



# INANOBIT PROJECT

First Email Newsletter

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Welcome by the Coordinator

In this issue, we introduce you to the iNanoBIT project.

The central aim of the project is to develop regenerative medicine solutions for Type1 diabetes. We apply nanotechnologies for imaging porcine pancreatic islet cellular transplants and induced pluripotent stem cell-derived beta-cells and subsequent regenerative processes in vivo in a porcine model. We will be present our progress in this newsletter.

Regenerative medicine is a potential paradigm shifting technology to cure chronic diseases.

The current COVID-19 crisis and the contribution of diabetes to the severity of the symptoms underlines the importance and urgency to progress with the iNanoBIT project.

The iNanoBIT project is being coordinated by BioTalentum Ltd. (Hungary) bringing together 8 leading scientific partners from academia and industry from across Europe.

We hope you enjoy reading our newsletter!

Prof. Dr. András Dinnyés  
CEO, BioTalentum Ltd.

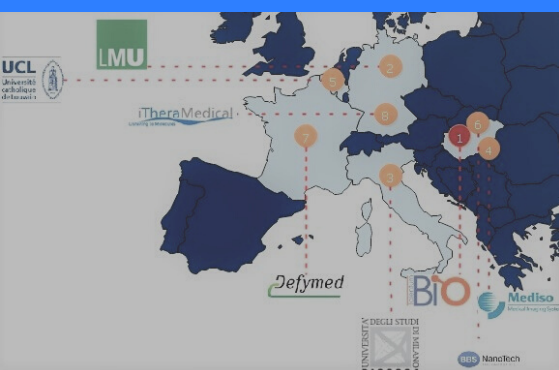


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## Partners



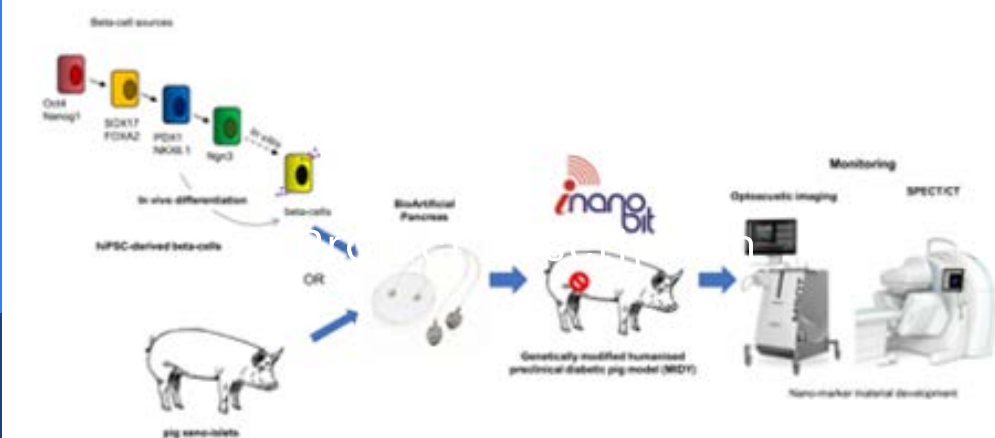
1. BioTalentum Ltd., Hungary – coordinator
2. Ludwig-Maximilians-Universität München, Germany
3. University of Milano-Bicocca, Italy
4. Mediso Medical Imaging Systems, Belgium
5. Université Catholique de Louvain, Belgium
6. BBS Nanotechnology Ltd., Hungary
7. Defymed, France
8. iThera Medical GmbH, Germany

