appears first. In DQ2/2, GADA dominates first. Therefore, he emphasised that diabetes is not associated with HLA but it is the appearance of autoantibodies that correlates with HLA.

Preliminary results in the TEDDY study were that febrile respiratory infection may precede the appearance of the first islet autoantibody. The study children that developed autoantibodies have had a febrile respiratory infection in the preceding three months and thus this may be the trigger for the disease.

The project studied gut microbiome and they detected an increased bacterial diversity in stool preceding the appearance of the first islet autoantibody but a decreased diversity at the time of clinical diagnosis of diabetes. Dr Lernmark argued that possible solutions for primary prevention could be to vaccinate against the trigger infection and to induce immunological tolerance. He drew attention to some studies in high risk infants with oral insulin that have resulted in immune response without hypoglycaemia. This treatment could prevent progression to overt disease.

The TEDDY study revealed that the higher the level of islet autoimmunity initially, the more rapid progression to open disease.

As regards secondary prevention, Professor Lernmark spoke of different clinical trials with different administration routes of insulin (nasal, oral) and other compounds, and gluten free diet trials. Some of those studies have failed.

TEDDY has also studied the prevalence of ketoacidosis (DKA) in type 1 diabetes children. Most likely due to the early diagnosis, intervention and close monitoring, the study children showed lower DKA rates compared to other similar studies.

To round off, Professor Lernmark emphasised that disentangling the aetiology (autoimmunity) of type 1 diabetes is an opportunity for primary prevention as well as deepening into the pathogenesis. He invited to perform early screening for islet autoantibodies to prevent DKA and to increase type 1 diabetes awareness.

Conclusions

The moderator of this session, Dr Magda Gunn wrapped up with the following conclusions:

10. It is important to find reliable biomarkers to diagnose, prevent and predict type 1 diabetes complications;
11. The use of -omics is relevant but also registries and observational data (cohorts, longitudinal studies) are needed;
12. In type 1 diabetes patients it is necessary to look at the autoimmunity for prevention and treatment.

3.2.3. Session 3- Working together for a better treatment and cure

- **Professor Ole Dragsbæk Madsen**

Professor Madsen presented a cell based therapy for type 1 diabetes. He made reference to the encapsulation/oxygenation technology as a vehicle for islet transplantation. He spoke of the proof of concept study (Shapiro et al, 2000) in 7 severe type 1 diabetes patients that received islet transplantation. This cell therapy restored euglycaemia in those patients. The Edmond protocol, a 5-year follow-up study of islet transplantation in patients with severe type 1 diabetes, showed that in 7.5% of patients glucose stability persisted presenting no hypoglycaemias and more than 80% produced C Peptide at the end of the study. Some of those patients are still benefiting from the intervention almost 15 years later since they do not need insulin. Professor Madsen referred to the state of art as regards stem cells derived from insulin-producing human beta cells: lines from pancreatic progenitors, mature beta cells derived in vitro from human pluripotent stem cells and

human embryonic stem cells. Dr Melton and his team have recently succeeded in curing type 1 diabetes in mice with mature in vitro beta cells. However, we seem to be far away from the commercialisation of these cells as stem cells do not have FDA's approval yet and their efficacy in humans needs to be proven.

Professor Madsen emphasised the role of oxygen in the regulation of functional beta cell mass. In vivo, the rate of glucose burning dictates the rate of insulin production. He stated that the higher the blood glucose, the higher the O_2 needed in the islets. In his opinion encapsulation strategies must ensure O_2 availability for success. Hypoxia (hypoglycaemia) can be deleterious for beta cell function and survival.

During his presentation the speaker referred to the FP7-funded project BIOSID that is currently working with encapsulation for the delivery of beta cell therapy.

He also mentioned the human beta cell lines developed by ENDOCELLS in IMIDIA (IMI1) as a very promising cell line for this purpose.

To wind up, Professor Madsen highlighted that for the application of beta cell therapy, a suitable device is required with the subsequent challenges: oxygenation, vascularisation and exchange of nutrients, insulin detection, immune-isolation and compliance with regulatory requirements. Such a device could also support cell based therapy using other cells.

