



**Automated Cellular Robot-Assisted Technologies
for translation of discovery-led research in Osteoarthritis**

2022 Newsletter

What is AutoCRAT?

AutoCRAT is an EU Horizon 2020-funded project that will develop novel sustainable cell and cell-derived therapies for osteoarthritis (OA). The project will use human induced pluripotent stem cells (iPSC) to generate articular chondrocytes for cartilage repair and human induced mesenchymal stem cells (MSC) for the prevention and treatment of established OA. As extended goals, the project will investigate the potential of the MSC cell secretome as a next-generation therapy and will produce the therapeutics identified in the project using cost-effective, robot-enabled processes in a novel manufacturing platform, with at line product testing, to expedite translation to patients.

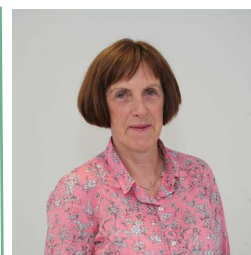
The AutoCRAT consortium is composed of nine expert scientific teams in five European countries specialising in regenerative medicine, OA, preclinical efficacy and safety demonstration, GMP and GAMP-compliant manufacturing of MSC, clinical trials for OA, regulatory affairs and health economics analysis.

Message from AutoCRAT Coordinator, Prof. Mary Murphy, NUI Galway

“The critical interactive engagement between partners enabled by in-person project meetings has resumed in AutoCRAT and the recent plenary hosted by UGOT in Gothenburg (with all partners in attendance) highlighted the excellent progress made to date.

Advanced protocols are now available for the production of chondrocytes, MSCs and related extracellular vesicles (EVs) using iPSCs as a sustainable cell source. Translation to automation is underway and the AutoCRAT automated platform build is progressing well, along with solutions for at-line testing. Results from ex vivo and in vivo studies of potential therapeutics are expected over the coming weeks and months.

As we enter an exciting phase for AutoCRAT, the extensive interactive discussion and planning in Gothenburg for the final 18 months of the project will help to deliver a successful outcome, with the potential to ultimately benefit patients with osteoarthritis or with compromised cartilage as a result of trauma.”



Prof Mary Murphy
AutoCRAT Coordinator

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SME in the Spotlight: PANAXEA

Panaxea (<http://panaxea.eu/>) is a leading health sciences research and consultancy organisation providing effective, evidence-based strategies for innovators and decision-makers within healthcare. By developing evidence-based knowledge and translating this into practice-oriented solutions, Panaxea aims to strengthen informed decision-making regarding health care innovations. The company is based in Amsterdam, the Netherlands, and started as a university spin-off in 2010.



Panaxea has a dedicated team of professionals with strong academic credentials and academic affiliations with leading universities. Being part of a network of healthcare innovators in Europe, the USA and South-East Asia, Panaxea services its clients with current local market intelligence and connections. This ensures they can guarantee the highest level of quality and flexibility to their clients .

Panaxea's mission is to accelerate market access and reimbursement for healthcare innovations with added value to the individual patient, the healthcare system and ultimately society. They do so by applying and developing rigorous methodologies for (early) Health Technology Assessment, Health Innovation Assessment and Health Systems & Services Research specifically for diagnostics, medical devices and complex healthcare programs at various (and often multiple) phases of the innovation life cycle.

Notably, Panaxea's founders have laid the academic groundwork for early-stage technology assessment approaches that are now used globally by health economists, healthcare decision-makers and innovative industries. Further, Panaxea holds vast international expertise in the evaluation of person-centred, integrated care models. In AutoCRAT, Panaxea is analysing the cost-effectiveness of cell-based treatments in comparison to usual care for patients with symptomatic osteoarthritis in the knee.

Our partners at the University of Gothenburg kindly hosted a consortium meeting on June 16th and 17th 2022.



Team photo from Gothenburg (Photo credit Elin Lindström)

The AutoCRAT Team



An AutoCRAT update from the University of Gothenburg

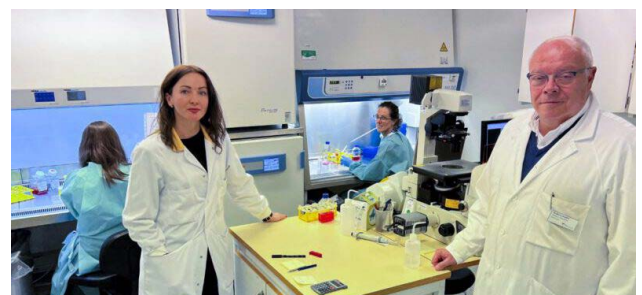
Within AutoCRAT, the University of Gothenburg is working with consortium partners to develop new cell-based products which have the potential to become future treatments for OA. “Soon, within the project, the consortium needs to agree on which cell source or cell-secreted vesicles are the best candidates to become cell-based therapies for osteoarthritis”, says Dr Kristina Vukusic.



