



Development of closed, scalable and AUTOMated robotic systems for therapeutic STEM cell manufacturing: aseptic systems from “Donor-to-Patient”

Welcome to the Summer 2018 AUTOSTEM Newsletter!

In this Edition

- AUTOSTEM in a Nutshell.....1
- The Story So Far (progress update)...2
- On the Road (recent events).....3
- Meet the Team.....4



AUTOSTEM in a Nutshell

AUTOSTEM is an EU H2020 project that is developing a closed, automated, sterile pipeline for large scale production of therapeutic mesenchymal stromal cells (MSCs).

Current MSC manufacturing protocols are inefficient and labour intensive. The project aims to enable lower-cost, higher quality and more consistent MSCs to be produced, ultimately helping patients to benefit from new cell therapies.

In AUTOSTEM bone marrow will be harvested from patients using a novel harvesting device. This bone marrow will then be delivered into the automated AUTOSTEM pipeline, where MSC will be selected, cultured and expanded. The environment in the pipeline bioreactors will be monitored (using sensor technology) to ensure optimum conditions are maintained. The AUTOSTEM process will require minimal direct manual intervention, thereby reducing the risk of error and contamination.

The AUTOSTEM consortium is a multidisciplinary mix of engineers, regenerative medicine scientists and high-tech companies from 4 European countries, led by Dr Mary Murphy of the National University of Ireland, Galway (NUIG). The project runs from 1 January 2016 to 31 December 2018.



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The Story So Far

Since our last newsletter, AUTOSTEM researchers have been working diligently on the different scientific work packages (WPs) in the project.

In WP2 the team in Crospon has finalized the design of the bone marrow harvest device. The system has been tested in pre-clinical studies and ethics approval has been received for clinical tests.

In WP3 researchers have achieved functionalisation of microcarriers with antibody CD362. This means that MSCs can be successfully selected onto beads. We are currently working on scaling up to larger beads and applying the process to isolate MSCs directly from bone marrow using serum-free medium.

Colleagues in WP4 continue to optimize procedures for MSC expansion, having now selected the bioreactor(s) for use in the platform. Researchers are working on the transfer of optimized procedures into the automated setting of the AUTOSTEM pipeline.

WP5 is focused on the development of sensors for the platform. We have demonstrated and evaluated longitudinal glucose sensing in a single channel context, in a bioreactor setting. The team is currently developing the second-generation sensors and system including the graphical user interface. The final system will include sensing for glucose, lactate and ammonia.

The team in WP6 from IPT Fraunhofer, are responsible for the platform build, which is now well advanced. We are currently working with suppliers on the delivery of hardware for the build (including the clean-room housing). Once the build is complete we will undertake acceptance testing, as well as risk and process analysis.

Researchers in WP7 are preparing the groundwork with regulators to ensure that the final pipeline is “GMP ready”.

The team in WP8 is working on biological characterization of the cells to be used in the AUTOSTEM pipeline and analysis of the AUTOSTEM cell secretome (the proteins that cells secrete). We have generated some encouraging results on the beneficial effects of extracellular vesicles (EVs) secreted by cells. In due course, colleagues in WP8 will validate the MSCs produced in the AUTOSTEM pipeline.

Finally, our team in WP9 has an oversight role – mapping and evaluating the pipeline process and technology development and assessing project risks, cost of goods and logistics analysis. Catapult (CGT) provide support to ensure both the platform and process are developed to the correct standards for future POC and commercial use.

“We believe that AUTOSTEM will ultimately help address technology gaps in commercial therapeutic MSC production. The project is also generating new knowledge about cell selection, cell expansion, bioreactor systems, sensor technology and MSC action.”

–Dr Mary Murphy (Coordinator)

AUTOSTEM Publications

Our publications to date include the following:

“Developing an automated robotic factory for novel stem cell therapy production” (Qasim A Rafiq et al). Regenerative Medicine 11/4 351-354. DOI: 10.2217/rme-2016-0040. Link to article [here](#).

“Cell and gene therapy manufacturing: the necessity for a cost-based development approach” (Richard P Harrison et al). Cell and Gene Therapy Insights 2/1 489-497. DOI: 10.18609/cgti.2016.014. Link to article [here](#).

“Automation in the context of stem cell production – where are we heading with Industry 4.0?” (Michael Kulik et al). Cell and Gene Therapy Insights 2/4 499-506. DOI: 10.18609/cgti.2016.060. Link to article [here](#).