<http://inanobit.eu/partners/>

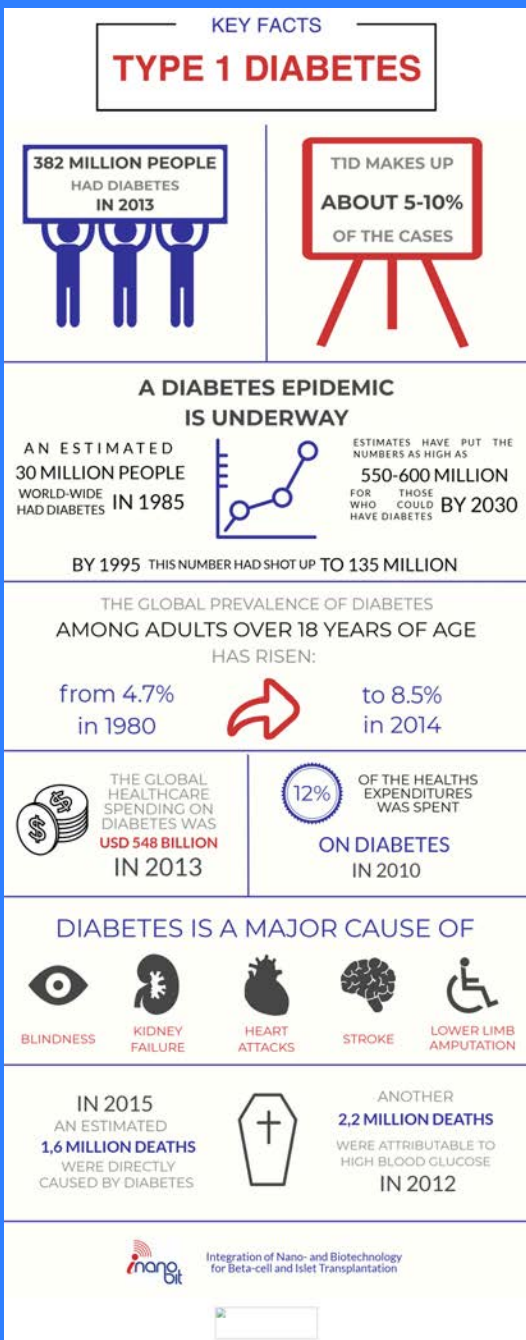


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The structure and toolboxes of the iNanoBIT project



Our focus is on diabetes, as one of the most challenging and economically important areas of medicine. A diabetes epidemic is underway: estimates have put the numbers as high as 550-600 million for those who could have diabetes by 2030.

The 5 years long iNanoBit project aimed generating new transgenic reporter pigs and human induced pluripotent stem cell (iPSC) lines for optoacoustic imaging and testing them in transplantable bioartificial pancreas devices. Additionally, novel highly sensitive nanotechnology-based imaging approaches allowing for monitoring of survival, engraftment, proliferation, function and whole-body distribution of the cellular transplants will be developed.