UNIVERSITY OF GOTHENBURG

In AutoCRAT, we are exploring the use of induced cartilage cells (chondrocytes), derived from induced pluripotent stem cells (iPSC) to repair cartilage tissue. We are also exploring the use of mesenchymal stem cells (MSC), which are a type of adult stem cell found in adipose tissue or bone marrow. We are also investigating the therapeutic potential of extracellular vesicles (sub-cellular packages released by cells with the potential to deliver therapeutic effects). As part of our work, we will generate economically sustainable and reproducible therapeutic cell sources.

“Our research team in Gothenburg has extensive clinical experience and a strong track record in cartilage repair. We provide AutoCRAT with this expertise and the cartilage cells against which the AutoCRAT end product will be compared. We grow cartilage cells and examine their EVs. We have developed novel lab protocols to direct iPSC to become cartilage cells. In this way, we hope to find a universal donor for osteoarthritis patients” says Dr Vukusic.



Group photo from UGOT (Photo credit Elin Lindström)

Anders Lindahl, professor at the University of Gothenburg and senior researcher in AutoCRAT, was one of the first in the world to start working with cell therapies. In the early 1990s, he and his colleagues began treating people with cartilage damage with their own cells. This is an approved cell therapy, which thousands of patients have received. Unfortunately, this treatment only works for patients with an isolated cartilage injury where there is healthy cartilage available and the patient can be his own cell donor. “The protocol that we developed within AutoCRAT describes in minute detail the management of the cells during the differentiation into chondrocyte-like cells so that the result is the desired one,” says Anders Lindahl.

The collaboration within AutoCRAT aims to demonstrate optimal automatic production, where expensive laboratory premises and high personnel costs are replaced by a cell culture platform. “The ultimate goal is to produce large amounts of cells and functional extracellular vesicles with a protocol that makes it possible to treat a large number of patients suffering from osteoarthritis,” says Anders Lindahl.



Dissemination Matters

Presentation highlights

On May 7th 2022, at the **Stem Cell Network NRW 13th internal Meeting** in Herne Fraunhofer IPT's **Ferdinand Biermann** presented: *Fully automated production of mesenchymal stem cells, chondrocytes and extracellular vesicles for osteoarthritis treatment.*

At the **OARSI 2022 World Congress**, April 7th to April 10th, 2022 in Berlin, **Prof. Ingrid Meulenbelt** of LUMC was the keynote speaker. Her talk was titled *Mechanobiology and OA: Elucidating Mechano-Pathology of Osteoarthritis.*

A poster "*Towards application of cell therapy using hiPSC-derived MSCs as stable 'off-the-shelf' cell source*" was presented by **Dr Yolande F. M. Ramos**, Leiden University Medical Center at the **Orthopedic Research Society 2022** meeting, Tampa, USA, February 4th- 8th 2022.

AutoCRAT Coordinator **Prof. Mary Murphy**, National University of Ireland Galway was a panellist during the "*Closed systems and automated manufacture: Manufacture & bioprocess*" session at the **Advanced Therapies LIVE conference**, October 5th, 2021.

Prof. Chiara Gentili and **Dr Elisabetta Palama**, University of Genova (UNIGE) presented at the **EV-Ita Symposium**, September 20th- 22nd, 2021 in Lucca, Italy. Prof. Gentili's poster was entitled: *Extracellular vesicles derived from mesenchymal stromal cells cultured in a clinical-grade medium promote human cartilage recovery.* Dr Palama's poster was "*Role of Extracellular Vesicles from adipose tissue and bone marrow mesenchymal stromal cells in endothelial proliferation and chondrogenesis*".

Publications

Rodríguez Ruiz, A., Dicks, A., Tuerlings, M., Schepers, Koen, van Pel, Melissa, Nelissen, Rob G. H. H., Freund, Christian, Mummery, Christine L., Orlova, Valeria, Guilak, Farshid, Meulenbelt, Ingrid and Ramos, Yolande F. M. "Cartilage from human-induced pluripotent stem cells: comparison with neo-cartilage from chondrocytes and bone marrow mesenchymal stromal cells". *Cell Tissue Res* (2021). DOI: <https://doi.org/10.1007/s00441-021-03498-5>.

Simon Staubach, Fabiola Nardi Bauer, Tobias Tertel, Verena Börger, Oumaima Stambouli, Denise Salzig, and Bernd Giebel, "Scaled preparation of extracellular vesicles from conditioned media". *Advanced Drug Delivery Reviews*, DOI: <https://doi.org/10.1016/j.addr.2021.113940>.

Gorgun, C., Palamà, M.E.F., Reverberi, D., Gagliani, M.C., Cortese, K., Tasso, R. and Gentili, C. (2021), "Role of extracellular vesicles from adipose tissue- and bone marrow-mesenchymal stromal cells in endothelial proliferation and chondrogenesis". *STEM CELLS Transl Med*. DOI: <https://doi.org/10.1002/sctm.21-0107>.

H. Evenbratt, L. Andreasson, V. Bicknell, M. Brittberg, R. Mobini and S. Simonsson, "Insights into the present and future of cartilage regeneration and joint repair", *Cell Regen* (2022). DOI: <https://doi.org/10.1186/s13619-021-00104-5>.



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