- **Professor Hans de Vries**

The speaker presented the results of one of the two final trials of the AP@home project (FP7), a trial to assess the efficiency of an artificial pancreas in 35 patients. The system consists of a glucose sensor, an algorithm for integration of data and release of insulin through a pump. The Closed Loop concept has to deal with a delay of up to 90 minutes from start of measuring a change in glucose to subcutaneously injected insulin taking full effect. To do so the system uses mathematical modelling. During the trial a combination of closed loop (at home from approximately 19:00 to 8:00 hours) and open loop treatment for the rest of the day when away from home was applied. The speaker justified this approach arguing that activities with high risk for glucose perturbations such as exercise and when driving a car are performed when not at home, and that at home is therefore a relatively safe environment to first implement this treatment mode. The meal time is also challenging for the closed loop, glucose being difficult to control. Professor de Vries stated that endpoint results are promising with better control of glycaemia (reduction of hyper- and hypoglycaemia), reduced HbA1c and less need for insulin. He said that some groups, such as AP@home deliver insulin only, whereas other groups such as PCDIAB also deliver glucagon.

Closing the presentation the speaker concluded that there is need for individualised, self-learning algorithms according to the personalised medicine concept, better control of exercise and meals and transition from tele-monitoring to automated detection and adjustment of algorithm settings.

In conclusion, despite the need for further research, the first generation of the artificial pancreas is moving to the market.

- **Professor Mark Peakman**

Professor Peakman presented the trends in immune-based therapies for intervention and prevention, the rationale, the proof of concept and the opportunities. The first treatment was with cyclosporine A in 1987. Since 2005 the science focuses on B lymphocyte depletion, whilst the current trend is to introduce more results from –omics and Next-Generation Sequencing (NGS). He emphasised that at present the immune based therapies are technology-driven and get the most interesting results from cohort studies. The speaker presented the Type 1 Diabetes Trialnet study that involves B lymphocyte depletion. Type 1 Diabetes TrialNet is an international network of researchers who are exploring ways to prevent, delay and reverse the progression of type 1 diabetes. B lymphocyte depletion is regarded as a safe intervention but there are some concerns as regards its maintenance. Another interesting approach is the Co-Stim blockade with excellent safety profile. He discussed some challenges: C-peptide decline returns post-treatment endpoints; is C-peptide retention a surrogate for reduced risk of complications? There is a need for new clinically relevant endpoints such as reduced hypoglycaemia as well as new stratification tools for biomarker discovery. He made reference to ways to reduce trial/size complexity such as addressing heterogeneity and endotypes, and personalised medicine. A good example for that is the Clustering Model of Arif et al, (Diabetes 2014) which underpinned the concept of type 1 diabetes heterogeneity.

As regards the INNODIA programme (IMI2), he anticipated that it will apply a systems biology approach. Interesting is the beta cell, immunome, genome, proteome and metabolo-/lipid-ome biomarker stratification. The speaker argued that combination therapies are promising since many

biologicals have limitations. The heterogeneity of the disease offers opportunities for personalised medicine. There is a need to have cohort data and to work on efficient trial design reducing length and complexity using biomarkers with clinically relevant endpoints. Combinations are challenging, have future and seem to have a high potential.

3.2.4. Session 4- Addressing the framework: regulatory aspects, national policy and data-sharing

- **Dr Paolo Tomasi**

Dr Tomasi introduced the regulatory frame for complex therapeutic solutions in the European Medicines Agency (EMA). EMA's Committee for Advanced Therapies evaluates the quality, safety and efficacy of advanced-therapy medicinal products (ATMPs). EMA, with its Committees including the Committee for Medicinal Products for Human Use (CHMP), provides scientific advice, issues guidelines and interacts with stakeholders. Innovative therapies as combined advanced therapy-device, tissue-engineered medicines, and others apply to type 1 diabetes. Particularly Dr Tomasi highlighted the role played by the Innovative Therapies Task Force (ITF), a multidisciplinary group that ensures a preparatory dialog and orientation across the Agency on innovative methods and medicines. Applicants can also seek an Orphan designation. At this point, Dr Tomasi referred to a few differences between the Food and Drug Administration agency (FDA) in the USA, and EMA as regards Orphan designation. FDA has already designated a number of orphan medicinal products for the condition 'treatment of recent-onset type 1 diabetes mellitus' whereas EMA has not designated any and this condition is not likely to be accepted by EMA mainly due to differences in legislation and guidelines.