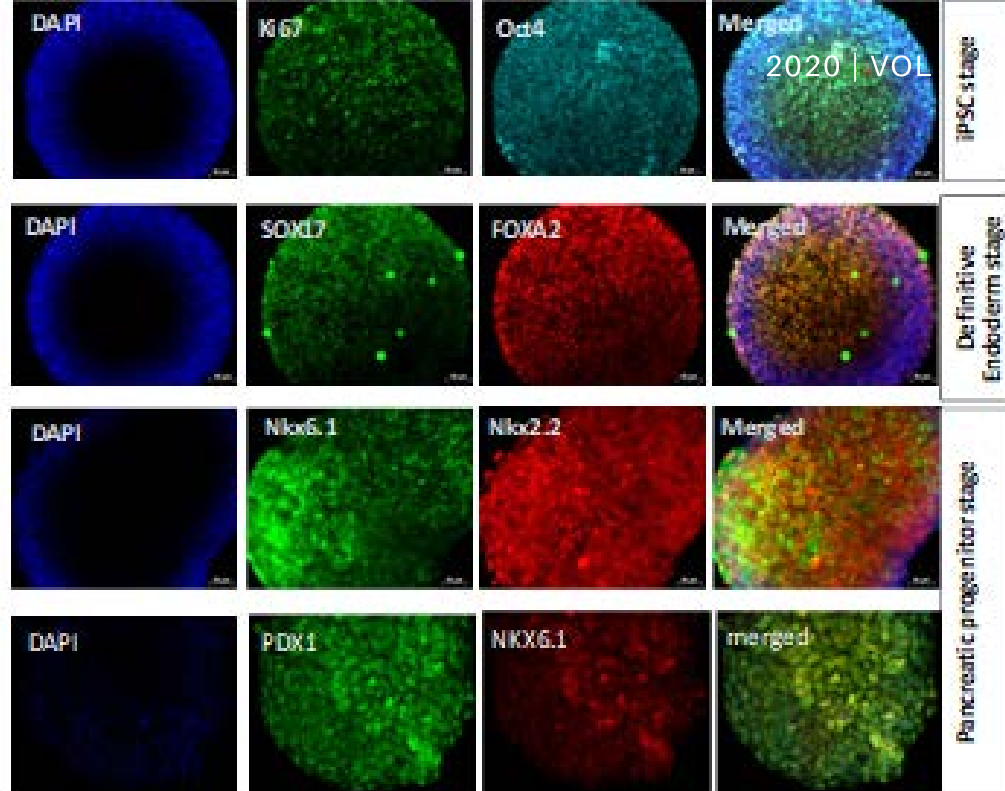


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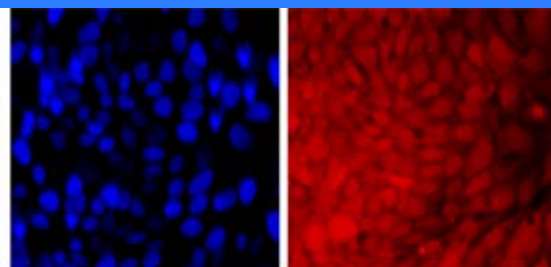


Schematic and representative images of 3D spheroids formation from iPSCs before and after differentiation



Representative immunofluorescent micrographs of different stages positive for pluripotency (Ki67, Oct4), Definitive Endoderm (FOXA2, SOX17) or pancreatic progenitor markers (NKX6.1, NKX2.2, PDX1). (Scale bar, 50 μm)

## Accomplished



Expression of iRFP720 in the targeted human iPSC clones. Blue: DAPI, red iRFP signal

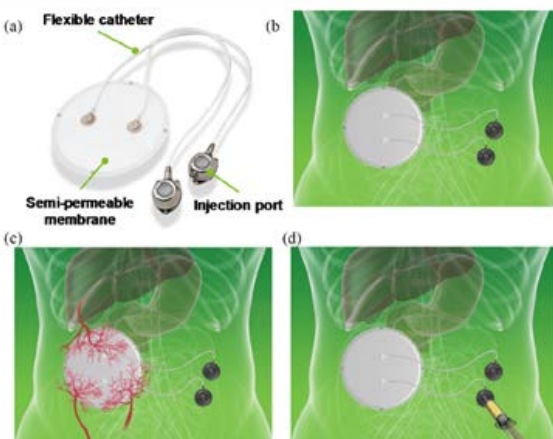


We have established the specified pathogen-free pig facility CiMM and have generated novel pig lines expressing near-infrared fluorescent protein iRFP720 which will allow us to monitor the viability of the transplanted xenoislets. Routine supply of NICCs from pig lines has been established.

We have also generated the iRFP720 protein expressing human iPSC line which was successfully differentiated into pancreatic progenitors and insulin secreting beta-like cells which are positive for appropriate markers. The generated pancreatic progenitors have been transplanted in mice for testing their ability to complete maturation in vivo and to normalize the blood sugar level. Nanoparticles have been designed for multimodality enhancing imaging, detecting agents and the ligand to specifically label beta-cells have been chosen and the first nanoparticles have been generated. Our artificial pancreas, MailPan has been successfully implanted in pigs, and the results showed the feasibility to implant MailPan® device subcutaneous as well as its integrity. PET/CT images of pigs have been established thus we will be able to perform imaging as soon as the transplantations will be available.

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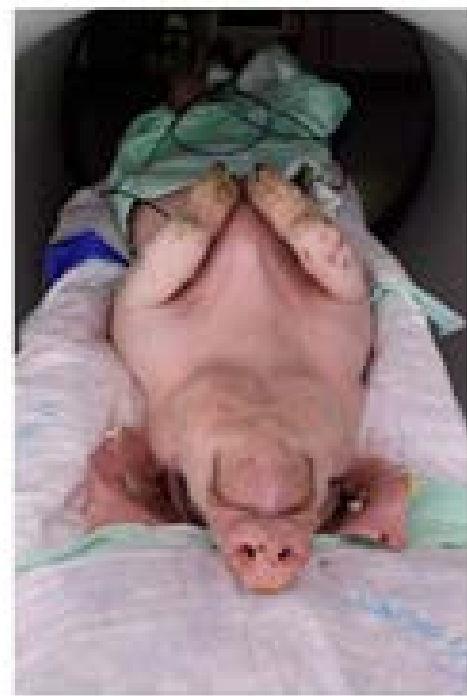
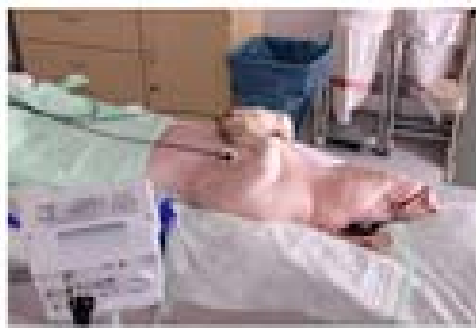


