HumEn: European Union's Seventh Programme for research, technological development and demonstration under grant agreement No 602889.

HumEn Publishable Summary Report

Up-scaling human insulin-producing beta cell production by efficient differentiation and expansion of pancreatic endoderm progenitors

EU-funded research partnership. Aiming to develop insulin-producing beta cells from pluripotent stem cells, for diabetes.

Work programme topic address: HEALTH.2013.1.4-1. Controlling differentiation and proliferation in human stem cells intended for therapeutic use.

FP7-HEALTH-2013-INNOVATION-1
Grant Agreement Number 602889

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Contents:

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1.0 Executive summary: Project Coordinator Professor Henrik Semb

The specific scientific goal of HumEn was to overcome the scientific and technological hurdles in expanding human pluripotent stem cell (hPSC)-derived endodermal progenitors. The underlying rationale for this idea was that such development will contribute to safe up-scaled manufacturing of future ATMPs in stem cell-based therapy in type 1 diabetes (T1D).

Having combined basic mechanistic research with various small molecule screens and bioengineering, HumEn now provides the following new innovative knowledge and technologies:

- Innovative functionalised 3D culture systems, with engineered chemical surfaces and topologies for directed expansion of hPSC-derived human anterior definitive endoderm and pancreatic endoderm.
- New protocols that direct differentiation of expanded hESC-derived pancreatic endoderm into functional beta cells with improved yield.
- New protocols for the establishment of hPSC-derived endodermal stem/progenitor cell lines.
- Identification of new cell surface markers for endodermal progenitors, and protocols for purification of pancreatic progenitors and their differentiation into beta cells.
- Experience from initial steps to implement pancreatic progenitor purification and their differentiation into beta cells under GMP-compliant conditions.

Some of these discoveries have been patented and published, some are in the process of being published. New IP has served as the basis for a new spinout company focusing on hPSC-based cell therapy in T1D. Thus, HumEn has not only delivered on its goals, but also set the stage for future efforts to develop and exploit safe manufacturing of future hPSC-based ATMPs for treatment of T1D (and other diseases). Thereby, HumEn work has clearly contributed to improving the health of European citizens, increasing the competitiveness and boosting the European innovative capacity of Europe.

To disseminate knowledge gained by the consortium, HumEn organized several outreach events, created informational and instructional videos, teaching materials, and built capacity for knowledge sharing within the partnership and beyond. By engaging students and postdocs in these events, HumEn has trained many young scientists in the research, technologies, platforms and dissemination aspects of translating basic stem cell research into clinical applications.

The success of HumEn is the result of an outstanding constellation of partners, collaborators, and Scientific Advisory Board members who all were fully engaged. We set high standards for working together synergistically and planted the seed for future collaborations that carries excellent potential for translational output.

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List of Project Beneficiaries and Lead Partners

#	Institute	Country	Lead partners/s[1]
1	Copenhagen University	Denmark	Henrik Semb, Joshua Brickman, Anne Grapin-Botton Palle Serup
2	Helmholtz Zentrum Muenchen Deutsches Forschungszentrum für Gesundheit und Umwelt GMBH	Germany	Heiko Lickert
3	The university of Edinburgh	United Kingdom	Wendy Bickmore Mark Bradley
4	Institut National de la Santé et de la Recherche Médicale , INSERM	France	Raphael Scharfmann
5	Uppsala University	Sweden	Olle Korsgren
6	Max Planck gesellschaft zur Foerderung der Wissenschaften e.v	Germany	Didier Stainier
7	CYTOO SA	France	Pauline Poydenot
8	MATERIOMICS BV	The Netherlands	Bernke Papenburg
9	MILTENYI BIOTEC GMBH	Germany	Sebastian Knöbel

2.0 Project contents and main objectives

Diabetes is a common life-long condition and the number of children being diagnosed with type 1 diabetes (T1D) is increasing. The symptoms can be controlled but there is no cure. There are currently no proven treatments for diabetes using stem cells. However, if pancreatic beta cells could be made in the lab, it could solve the problem of obtaining the right number and quality of cells to replace a patient's missing or dysfunctional beta cells through islet transplantation.