Dr Tomasi discussed about the guidelines that EMA developed in 2012 where among other aspects of type 1 and 2 diabetes they refer to specifications for studies aiming at preservation of beta cells in type 1 diabetes. Dr Tomasi also spoke about the process of qualification of biomarkers.

Finally, Dr Tomasi summarised the paediatric regulatory aspects of treatments for type 1 diabetes and that applications for Paediatric Investigation Plans (PIP) must be sent with sufficient advance, prior to start studies in children, as agreeing a PIP with the Paediatric Committee (PDCO) takes on average 8-12 months. He stated the PIPs are not irreversible and can be modified later on after adoption of the EMA Decision.

In conclusion, Dr Tomasi's main message to future applicants was to seek EMA's advice early and often through any of its multiple bodies.

- **Professor Nick Wareham**

Professor Wareham illustrated the challenges of data sharing through three different classical models and a novel approach. The first model assembles data in a consortium and participating cohorts supply data to be analysed by a central analysis team. This model can create transactional burdens as it needs to be governed by data transfer agreements, which can be complex as the number of partners increases. The model is not particularly engaging for participating cohorts and the intended use of data can be difficult to control. In the second approach, responsibility for analyses is left at the cohort level, each of which has cohort-specific analytical teams who contribute summary results to the central analysis team. This model is burdensome for the cohorts and can present difficulties for data harmonisation. It has worked very well for genetic analyses, but this form of meta-analysis of results can be limited for other questions. Professor Wareham presented a third approach based on central data deposition in which cohorts provide data to a central repository which can then provide data to approved researchers. This model poses governance, ethical and legal challenges and may not work well with complex forms of data or in collaborations that include cohorts from multiple countries.

Finally Professor Wareham referred to the approach being promoted by the FP7-funded InterConnect[22] project. InterConnect aims to optimise the use of existing data to enable cross-cohort analyses. This project includes three key elements; a study registry to enable data discovery, a platform for data harmonisation and support for federated meta-analysis. In this approach the data stays within the governance structure of the source cohort and analyses are

[22] InterConnect, Global initiative on gene-environment interaction on diabetes/obesity risk, http://www.interconnect-diabetes.eu/

conducted using a federated approach (Datashield) that takes the analysis to the data rather than the data to the analysis.

- **Professor Soffia Guđbjörnsdóttir**

Professor Guđbjörnsdóttir, its current director, presented the Swedish National Diabetes Register[23]. It was created in 1996 and Dr Guđbjörnsdóttir stated that its main aim was to improve diabetes care in Sweden. It is a quality registry, an internet-based open system (all results are public), able to provide online feedback and real time statistics and reports. It contains data from almost 90% of all known patients with diabetes in Sweden and they are registered at least once a year. Dr Guđbjörnsdóttir emphasised that the patient profile consists of clinical characteristics, risk factor control, treatment and complications and it is linked to other external registries (Cancer Register, Causes of Death Register, Medical Birth Register, Education Register, etc). She drew attention to the continuous referral to the existing guidelines for the clinical management of diabetic patients. The registry has contributed to clinical improvement through measurement since the involved teams participate in the overall clinical process as well as in training for improvement. Dr Guđbjörnsdóttir emphasised that the registry has provided opportunities for large population-based studies. Some of these applications are the estimation of type 1 diabetes incidence rates in children and young adults, risk for heart failure in type 1 diabetes, excess mortality or the association between type 1 diabetes and cancer. Other very interesting findings are the impact of socioeconomic status on CVD (cardiovascular disease) and death in type 1 diabetes or how insulin pump seems to be protective from CVD death in type 1 diabetes (type 1 diabetes cohort of over 18.000 patients followed up to 7 years).

In the end, Dr Guđbjörnsdóttir acknowledged that ethical considerations were taken into account through the development of the project such as data ownership (it stays with the patient) and there is also concern about the financial sustainability of the project and the cost-benefit ratio of the set-up and maintenance of the system.

4. PARTICIPANTS' DISCUSSIONS

4.1. Session 1- Aethiology/Pathophysiology-state of play and perspectives

Connection between different –omics signatures
Would it be possible to look at the transcriptomics signature? In vitro models can be used and see how they interact with candidate genes and environmental cues. The idea is to enhance collaboration. The first step would be to compare mRNA with metabolomics and other signatures to obtain a global picture of both beta cells and immune cell responses.