“The evolving role of automation in process development & manufacture of cell & gene-based therapies” (Qasim A Rafiq et al) Cell and Gene Therapy Insights 2/4 473-479. DOI: 10.18609/cgti.2016.058. Link to article [here](#).

“Advances in automation for the production of clinical-grade mesenchymal stromal cells: the AUTOSTEM robotic platform” (Jelena Ochs et al) Cell and Gene Therapy Insights 2017; 3(8), 739-748. DOI: 10.18609/cgti.2017.073. Link to article [here](#).



AUTOSTEM: On the Road

Our team have been spreading the word about Autostem since the project began, with over 50 different dissemination activities recorded so far. Some examples of recent events, conferences and presentations are set out below.

NUIG and Orbsen made a number of presentations about AUTOSTEM at the **ISCT Annual Conference** in London on 3 to 6 May 2017. Prof Frank Barry presented “*MSC Biology and Manufacturing Challenges*”. A number of posters were also presented at the event.

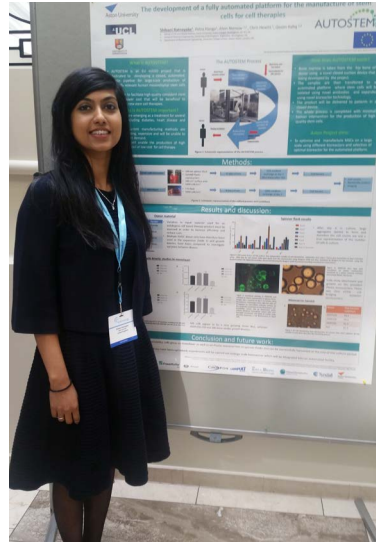
Several partners from AUTOSTEM contributed to the **Phacilitate Automation Special Interest Group Conference** held in Edinburgh on 30/31 May 2017. Dr Qasim Rafiq led the workshop focused on “*Automation and allogeneic cell therapies*”. Researchers from Fraunhofer IPT presented “*Towards automated stem cell manufacture*” and hosted an exhibit in the Tech Hub (pictured below).



Several members of the AUTOSTEM team attended the European Chapter Meeting of **TERMIS** (the Tissue Engineering and Regenerative Medicine International Society) held in Davos, Switzerland on 26-30 June 2017. Dr Mary Murphy (NUIG) presented at the Symposium on Stem Cells for Bone Regeneration. There were also several AUTOSTEM posters presented at the Conference.

AUTOSTEM was presented at the **EU MSC2 2017** meeting hosted by Leiden University Medical Center in Leiden, NL on September 12th and 13th 2017. This event assembled twelve EU-funded, MSC-focused consortia to network and explore issues of common interest.

Jelena Ochs of the Fraunhofer Institute for Production Technology IPT in Aachen, Germany presented AUTOSTEM at the **German Stem Cell Network Annual Meeting** held in Jena, Germany on September 11th-13th 2017.



Dr Shibani Ratnayake presenting a poster at the 1st Eppendorf Stem Cell Community Day (Hamburg, Germany, 4 April 2017).

Dr Mary Murphy presented “*Mesenchymal stromal cells for musculoskeletal indications: from mechanistic insights to robotic cell production*” at the **ESACT-UK 2018 Conference**, Leeds on 13 January 2018.

AUTOSTEM has also exhibited at several public-facing events, including the **START** competition for students (Galway, 19 May 2017), the **International Clinical Trials Open Day** (Galway, 20 May 2017) and the **Galway Science & Technology Festival** (Galway, 26 November 2017).

Finally, in August 2017 the **AUTOSTEM explainer video** was launched. This short video provides an easy-to-understand summary of the project. Watch the video on the project website or on YouTube [here](#).



Meet the Team

The AUTOSTEM consortium is a multidisciplinary mix of engineers, regenerative medicine scientists and high-tech companies from 4 European countries, led by Dr Mary Murphy of the National University of Ireland, Galway. The partners in the project are set out below.

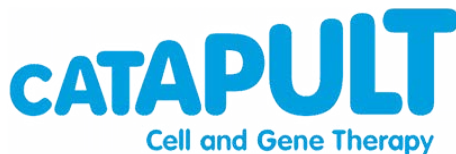
For more details see <http://www.autostem2020.eu/>



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For further information on the project please see the Project website

<http://www.autostem2020.eu/>

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