Key facts on diabetes[2] [3]

- The number of people with diabetes has risen from 108 million in 1980 to 422 million in 2014.
- The global prevalence of diabetes among adults over 18 years of age has risen from 4.7% in 1980 to 8.5% in 2014 *(1)*.
- Diabetes prevalence has been rising more rapidly in middle- and low-income countries.
- Diabetes is a major cause of blindness, kidney failure, heart attacks, stroke and lower limb amputation.

[1] List of scientists and group leaders
[2] WHO November 2017, http://www.who.int/mediacentre/factsheets/fs312/en/
[3] See possible complications of T1D on NHS, https://www.nhs.uk/conditions/type-1-diabetes/complications/

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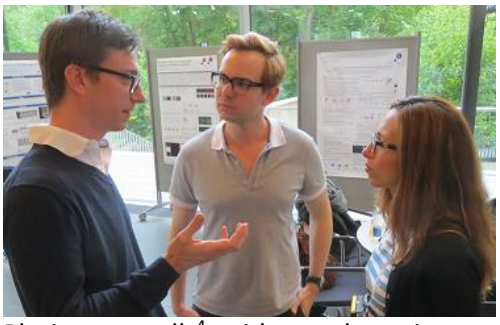
- In 2015, an estimated 1.6 million deaths were directly caused by diabetes. Another 2.2 million deaths were attributable to high blood glucose in 2012**.
- Almost half of all deaths attributable to high blood glucose occur before the age of 70 years. WHO projects that diabetes will be the seventh leading cause of death in 2030 *(1)*.
- Healthy diet, regular physical activity, maintaining a normal body weight and avoiding tobacco use are ways to prevent or delay the onset of type 2 diabetes.
- Diabetes can be treated and its consequences avoided or delayed with diet, physical activity, medication and regular screening and treatment for complications.

2.1 Making beta cells from pluripotent stem cells



Diseases related to the endodermal organs, such as the gastrointestinal tract, liver and pancreas are rapidly becoming some of the most significant health problems facing the 21st century European societies. To better treat diseases where cells are lost or damaged, such as in diabetes, cell-replacement/regenerative strategies have been proposed.

Pluripotent cells[4] - either embryonic stem cells or induced pluripotent stem cells - can make any cell type in the body and the scientific challenge is how to direct these to make fully functional beta cells. Such cells could replace the scarce amount of donor pancreatic islets of Langerhans[5] and in theory, offer an unlimited source for transplantation and ultimately the possibility of a curative treatment for T1D. Initially, it was only possible to differentiate human pluripotent stem cells into pancreatic progenitors, which are capable of maturing into all pancreatic cell types, including beta cells. The first phase 1/2 clinical trial using human embryonic stem cell-derived pancreatic progenitor cells, which are capable of maturing into insulin-producing beta cells upon engraftment in mice, for the treatment of T1D started in the US in July 2014. More recently, researchers have succeeded in producing cells from human pluripotent stem cells that share functional properties with normal beta cells both in vitro and in diabetic mice after being transplanted. These stem cell-derived beta cells provide the first expandable exogenous source of beta cells to test in T1D patients.

Facing the scarcity of donor material, the generation of replacement cells from pluripotent stem cells is a promising avenue. Production lines following the paths that embryonic cells naturally use during development provide molecular triggers and quality control criteria at each step of the process.

By understanding the molecular, epigenetic and three-dimensional (3D) niche factors that control the balance between differentiation and proliferation in embryonic progenitor, (stem cells) of the human endoderm lineage, the consortium was aiming to robustly generate functional beta cells from human pluripotent stem cells (hPSCs), and to make significant progress towards up-scaling the generation of insulin-producing beta cell for cell replacement therapy.

[4] https://en.wikiversity.org/wiki/Pluripotent_stem_cells
[5] https://www.britannica.com/science/islets-of-Langerhans

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2.2 Clinical prospective

Insulin deficiency, absolute or relative, underlies all forms of Diabetes and currently affects over 422 million[6] people worldwide. In Europe alone, the number of people with Diabetes is estimated to be 60 million, with an average prevalence of 8.1%. Treatment of Diabetes related complications currently consumes ~11% of the health care budgets. Currently, the only way to replace lost or dysfunctional beta cells is via transplantation of donor whole pancreas or islets of Langerhans. Replacing destroyed beta cells prevents not only the diabetes-causing hyperglycaemia but also the life threatening hypoglycaemia, caused by excessive insulin administration. Although these results provide proof-of-concept for cell-replacement therapy in T1D, too few patients could be offered this treatment due to lack of donors.