The role of microbiome
Could we also consider 2015 as a year of microbiome? There is a need to look not only to intestinal microbiome but also to other microbiome systems in the body. Mechanisms involved in microbiome's impact need further study.

Maternity factors
Maternity factors such as diet can confer some risks to newborns in mothers with gestational diabetes, including increased adiposity and impaired glucose tolerance at childhood. Is there also a risk for developing type 1 diabetes in offspring born to gestational diabetic or obese mothers?
There are indeed some reports claiming such a risk and we shall have to begin to regard pregnancy as an important period, which may contribute to the children's risk for developing type 1 diabetes.

Beta cells response to viral challenges
Beta cells have limited capacity in their response to viral challenges maybe due to an advantageous adaptation from the evolutionary point of view. The absence of an intense response to virus might

[23] NDR, Swedish National Diabetes Register, https://www.ndr.nu/

constitute a more adaptive behaviour, but with the risk of enabling long term non-cytololitic infections that may lead to autoimmunity.

The role of metabolomics profile
Metabolomics profile can have a role in guiding secondary prevention therapy in the future. It is 'doable' but the main issue is to find good markers.

Different stress factors on beta cells
The whole expression of beta cell key gene networks differs depending of the stressor. The response varies according to the type of stressor, be it a virus, immune or metabolic stress, which may have an impact in the design of novel therapies to protect beta cells (in other words, it is unlikely that "one therapy will fit all").

The role of molecular imaging for beta cells
There is ongoing research to apply imaging for detection of beta cell function and mass. This is a major unmet need in the field, but the available techniques are not yet accurate enough to detect subtle differences in beta cell loss.

Differentiation in beta cells
Beta cells can differentiate in vitro. ENDOCELLS has a model and information about the number of genes involved in differentiation for their human beta cell line.

The role of the HLA complex
How much does the HLA complex relates to disease in type 1 diabetes? HLA is mostly related to developing autoimmunity or not. Overt disease and disease progression seem to be more related to non-HLA candidate gene families.
The alpha and beta cells experimental model presented correlates well with reality. Some viruses seem to display tropism for those cells. In studies of acute infection of human islets, both alpha and beta cells get infected after 8 hours. Beta cells are destroyed whereas alpha cells survive. This may explain beta cells demise in type 1 diabetes.

Early screening for type 1 diabetes
To identify individuals at risk, genetic screening at birth and then follow up by pancreatic beta cell autoantibodies could be used. Besides providing valuable research information, this is relevant for preventing ketoacidosis in children as the disease first onsets.

4.2. Session 2- Prevention and Diagnostics-turning progress into every-day solutions

Single drug approach
Diabetes is a very complex disease. However, why do we continue attempting to prevent it with single drug approaches? Clinical research on combination of drugs is needed.

Life expectancy
Life expectancy is increasing in the population at large, both in men and in women. Therefore it is expected that this trend translates into type 1 diabetes population.

Diabetes nephropathy
Is diabetes nephropathy considered a kidney microvascular disease or a generalised disease? In diabetes, co-appearance of complications affecting different organs suggests that it might be a generalised disease. Nevertheless, more combined studies and biopsies are needed before drawing conclusions.

Benefits of early diagnosis in type 1 diabetes
Are there additional benefits from an early diagnosis of the disease? Preparedness in those families facilitates a better management of the disease and improves outcomes. Follow-up studies show that the study cohort children starts with a higher C-Peptide and thus require less insulin from the beginning. C-Peptide decline occurs faster in the general population. Having well-educated parents at the time of the onset of the disease has led to a reduced number of ICU admissions, an earlier treatment of the disease, an increase on the life expectancy and decrease rates of nephropathy.

The role of islet autoantibodies (IA)
What are the implications of detecting IA for the progression to overt disease? If IA persist overtime the risk for progression to overt disease increases

Next steps
What are the next steps? Prospective validation across many cohorts is a clear objective since the whole profile of patients is also changing. In this sense, IMI and EFPIA[24] may contribute by making available samples and enhancing collaboration. Collaboration is crucial to validate, replicate and conduct prospective studies for biomarkers. Integration of -omics and establishing a collaborative platform including diagnostics will confer a wide range of perspectives.