*Principle of MailPan® device*

Coming next



*AnyScan TRIO system with multi-pinhole collimator design focusing on the pig's liver*



Our 3D culture based pancreatic progenitor differentiation protocol will allow us to scale-up spheroid production in order to provide sufficient number of cells for the treatment of large animals. Currently, upscaling the beta-cell production from iPSCs and cost-optimization of the protocol is in progress in order to provide the consortium sufficient amount of iPSC derived beta-cells for porcine transplantation. The toxicity effect of generated nanoparticles and functionalized polymers will be tested in vitro on porcine neonatal islet-like clusters and hiPSC derived beta cells. Biocompatibility studies will be performed to test their possible interaction with the components of blood both in vitro and in vivo. In the upcoming two years Mailpan device, filled with either porcine islets or human beta cells will be implanted in the extraperitoneal space of porcine. Finally, imaging of the transplanted pigs with PET/SPECT and MSOT will be performed applying the novel nanotools, reporter pigs and cell lines.



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## Project meetings



iNanoBIT kick-off meeting - Brussels, 3 October 2017



iNanoBIT Annual Meeting - Budapest, 7-9 October 2018



iNanoBIT Review Meeting - Brussels, 9 April 2019



iNanoBIT Annual Meeting - Munchen, 6 October 2019



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## Upcoming events, meetings



# COVID-19

The iNanoBIT Project is facing the Covid-19 situation as many of H2020 projects over the world since many weeks. However, this pandemic did not stopped the partners' motivation work forward this great research project!

The members of the consortium have decided to maintain the 3rd Annual and Review Meeting that is supposed to take place on **October 6th 2020** in Brussels (Belgium) to make it happen remotely, via GoToMeeting platform.

Our Project Officer, Matteo Bonazzi and the Project Monitor, Prof. Giuseppe Cacace will attend to talk about the solutions brought by the EU Commission to face the pandemic situation.

Each Work Package leader will present their main results since the last Annual Meeting and the action plan for the next 12 months to come.

Despite those particular times, all members of the consortium are motivated to contribute to this project and participate to an effective meeting soon.





## Publications

PUBLICATIONS are key points  
in dissemination activity.

On publications that are  
included research funded by  
iNanoBIT it is compulsory to  
acknowledge the project in a  
pre-defined form.



Integration of Nano- And Biotechnology for Beta-Cell and Islet Transplantation in type-1 Diabetes Treatment  
Andras Dinnyes, Andrea Schnur, Suchitra Muenthaisong, Peter Bartenstein, Charles-Thibault Burcez, Neal Burton, Clemens Cyran, Pierre Gianello, Elisabeth Kemter, Gabor Nemeth, Francesco Nicotra, Eszter Prepost , Yi Qiu , Laura Russo , Andras Wirth, Eckhard Wolf, Sibylle Ziegler, Julianna Kobolak, Cell Prolif . 2020 May;53(5):e12785. doi: 10.1111/cpr.12785. Epub 2020 Apr 27. DOI: 10.1111/cpr.12785

Glycans in nanomedicine, impact and perspectives  
Susanna Sampaolesi, Francesco Nicotra, Laura Russo  
Future Medicinal Chemistry, Issue 11/1, 2019, Page(s) 43-60, ISSN 1756-8919 DOI: 10.4155/fmc-2018-0368

Recent progress in porcine islet isolation, culture and engraftment strategies for xenotransplantation  
Elisabeth Kemter, Eckhard Wolf, Current Opinion in Organ Transplantation, 2018, Page(s) 1, ISSN 1087-2418 DOI: 10.1097/mot.0000000000000579