Therefore, in order to increase the number of patients who can receive cell-replacement therapy and thereby improve the life quality for the increasing population of diabetic patients, it is crucial to identify alternative sources of transplantable beta cells. Current approaches to generate functional pancreatic cell types from exogenous sources, such as human pluripotent stem cells (hPSCs), are promising, but have not reached the goal of efficient production of fully functional beta cells in vitro. The advantage of hPSCs as a source for beta cells is that, in theory, they offer an unlimited source of beta cells. Additional advantages of using hPSCs as a source for new beta cells are reduced cost and potentially less invasive surgery compared with whole pancreas and islet transplantations.

2.3 Objectives in relation to the EU Health Theme

HumEn aimed to contribute significantly to the translation of basic discoveries into clinical applications related to new cell-based therapies. The overall aim of HumEn was to identify, understand, and expand human endodermal progenitors as a consistent and renewable source of cells for transplantable pancreatic beta cells in future cell therapy in T1D.

The HumEn project aimed:

1. To create a critical mass of European scientists including research intensive SMEs and larger industries, working together towards the same overall goal thereby overcoming important bottlenecks in research and technology development within cell therapy.
2. To contribute to the strategic objective of developing the knowledge, tools, and resources needed to exploit the full potential of pluripotent stem cells and apply it to human health while at the same time stimulating industrial and economic activity.
3. To fulfil EU policies targeted at strengthening the competitiveness of the European economy, generating a knowledge-based economy, and solving major societal questions. Through its contribution to the development of new regenerative cell therapies, HumEn on the level of the individual citizen aimed to improve the future quality of life of people diagnosed with type 1 and type 2 diabetes.

[6] http://www.who.int/mediacentre/factsheets/fs312/en/

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2.4 Scientific objectives

The scientific objective of HumEn was to understand the balance between differentiation and proliferation in embryonic progenitor cells of the human endoderm lineage with the aim of achieving robust generation of functional beta cells from hPSCs (hESCs)/hiPSCs). Ultimately, these results were expected to be essential for up-scaled beta cell generation for cell-replacement therapy.

HumEn's starting point was to understand the cues that promote and halt differentiation at different points in the progression of hPSCs to beta cells as a means to develop "real" beta cells from hPSCs in vitro. The scientific objective was to exploit these cues as a means to identify and expand endodermal progenitors as a consistent and renewable source of cells for pancreatic beta cell differentiation. HumEn aimed to provide mechanistic insight into the signaling pathways and downstream targets that control the expansion of DE and PE and their differentiation into functional beta cells.

2.5 Technological objectives

The technological objectives of HumEn were to develop new, innovative tools including:

- New genetically modified hESC lines to track heterogeneity of lineage choices and cell cycle regulation that is widely available after completion of the project.
- Micropatterned extracellular matrix substrates for the guidance of stem cell lineages in 3D-like structures, compatible with High Content Imaging.
- Topologically patterned polymers and screening services to identify optimized surfaces for cell expansion and differentiation.
-

3.0 Overall project results

Specifically, the main findings of HumEn were:

- Isolation, characterization and expansion of hESC-derived anterior endodermal (ADE) progenitors with capacity to differentiate into pancreatic islet cells
- Improved understanding and exploiting self-renewal in ADE
- Molecularly define hESC-derived multipotent pancreatic endoderm (PE) progenitors capable of differentiation into beta cells
- Understanding the underlying mechanism for PE expansion as a means to control expansion of hESC-derived multipotent PE progenitors
- Understanding the underlying mechanism for PE differentiation into beta cells as a means to control differentiation of hESC-derived multipotent PE progenitors into beta cells
- Functional validation, in vitro and in vivo, of beta-cells generated from hESCs
- Increased awareness of the current position of stem cell biology and underpinning developmental biology research in Europe in a manner understandable to the general public.

While it is not practical to differentiate hPSCs directly to beta cells when needed, the creation of frozen stocks of purified and hPSC-derived, expanded endodermal progenitor cells (derived from hPSCs) that could readily be transformed to functional beta cells addresses several concerns in the manufacturing of beta cells from pluripotent stem cells. For example, such a strategy will improve safety, robustness, cost effectiveness, and distribution of multiple future medicinal products.