Comorbidities and polymedication
Could anti-hypertensive therapy or other treatments mask biomarkers? In order to optimise thresholds the first need is to test associations. One possibility is to establish a risk score with peptides to avoid the bias of a single marker.

Genetic biomarkers
In nephropathy, is it worth it to continue investing on genetic biomarkers? Until the present the biggest efforts have been put into conventional phenotypes. There are many difficulties in finding a good predictor and we may need a different approach. A higher dimensional predictor is needed. Exploiting GWAS for predicting requires a different methodology. Novel discovery pathways of newer variants have not been exploited yet. There might be a way of optimising the process to obtain more intermediate biomarkers from genetic data.

The role of HLA and non-HLA genetic factors in disease progression
A major challenge is understanding the genetic factors that support disease progression that may be different from those linked to the risk of developing autoantibodies.

Marker of early immune response
A marker of early immune response is needed, maybe a non-age linked antibody such as an IgM response.

Triggers in type 1 diabetes
Professor Knip believes that there are two external driving factors: one favours the initiation of the disease and the other is related to the progression. However, he considers that we will talk about autoantibodies as biomarkers of progression to type 1 diabetes for a long period.

Impact of external factors on the aetiology of type 1 diabetes
Severe life events such as accidents, or emotional (divorce, stress) may be contributing factors although not the trigger. For instance, the role of vitamin D has been studied and there was no association. Environmental factors could also act as trigger or protective factors (i.e. seasonal distribution of type 1 diabetes).

---

[24] EFPIA, the European Federation of Pharmaceutical Industries and Associations, http://www.efpia.eu/

Impact of geographical distribution of HLA
Geographical distribution of HLA throughout Europe varies. Does this geographical distribution have an impact in the onset of the disease? A number of studies addressed the issue of genetic background for type 1 diabetes in migrant families in Sweden. These studies concluded that children born to immigrant parents in Sweden did not have an excess risk to suffer type 1 diabetes whereas the risk was correlated to Swedish genetic background.

4.3.Session 3- Working together for a better treatment and cure

Collaboration
How can we collaborate on bringing the different resources together successfully? By focusing on big questions, facilitating collaborative interactions, for instance the artificial pancreas projects benefit from collaboration with pharmaceutical companies.

Smart phones
Have smart phones been used in artificial pancreas for monitoring exercise? They are currently working on it.

Patient's input in artificial pancreas
How physiological would it be that the patient activates the infusion of insulin before starting the meal? This question referred to the difficulties to function as a close loop during the whole day. Some discussions about an autonomous functioning of the artificial pancreas followed.

Combination therapies
What would be the preferred combination therapy? That would depend on the patient's phenotype. More studies are needed in this field. As regards encapsulation, a crucial step is the correct supply of O_2 in the encapsulation device. The projects BIOSID and BetaO_2[25] are two projects currently developing an encapsulation device, although daily refilling of O_2 seems to be a limiting factor for the second. Preliminary results showed certain survival of beta cells and blood glucose regulation.
Combination therapy appears to provide the highest potential for maintaining insulin secretion, but which kind of studies should be used? There is need for both preclinical studies and for repurposing of existing drugs for combination therapy. However, there have not been robust opportunities so far. Currently only one company seems to be working on a combination therapy.

It is fairly safe to claim that in a short time researchers will have validated stem cells either from embryonic or IPCs cells. There are also ongoing studies to prevent immune cells to kill beta cells, and these approaches will need to be combined to lead to clinical success.

Registries
Why is Europe lagging behind USA as regards diabetes registries? Things are moving forwards in Europe. For instance, INNODIA (IMI2) is dealing with early diabetes and prediabetes and working on developing registries. However, a major drawback is that not all EU countries have electronic medical records. The development of registries is 'doable' but requires important investments. Registries are very useful to study heterogeneity.

Other autoimmune diseases
Are there any plans to address concomitant to type 1 diabetes other autoimmune diseases, i.e. celiac disease, rheumatoid arthritis, multiple sclerosis etc ? Yes, there is a plan, but both the tissue collections and the processes to be studied must be clearly defined.