Will Genetic Engineering Carry Xenotransplantation of Pig Islets to the Clinic? Elisabeth Kemter, Joachim Denner, Eckhard Wolf, Current Diabetes Reports, Issue 18/11, 2018, ISSN 1534-4827 DOI: 10.1007/s11892-018-1074-5

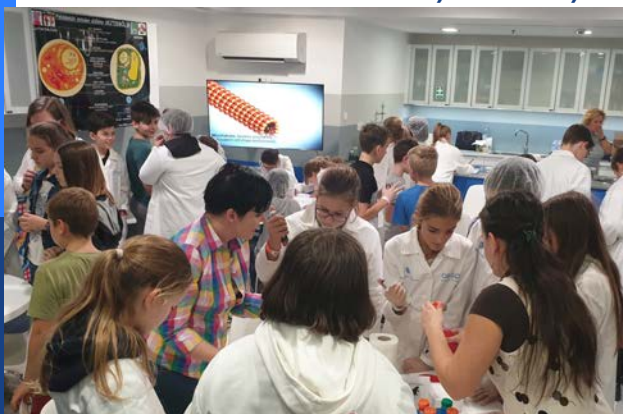




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Researchers' Night - Milano, Budapest  
2017, 2018, 2019



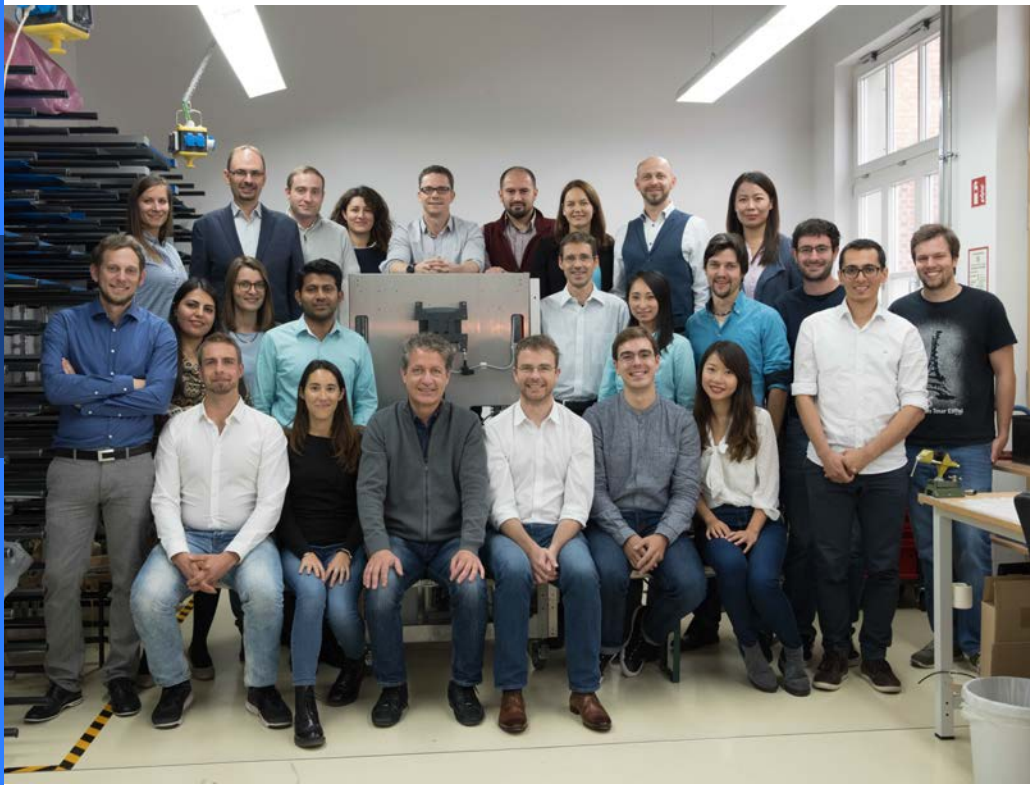
IXA 2019  
Congress

## Dissemination activities



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## Recent news from IThERA

The logo for iTheraMedical, featuring the text 'iTheraMedical' in a blue serif font, with a stylized blue wave graphic underneath the word 'iThera'.