Based on new knowledge and IP generated a new spin-off company, PANCRYOS[7] , was launched in 2017. This new start-up company will develop next generation stem cell-derived allogeneic cell therapy medicinal products for future cell therapy in T1D.

HumEn delivered

- Knowledge, tools, and resources for exploiting the full potential of Pluripotent Stem Cells.
- Contribution to development of new regenerative cell therapies for Diabetes.
- A new, in depths understanding of the balance between differentiation and proliferation in embryonic progenitor cells of the human endodermal lineage.
- Mechanistic insight into the signalling pathways and downstream targets that control expansion of ADE and PE, and their differentiation into functional beta cells.
- Robust generation of functional beta cells from hESCs/hiPSCs.

3.1 Translation of research to the clinic

HumEn scientists (partner 1, Semb group) have identified a unique cell surface protein present on human pancreatic precursor cells providing for the first time a molecular handle to purify the cells whose fate is to become cells of the pancreas – including insulin producing cells. The work, outlined in a landmark study entitled 'Efficient generation of glucose-responsive beta cells from isolated GP2+ human pancreatic progenitors' has been published in Cell Reports[8]

The partners have engineered a streamlined and simplified differentiation process to generate insulin-producing cells for future treatment of type 1 diabetes patients. The process will enable cost-efficient manufacturing and exploits at its core an intermediate cell bank of purified pancreatic precursor cells.

Another stem cell study conducted by HumEn Partner 1, showed how we may increase the vital production of insulin in patients suffering from diabetes. It showed explicitly how, in a more efficient manner and at a lower cost, we can produce insulin-producing beta cells from human stem cells. This technique paves the way for more effective treatment of diabetes. The benefit of this method may also prove significant to the treatment of a series of other diseases[9].

[7] See more on section 4.1

[8] Ameri, Jacqueline, Rehannah Borup, Christy Prawiro, Cyrille Ramond, Karen A. Schachter, Raphael Scharfmann & Henrik Semb (2017). Efficient Generation of Glucose-Responsive Beta Cells from Isolated GP2+ Human Pancreatic Progenitors. Cell Reports, 19(1), 36-49, doi:10.1016/j.celrep.2017.03.032.

[9] Löf Öhlin, Zarah, Pia Nyeng, Matthew Bechard, Katja Hess, Eric Bankaitis, Thomas U. Greiner, Jacqueline Ameri, Christopher V. Wright & Henrik Semb (2017). Context-specific regulation of apicobasal polarity by EGFR orchestrates epithelial morphogenesis and cellular fate. Nature Cell Biology, doi: 10.1038/ncb3628.

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4.0 Potential impact and the main dissemination activities and exploitation of results

HumEn aimed to scale up and improve efficiency of beta cell generation, from accessible and storable endodermal intermediates.

By combining basic mechanistic research with various small molecule screens and bioengineering, HumEn provided the following new innovative knowledge and technologies:

- Innovative functionalised 3D, engineered chemical surface and topology culture systems for directed expansion of hPSC-derived human anterior definitive endoderm and pancreatic endoderm.
- New protocols for directed differentiation of expanded hESC-derived pancreatic endoderm into functional beta cells.
- New protocols for the establishment of hPSC-derived endodermal stem/progenitor cell lines.
- Identification of new cell surface markers for endodermal progenitors, and protocols for purification of pancreatic progenitors and their differentiation into beta cells.
- Experience from initial steps to implement pancreatic progenitor purification and their differentiation into beta cells under GMP-compliant conditions.

Creation of new knowledge by significantly contributed to solving key bottlenecks towards generating functional beta cells for future cell therapy in diabetes, as well as to creating more relevant beta cell models for in vitro drug discovery and target validation. In addition, HumEn went one step further, in its attempts to solve the problem of efficient beta cell generation, from accessible and storable endodermal intermediates. The differentiation of these cell lines to beta cells should be less complex (avoiding unnecessary early steps), less expensive and more efficient.