Immunosuppression
In encapsulation, how to avoid the destruction of insulin-producing cells by molecules (e.g. cytokines) that enter the capsule due to their small size? Is there an ethical threshold for when to

[25] BetaO_2, http://beta-o2.com/type-1-diabetes/#

introduce immunosupressors? Apart from ethical issues, the earlier the better, always assessing the risk-benefit.

4.4. Session 4- Addressing the framework: regulatory aspects, national policy and data-sharing

Funding and maintaining registries
Funding to create and maintain registries is needed. A debate started on the need of registries in Europe and how the European Commission could support these registries. Karim Berkouk clarified that the European Commission's mandate in the area of research is to support research projects up to their completion. Due to the multiannual budgetary planning of the European Commission and the competitive selection for financial support in Framework Programmes for R & I, scenarios for ensuring the financial sustainability of registries should be explored beyond the only support from the Commission.
Moreover, approximately only 5-10% of European research funds are managed by the European institutions whilst 90-95% remains with the Member States. In this sense, Dr Berkouk explained the catalyst role of the European Union in initiating research projects but further maintenance and development corresponds to Member States.

Prof Guđbjörnsdóttir was also asked if they had performed cost-utility studies to demonstrate the benefits of the Swedish registry.

Legal restrictions to registries
Quality registries are allowed in Denmark. However they cannot be used to guide individual treatment, i.e. they can be used to generate statistics like means or the deviation in one clinic from other clinics on an average level, but cannot be used for example, to identify subjects that need specific treatment.
Does the same occur in Sweden?
The situation is similar in Sweden. Treatment decisions cannot be made based on an online quality registry.

Data ownership
Professor Wareham was asked on data ownership in his model. He said that data could be easily downloaded locally since data stay within the local governance structure.

Interrelationships between EMA and other regulatory agencies
Dr Tomasi explained that EMA keeps regular contacts with other regulatory agencies such as FDA, and the Canadian or the Japanese regulatory agencies, considering a common approach to certain issues. Nevertheless, the conclusions of these contacts need to be made public and EMA is working on new means for disseminating them.

Biobanking
Prof Guđbjörnsdóttir was asked whether the Swedish registry collected samples. She affirmed that at the moment there is no biobank at the registry. The registry encountered certain difficulties in its inception and thus developed slowly at the beginning. Nevertheless, thanks to the support of some actors such as nurses in charge of diabetes care and the Swedish government, it started to develop. Online feedback was very well accepted. Therefore, she envisions that biobanking will happen although it may take some time.

5. CONCLUSIONS, RECOMMENDATIONS AND NEXT STEPS

- **Dr Richard Insel**

Dr Insel thanked the speakers and audience for the very interesting discussions held and rounded off by emphasising a number of scientific developments and prospects. He put high on the agenda the need for increasing our understanding of pathogenesis and heterogeneity of type 1 diabetes as critically important for the future of precision, predictive medicine. Correlates of this are to develop improved phenotyping, better models of human disease, and discovery and validation of prognostic and predictive biomarkers to stratify clinical trial subjects and optimize the design of type 1 diabetes clinical trials. As a component of improved phenotyping, it will be important to conduct small, mechanistic trials that perturb pathways. Systems based approaches with large databases and biorepositories need to be developed. Dr Insel emphasized the importance of investigating transgenerational and epigenetic effects on type 1 diabetes and the capacity to dissect defects of immunoregulation through *immunomic*s. He also championed a major effort of FP7 and Horizon 2020 to elucidate the role of microbiome in pathogenesis of disease in general and specifically in type 1 diabetes.

As regards treatment, he addressed the potential of the artificial pancreas, population-based screening for detecting risk of disease and efforts to prevent symptomatic disease, and the future approaches of replacing functional beta cell mass with stem-cell derived islets.

Dr Insel confirmed that JDRF would continue investing in Europe and supporting European research and welcomed effective collaboration between academia, private sectors and funders with the ultimate goal of making progress at the clinical level to improve the life of type 1 diabetes patients and to prevent and cure the disease.

