# DIGIPREDICT FIRST PUBLISHABLE SUMMARY

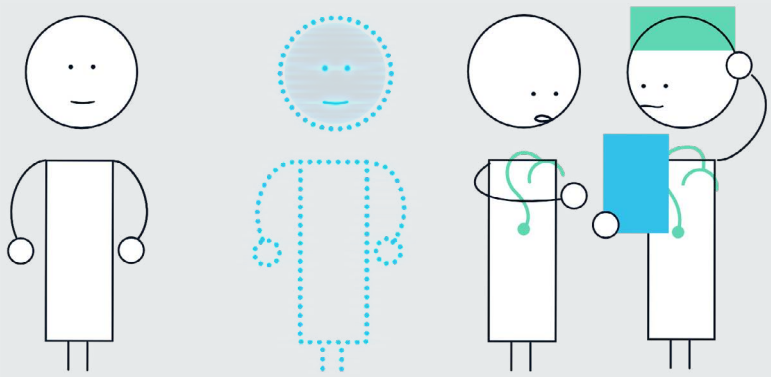
*February 2022*

DIGIPREDICT proposes a digital twin vehicle, which represents patient-specific (patho)physiology and is capable to predict progression of infectious viral diseases. The main objective of the project is to allow identifying, monitoring and screening of high-risk patients, and to provide them with the right supportive therapy based on referral decisions that can be personalized. For instance, the interplay between viral infection, host response, development of (hyper)inflammation and cardiovascular injury in COVID-19 is currently poorly understood which makes it difficult to predict which patients remain with mild symptoms only and which patients rapidly develop multi organ failure. Therefore, DIGIPREDICT explores the first of its kind digital twin – designed, developed and calibrated on patient measurements of various digital biomarkers and their interaction, starting from needs identified in the global pandemic period.

During the 1st reporting period, the DIGIPREDICT project made significant progress towards the general project objectives and achieved a significant number of scientific milestones.

The consortium organized an internal workshop where the medical end-users presented and discussed needs for the development of biomarker sensors and physiological sensors as well as of organ-on-chip (OoC) technology. With the main goal of building digital twins, data flow and data management specificities concerning standard monitoring in hospitals, as well as opportunities of machine learning and artificial intelligence driven methods, including ethical aspects, have been discussed. A prioritization of major biomarkers for inflammation and cardiovascular disease progression has been made based on their dynamics. The consortium also progressed with the preparation of the ethics documents and a study protocol for the *in-vivo* deployment of the DIGIPREDICT-Physio demonstrator.

We made major advancement concerning the demonstration of C-Reactive Protein (CRP) inflammation marker detection with a complementary metal–oxide–semiconductor (CMOS) compatible technology platform as reported at IEEE IEDM 2021[1]. This breakthrough is in the context of the evaluation of two different technologies for the transduction mechanism of the sensing platform: Silicon Nanowire field-effect transistor (FETs) and 2D material FETs. This integrated sensor is compatible with the size and the volumes of interstitial fluid (ISF) needed for sensing with the ISF microneedle array technology proposed in our consortium. A number of preparatory activities to address delays related to medical device reulation (MDR) and advance towards the in-vivo deployment of their technology have been performed using an earlier microneedle chip generation with a MDR class IIa device.



*Visual representation of a digital twin as seen in the DIGIPREDICT introductory video, available at www.digipredict.eu/outcomes*

[1] Capua, L., Sprunger, Y., Elettro, H., Grammoustianou, A., Midahuen, R., Ernst, T., Barraud, S., Gill, R. & Ionescu, A. Double-Gate Si Nanowire FET Sensor Arrays For Label-Free C-Reactive Protein detection enabled by antibodies fragments and pseudo-super-Nernstian back-gate operation. in 2021 IEEE International Electron Devices Meeting (IEDM) 16.2.1–16.2.4 (IEEE, 2021). doi: 10.1109/IEDM19574.2021.9720670.

The consortium devised a complementary strategy for the data analytics, to parallelize and speed-up the work on digital twin models and their validation, using several intensive care unit (ICU) databases as complementary sources to DIGIPREDICT data to advance from an early-stage model developments and validation, without waiting for the data generated by the emerging wearable sensor technology.

An important technical highlight of the period is the GISMO interface chip capable to feature both voltametric and amperometric readouts. The multi-modal analogue readouts have the following features: 4 multiplexed channels differential ISFET, pA input bias potentiometric (POT), 2 high dynamic range potentiostat (PSTAT), die temperature, 3 programmable voltage drivers, 12-bit SAR ADC for signal digitization, digital controllers for power optimization and SPI communication. The chip has been designed and fabricated in 0.180nm CMOS with 1.8V Supply, with a die area of 9mm$^2$.

The development of flexible membrane multielectrode array chip (FMMC) using a custom CMOS fabrication was advanced and different designs of the mesh have been developed and tested to fulfil the specifications and toxicity conditions of the OoC applications. In addition, a set-up and related protocols to operate this blood vessel-on-chip model; enabling operational blood vessel-on-chip that can be used to test and study various cytokine mixtures have been achieved.

In the perspective of deploying digital twin wearable data generators as edge devices, the consortium delivered in-time and according to project specifications a small batch of fully functional PhysioPatch miniaturized wearable, battery operated and radio-enabled devices capable to monitor the patient's skin temperature, bioimpedance-based respiratory rate and blood oxygenation ($SpO_2$).

The consortium achieved the successful implementation of the project website, a DIGIPREDICT flyer, video and social media presence, ensuring an excellent international visibility of project (https://www.digipredict.eu).

Dissemination activities have been successfully started and ramped-up, with involvement of the consortium in five online international events (SMART MedTech Forum, ICDDMAP2021, CIS Digital Twin Days, SelectBIO 3D Culture, Organoids & Organ-on-a-Chip Europe 2021 World Congress on Alternatives and Animal Use in the Life Sciences 2021) and 7 conference and journal papers.

The project is expected to propose beyond state of the art solutions in multiple domains: (i) new models representing patient-specific (patho)physiology to early detect and predict the progression of infectious viral diseases and cardiovascular implications, (ii) unique multi-modal data generator wearable technologies to support building and sourcing the Digital twin models, based on both *in-vitro* and *in-vivo* validations, (iii) new physical vascular OoC technologies, beyond the current state design to support de developments of (i) and (ii). As explicitly mentioned earlier, in all the three mentioned domains and their interactions the project made significant progress during the 1st reporting period.