The progress made with HumEn has paved the way for future translational research consortia to develop innovative approaches and tackle the challenges of advanced therapy medicinal products

4.1 Spinoff Company

PANCRYOS – INSULIN NATURALLY

PANCRYOS[10] is a spinout company arising from the Novo Nordisk Foundation Center for Stem Cell Biology (DanStem) at the University of Copenhagen (P1) as a result of HumEn scientific and collaborative efforts. The company aims to develop a next generation stem cell derived allogeneic cell therapy (PanINSULA™) for type 1 diabetes. Based on novel IP, PANCRYOS will, for the first time, enable the definitive safety and large-scale manufacturing of insulin cells for therapeutic use. PANCRYOS is in the pre-clinical stage of development and is addressing cost effective scalability and manufacturing of the cell therapy early on to ensure successful commercialization.

[10] http://pancryos.com/

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PANCRYOS is founded by stem cell biologists Assistant Professor Jacqueline Ameri (HumEn associate, the Semb group, UCPH, P1) and Professor Henrik Semb, (HumEn coordinator), who have assembled a team of highly experienced business advisors, regulatory consultants, islet transplantation experts and cell manufacturing CMOs with the goal of testing a mature beta cell therapy in a phase 1/2 clinical trial. The company's goal is to provide a long-term vision of a brighter and healthier future for diabetes patients.

PANCRYOS 's technology is based on several publications, which credited HumEn, and patent[11] that lay the foundation for the company. Most recently, the founders published a ground-breaking study entitled: "Efficient generation of glucose-responsive beta cells from isolated GP2+ human pancreatic progenitors"[12]. The work is the culmination of several years of extensive effort, a few of them under the HumEn project. It describes the identification of GP2 as a specific marker of human pancreatic endoderm cells (PECs) and demonstrates that the isolated GP2+ PECs generate cultures enriched in glucose-responsive insulin-producing cells. By eliminating undifferentiated hESCs this work provides a new concept for safe manufacturing of endocrine cells for future diabetes cell therapy.

4.2 Dissemination activities

HumEn outreach activities were specifically focused on:

- Conveying the importance of complex 3D and multi-cellular environments to support stem cell differentiation, proliferation, and the link between them,
- Communicating clearly about the potential that HumEn holds with regards to future cell-replacement therapies for diabetes and other chronic diseases in the endodermal organs.

In the outreach and dissemination approach, HumEn aimed to increase awareness of current stem cell biology and underpinning developmental biology research by addressing the complexity of stem cell biology in a manner understandable to lay audience.

To achieve the broadest impact, HumEn engaged in common training, dissemination and outreach activities with like-minded consortia supported under HEALTH.2013.1.4-1. Controlling differentiation and proliferation in human stem cells intended for therapeutic use.

[11] ISOLATION OF BONA FIDE PANCREATIC PROGENITOR CELLS. Inventors: Jacqueline Ameri and Henrik Semb, Applicant: University of Copenhagen. WO/2016/170069

[12] The work, published in the journal Cell Reports in April 2017, https://www.sciencedirect.com/science/article/pii/S2211124717303649

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4.2.1 Detailed outreach objectives

- HumEn created 3D movies/animations, short films, illustrating the importance of the 3D architecture (niche) and cell based community effects on stem cell differentiation.

- The project established a website which was up and running shortly after the project launched, with the aim of dissemination of project results and findings at all levels

- HumEn contributed to development of Wikipedia resource on endoderm and hESC differentiation to endoderm. Wikipedia resources that accurately reflected current work in the field and particularly the work of the work of HumEn.

- The project Initiated several popular science presentations and events: production and collection of outreach material relevant for popular science presentations and events at secondary school, events arranged by special interest groups, as well as active participation in national, European and international Science Festivals.

- The project released press announcements related to the project and project results. All press releases, articles and interviews were posted at the HumEn website and on relevant, national communication channels.

- HumEn contributed to Hydra, European Summer School on Stem Cells and Regenerative Medicine: in collaboration with other stem cell, training dozens of junior scientists every year.

- HumEn was active with dissemination of scientific results to peers: peer-reviewed poster presentations, conference presentations, invited talks, and Publications at international, high-profile conferences and journals for basic and applied stem cell and developmental biology in Europe and internationally.