After receiving CE certification on the MSOT Acuity system (optoacoustic imaging system without the integration of ultrasound) last year, we started integrating ultrasound to the system. After one year of hard work, we finished the development of the new MSOT Acuity Echo system, which is the optoacoustic imaging system with integrated ultrasound. Recently we successfully finished the verification and validation tests for the MSOT Acuity Echo system. This will serve as a basis for the next generation MSOT research imaging system for clinical and large animal research. Efforts for certifying the MSOT Acuity Echo research system will begin in autumn this year.



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## Recent news from Defymed



Defymed is pleased to announce the publication of their article Magisson et al., Journal of Tissue Engineering (2020) 1-16; DOI 10.1177/2041731420924818

### **Safety and function of a new pre-vascularized bioartificial pancreas in an allogeneic rat model**

Cell encapsulation could overcome limitations of free islets transplantation but is currently limited by inefficient cells immune protection and hypoxia. As a response to these challenges, we tested in vitro and in vivo the safety and efficacy of a new macroencapsulation device named MailPan®. Membranes of MailPan® device were tested in vitro in static conditions. Its bio-integration and level of oxygenation was assessed after implantation in non-diabetic rats. Immune protection properties were also assessed in rat with injection in the device of allogeneic islets with incompatible Major Histocompatibility Complex. Finally, function was assessed in diabetic rats with a Beta cell line injected in MailPan®.

In vitro, membranes of the device showed high permeability to glucose, insulin, and rejected IgG. In rat, the device displayed good bio-integration, efficient vascularization, and satisfactory oxygenation (>5%), while positron emission tomography (PET)-scan and angiography also highlighted rapid exchanges between blood circulation and the MailPan®.

The device showed its immune protection properties by preventing formation, by the rat recipient, of antibodies against encapsulated allogeneic islets. Injection of a rat beta cell line into the device normalized fasting glycemia of diabetic rat with retrieval of viable cell clusters after 2 months. These data suggest that MailPan® constitutes a promising encapsulation device for widespread use of cell therapy for type 1 diabetes.





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## Recent news from LMU



Eckhard Wolf  
[ewolf@genzentrum.lmu.de](mailto:ewolf@genzentrum.lmu.de)

The Center for Innovative Medical Models (CiMM) at LMU Munich is a unique research environment for the generation, characterisation and implementation of large animal models in biological and biomedical research.

CiMM is operated by staff from the Chair of Molecular Animal Breeding and Biotechnology, Gene Center and Department of Veterinary Sciences, LMU Munich. CiMM welcomes guest scientists from academia and industry to perform their research projects with large animal models in collaboration with experts from the CiMM facility.



CiMM is a core infrastructure for a number of research networks, such as the German Center for Diabetes Research (DZD), the DFG Transregional Collaborative Research Center 127 "Biology of Xenogeneic Cell, Tissue and Organ Transplantation - from Bench to Bedside", and the EU H2020 Project **iNanoBIT**.

Currently, CiMM is active in the following research areas:

- Genetically Tailored Porcine Disease Models
- Donor Pigs for Xenotransplantation
- Biology and Biotechnology of Reproduction

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## Recent news from BioTalentum



BioTalentum Ltd. is a leading technology provider in Central & Eastern Europe since 2005 so we turned 15 years in 2020.

In these 15 years BioTalentum Ltd. has grown significantly, our research and management team now comprised of 22 personnel.

However, our mission is still the same: developing and providing human stem cell-based solutions for disease modelling, in vitro toxicology and regenerative medicine.

In FP7 BIOT has successfully participated in 17 projects, (in 9 as scientific coordinator), and in H2020 programme BIOT takes part in 13 projects:

CasR, IN3, NABBA, PurinesDX (MSCA ITNs), EuToxRisk (large RIA), SciChallenge (SEAC), DRYNET (RISE), GROWTH, TUBE, EMAPS-Cardio (RIA) ADAIR and as coordinator of **iNanoBIT** (RIA) and DohART-NET (MSCA ITN).

We would like to thank all of our partners for their valued support over the past 15 years.

Please also visit our renewed website from November: [www.biotalentum.hu](http://www.biotalentum.hu)