- **Dr Karim Berkouk**

Dr Berkouk summarised the main topics discussed throughout the workshop and identified needs and perspectives for future research. He listed further studies in gestational diabetes, deepening in the role of microbiome, integration of –omics, robust statistical analysis and validation of new or existing biomarkers, and meaningfulness and usefulness of biomarkers for prevention and progression, as important avenues for research. Concerning research methodology, Dr Berkouk highlighted the relevant role of well characterised cohorts and the proven need for better phenotypes. He also pointed at the necessity for re-designing clinical trials enforcing stratification of patients to target low or high risk populations, addressing early phases of the disease.

He endorsed the open data and data sharing policies and emphasised the value of registries, biobanks and observational data.

To conclude, Dr Berkouk called researchers for betterment of regulatory processes of new therapies, particularly advanced therapies, for a better and faster delivery of new treatments to patients and to make use of existing resources within EMA.

6. ANNEX 1- AGENDA

European Commission – JDRF workshop
'Type 1 diabetes research: taking stock and maximising collaboration'
23 June 2015
DG RTD, Champ de Mars 21, 1050 Brussels

08:00 – 08:30	Registration and Reception
08:30 – 08:50	Opening remarks **Ruxandra Draghia-Akli, Director, Directorate Health, European Commission** **Richard Insel, CSO, JDRF**
08:50 – 09:35	**Aetiology/Pathophysiology – state of play and perspectives** *Moderator*: Miriam Cnop (ULB, Belgium) Mikael Knip (Helsinki University Hospital, Finland) Raphael Scharfmann (INSERM, France) Decio Eizirik (ULB, Belgium)
09:35 – 10:20	Q&A
10:20 – 10:35	Coffee Break
10:35 – 11:35	**Prevention and Diagnostics – turning progress into every-day solutions** *Moderator*: Magda Gunn (Innovative Medicines Initiative) Peter Rossing (Steno Diabetes Center & Aarhus University, Denmark) Helen Colhoun (University of Dundee, UK) Åke Lernmark (Lund University, Sweden)
11:35 – 12:30	Q&A
12:30 – 13:30	Lunch
13:30 – 14:15	**Working together for a better treatment and cure** *Moderator*: Philip Just Larsen (Sanofi Aventis, Germany) Ole Dragsbæk Madsen (Novo Nordisk & University of Copenhagen, Denmark) Hans de Vries (University of Amsterdam, The Netherlands) Mark Peakman (King's College, UK)
14:15 – 15:00	Q&A
15:00 – 15:15	Coffee Break
15:15 – 15:45	**Addressing the framework: regulatory aspects, national policy and data-sharing** *Moderator*: Karim Berkouk (DG Research & Innovation) Paolo Tomasi (European Medicines Agency) Nick Wareham (University of Cambridge, UK) Soffia Guđbjörnsdóttir (Gothenburg University, Sweden)
15:45 – 16:15	Q&A
16:15 – 17:00	Closing remarks & conclusions

7. ANNEX 2- LIST OF PARTICIPANTS

Name	Organisation	Country
Speakers		
Knip, Mikael	Helsinki University Hospital	Finland
Scharfmann, Raphael	INSERM	France
Eizirik, Decio L.	Center for Diabetes Research, Université Libre de	Belgium
Rossing, Peter	Steno Diabetes Center; Aarhus University	Denmark
Colhoun, Helen	University of Dundee	United
Lernmark, Åke	Lund University	Sweden
Madsen, Ole Dragsbaek	Novo Nordisk Camp; University of Copenhaguen	Denmark
De Vries, Hans	University of Amsterdam	Netherlands
Peakman, Mark	King's College	United
Tomasi, Paolo	EMA	United
Wareham, Nick	University of Cambridge	United
Gudbjorndsdottir, Soffia	Gothenburg University	Sweden
Moderators		
Cnop, Miriam	Center for Diabetes Research, Université Libre de	Belgium
Gunn, Magda	Innovative Medicines Initiative	Belgium
Larsen, Philip Just	Sanofi Aventis	Germany
Berkouk, Karim	European Commission	Belgium
European Commission		
Draghia-Akli, Ruxandra	DG Research and Innovation	Belgium
Vidal-Ragout, Maria	DG Research and Innovation	Belgium
Lizaso, Miguel	DG Research and Innovation	Belgium
Navarro Torné, Dora	DG Research and Innovation	Belgium
Nieto, Pilar	DG Research and Innovation	Belgium
Juvenile Diabetes Research Foundation		
Insel, Richard	JDRF	USA
Dutta, Sanjoy	JDRF	USA
Arnaud, Olivier	JDRF	France