4.2.2 Development of outreach materials

1. Science Festivals: HumEn successfully applied to the **Edinburgh International Festival** to develop and deliver an 'Unfolding Organogenesis' at the festival on the 3rd and 4th April 2016. Collaborating with ThymiStem, Eurostemcell and the MRC-Centre for Regenerative Medicine, Edinburgh, 4 HumEn scientists and the science communicator connected with around 2,000 general public in The National Museum of Scotland through a range of stimulating and innovative activities aimed at revealing how

organs arise during development and how scientists use this knowledge in the lab. Co-developed with an origami artist, we made parallels with making origami organs from instructions and the work of scientists deciphering the instructions to make human organs. A time-lapse video of the event can be seen here: https://youtu.be/6RzFsucp-h8

Accounts of the event:

http://www.eurostemcell.org/story/unfolding-organogenesis

http://www.hum-en.eu/news-and-events/edinburgh-international-science-festival

Origami resources made available for stem cell scientists and science communicators to use on Eurostemcell:

http://www.eurostemcell.org/resource/unfolding-organogenesis

2. Science events with those affected by Diabetes:

The Young people arm of Diabetes UK Scotland visited HumEn Edinburgh labs (WB) for a day of discussion and tours in collaboration with the Institute for Genetics and Molecular Medicine and The Centre for Regenerative Medicine. A Swedish diabetes patient group visited Danstem, a first for the Centre for talks, activities and lab tours.

Accounts of the events:

http://www.hum-en.eu/news-and-events/sharing-our-work-diabetes-uk

http://danstem.ku.dk/news/coffee-meeting-with-scientists/

3. Schools and teachers: DanStem delivered second Stem cell day and develop plans for a stem cell module for a younger school age group

http://www.hum-en.eu/news-and-events/second-year-danstem-day

4. Short 3D film/animations produced

In collaboration with Revive consortium http://www.revive.fr/en as joint funders, two animations have been developed and launched: 1.Early Pancreas Development and the 2. The Birth of Beta Cells. A spliced version ' The Birth of beta Cells' with English voice over (Robert Illingworth P3) was launched on Stem Cell Awareness Day 12th October 2016 in collaboration with Eurostemcell for maximised exposure. The 3D computer animations were developed by a science working group (Anne Grapin-Botton, Henrik Semb (P1), Raphael Scharfmann (P4)), the Science Communicator (P3) and Nymus 3D http://www.nymus3d.nl .

5. Wikipedia resource

Creation of a Wikipedia resource that accurately reflects current work in the field and particularly the work of HumEn. A series of articles for Wikipedia on the endoderm, pancreas and hESC differentiation

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Collaborated with Wikimedia UK to develop a strategy and training for scientists in writing for Wikipedia. Created a Wikipedia page as a focal point for scientists: Eurostemcell Editathon . The page houses the 'Hit list', created through advice from Wikipedia on what contribution would create the widest impact.

Delivered two 'Wikithons' (a gathering of people with the aim of a collaborative Wikipedia edit) with a focus on the 'Hit list' at The University of Edinburgh and Danstem (UCPH) together with Wikipedians from Edinburgh and Copenhagen, providing the legacy of a support network. Collaborated with other EC Health consortia (ThymiStem) and Eurostemcell. The Eurostemcell Digital Communications Manager and translation Manager trained as 'Wikipedia Trainers' to provide continued support for the initiative begun by HumEn.

6. Summer school

Collaboration with other stem cell consortia in the financing and delivery of the European Summer School on Stem Cells and Regenerative Medicine in Hydra, Greece

Five HumEn participants at each Summer School

7. Building capacity through training for junior researchers on science communication

1. Planning and delivery of training in science communication at Hydra Summer School 2015 and 2016 (10 HumEn participants)

2. Sharing best practice workshops, November 2015 Edinburgh; November 2016 Berlin: In collaboration with Eurostemcell and other FP7 stem cell consortia, HumEn has taken a lead role in the conception and development of two 2-day training events for stem cell communicators across the Eurostemcell partnership, including HumEn members. The workshops allow for professional development in public engagement and serve as a networking opportunity to strengthen partnership working and idea development.

3. Bespoke mentoring to support HumEn researchers in their engagement activities

4. Science Communication training at HumEn GA meetings: Writing for Wikipedia

8. Diabetes and Stem Cells Film

HumEn, in collaboration with Eurostemcell completed the production of a 12 minute short film *Diabetes and Stem cells* to complement the Eurostemcell film series. The multi-functional educational tool shows footage from HumEn labs, interviews with HumEn scientists and was scientifically edited by Henrik Semb. Disseminated via Eurostemcell, all partners, Teacher networks and The Science Learning Centre UK resource depository, the short film will be used by scientists, educators, science communicators, patient organisations and online public audiences**.** The film is currently available with English voice over and French subtitles: https://www.eurostemcell.org/video-diabetes-and-stem-cells

4.2.3 Launch events in relation to the World Diabetes Day

To celebrate *World Diabetes Day* 14/11/2017 HumEn launched the short film *Diabetes and Stem Cells* in Edinburgh, UK and Paris, France. http://hum-en.eu/news-and-events/diabetes-and-stem-cells-film-

launched. Collaborating with Eurostemcell a digital launch coincided with *World Diabetes Day* through Twitter and Facebook channels.

Edinburgh 2017 The evening event to launch *Diabetes and Stem Cells* attracted a diverse audience (approx. 60) including families and individuals affected by diabetes, school teachers, pupils and general interest public. The film was shown followed by a Q&A session with a panel including HumEn's Professor Wendy Bickmore, Dr Cathy Southworth, the film's director and animator and a young person affected by diabetes who appears in the film. The reception allowed for informal discussion amongst the panel and audience.

Paris 2017 Collaborating with Revive, Institute Pasteur launched Stem Cells and Diabetes alongside the film *Pour quelques barres de chocolat to an audience of 50.*

1. **Unfolding Collaboration – short film**

HumEn worked with Eurostemcell to share their expertise of working in collaboration developing and delivering public engagement events. Using The Edinburgh International Science Festival in 2016 as the case study, the learning was synthesised into a short film and shared via Eurostemcell as a tool for science communicators: https://www.eurostemcell.org/it/node/604

2. **Using origami as a tool to engage about stem cells**

To share learning from the engagement HumEn undertook at the Edinburgh International Science Festival 2016 an abstract entitled *Unfolding organogenesis* has been submitted to **The 7th International Meeting on Origami in Science, Mathematics and Education (7OSME,** http://www.osme.info/7osme/**)** which will take place in Oxford, United Kingdom between 5th and 7th September 2018.

3. **Engagement with schools – UK and Danstem**

Alongside the 3rd 'Danstem Day' http://danstem.ku.dk/news/stem-cell-day-2017/ HumEn also supported the work with a local schools and community project in Edinburgh, UK which aims to connect young people and teachers with cutting edge and real-world science. HumEn's science communicator shared the world of stem cells with Primary and Secondary school pupils, teachers and the local community through a collection of professional development, a community science festival and lab tours.

4.3 Building capacity through training junior researchers

Planning and delivery of training in science communication at Hydra Summer School 2017

Sharing best practice workshop November 2017 Vienna: In collaboration with Eurostemcell and other FP7 stem cell consortia, HumEn took a lead role in the conception and development of a two 2-day training event for stem cell communicators across the Eurostemcell partnership, including HumEn members. The workshops allow for professional development in public engagement and serve as a

networking opportunity to strengthen partnership working and idea development (2017 was the third in the series).

Training in Science Communication at the Joint Health Consortia Meeting, May 2017, Amsterdam

The work extended to provide a comprehensive science engagement programme for HumEn. Audiences reached included those affected by Diabetes, patient organisations, school teachers, school pupils, science communicators (as multipliers) and general public, non-specialists**.**

5.0 The project's public website and relevant links

HumEn public website: http://hum-en.eu/

Diabetes and Stem Cells:

https://www.youtube.com/watch?v=agFhYc6BV_M&t=5s

https://www.eurostemcell.org/video-diabetes-and-stem-cells

The birth of beta cells:
https://youtu.be/r3CCm1CXQl8?list=PLO0_bpy1MW5DDo76oFKFWabjswB10gaWe

Stem cells and their awareness of future self:

https://www.youtube.com/watch?time_continue=1318&v=jtp01ImddGc

Stem Cells Pave the Way for Cure for Diabetes:

http://video.ku.dk/stem-cells-pave-the-way-for-cure-for-diabetes

A new role for Insulin as a vital factor in maintaining stem cells: https://vimeo.com/230455281

Outreach stories:

http://www.eurostemcell.org/story/unfolding-organogenesis

http://www.hum-en.eu/news-and-events/edinburgh-international-science-festival

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