Name	Organisation	Country
Juvenile Diabetes Research Foundation		
McVicker, Clare	JDRF	United
McKeever, Conor	JDRF	United
Kristensen, Finn	JDRF	Denmark
van Lookeren Campagne,	JDRF	Netherlands
Gildor, Boaz	JDRF	Israel
Participants		
Bondia Company, Jorge	Universitat Politécnica de Valencia	Spain
Brozzi	Université Libre de Bruxelles (ULB)	Belgium
Cardozo, Alessandra	Université Libre de Bruxelles (ULB)	Belgium
Carey, Emma	Research Office	United
Castantildejo Gonzalez,	Instituto Biocruces - Hospital Cruces - Bilbao	Spain
Chockalingam,	Staffordshire University	United
Danne, Thomas	SWEET Project; BULT Diabetes Center for Children	Germany
de Beaufort, Carine	ISPAD	Luxembourg
Desoye, Gernot	Medical University of Graz	Austria
Gauthier, Benoit	Andalusian Center for Molecular Biology	Canada
Hills, Sarah	EURADIA	
Hyoty, Heikki	University of Tampere	Finland
Ilonen, Jorma	University of Turku	Finland
Keymeulen, Bart	UZ	Belgium
Maedler, Kathrin	University of Bremen	Germany
Martinez Garcia,	INCLIVA Health Research Institute Unit of Internal	Spain
Mougiakakou, Stavroula	University of Bern	Switzerland
Napolitano, Antonella	GlaxoSmithKline	
Oresic, Matej	Steno Diabetes Center Camp; H2020 Advisory Group	Denmark
Pieber Thomas Univ.-	Medical University of Graz	Austria
Piemonti, Lorenzo	Diabetes research Institute IRCCS San Raffaele	Italy
Ronfini, Pier Francesco	Progetto "Rete IRCCS/DI per	Italy
Schloot, Nanette	Lilly	Germany

Name	Organisation	Country
Participants		
Strollo, Rocky	University Campus Bio-Medico	Italy
Toppari, Jorma	Departments of Physiology and Paediatrics, University	Finland
van Eimeren , Michael	European Association for the Study of Diabetes	
Veijola, Riitta	Department of Paediatrics, University of Oulu	Finland
Walker, Lucy	University College London	United

How to obtain EU publications

Free publications:

- one copy:
  via EU Bookshop (http://bookshop.europa.eu);
- more than one copy or posters/maps:
  from the European Union's representations (http://ec.europa.eu/represent_en.htm);
  from the delegations in non-EU countries (http://eeas.europa.eu/delegations/index_en.htm);
  by contacting the Europe Direct service (http://europa.eu/europedirect/index_en.htm) or
  calling 00 800 6 7 8 9 10 11 (freephone number from anywhere in the EU) (*).

(*) The information given is free, as are most calls (though some operators, phone boxes or hotels may charge you).

Priced publications:

- via EU Bookshop (http://bookshop.europa.eu).

Diabetes is a chronic disease that constitutes a major cause of morbidity and mortality worldwide. Diabetes rates are alarmingly increasing both in developed and developing countries across the world. It poses a considerable burden to patients and healthcare systems.

The European Commission Directorate General for Research and Innovation (DG RTD) and the JDRF (formerly Juvenile Diabetes Research Foundation)[26] jointly organised a workshop on type 1 diabetes held in Brussels on 23 June 2015 with the ultimate goal of defining the state-of-art in the field, identifying gaps, and brainstorming about the possibilities offered by personalised medicine approaches in this area.

The presentations addressed the latest advances and challenges concerning type 1 diabetes. They were very interactive and were followed by vivid discussions reflecting the wide range of interests of the participants.

The speakers laid out that time frame for the next major advances in type 1 diabetes have never been so close for patient access (a matter of few years for closed loop artificial pancreas system, encapsulation, immunomodulation, etc) and that efforts and investment have to be pursued to reach the goals.

Studies and reports

[26]JDRF, Juvenile Diabetes Research Foundation, http://jdrf.org/

ISBN 978-92-79-52211-6

Publications Office