







Press release - 22 March 2021

Non-hormonal female contraception using antibody fragments

Accelerating Discovery for Non-Hormonal Contraceptives is one of the Grand Challenge programmes launched by the Bill & Melinda Gates Foundation for the coming years. A research project has just started in the context of this programme, having received funding worth \$1.8 million. The project is being managed by a consortium led by INRAE and involving IN-CELL-ART, a French biotechnology company specialised in nanotransporter technologies called NANOTAXI®, the Italian university UNIMORE¹, and MAbSilico, an INRAE start-up that proposes software based on artificial intelligence technologies for the development of antibodies. The aim is to design biological products based on antibody fragments to block ovulation and thus enable non-hormonal contraception that causes fewer adverse effects.

In this collaborative project, the INRAE research team², which specialises in studying the membrane receptors that control reproduction, is focusing in particular on the contraceptive mechanism that blocks the molecular regulators of ovulation. Antibody fragments that target receptors present in ovarian cells can very selectively modulate the effects of natural hormones within these cells. Studies will aim to develop antibody fragments that can selectively block ovulation without disturbing the endogenous production of steroid hormones. These antibody fragments will then be modified to produce sufficiently durable effects to guarantee contraception, while ensuring the reversibility of the ovulation blockade after treatment is discontinued.

The software platform developed by MAbSilico is being used for the selection, characterisation and optimisation of antibody fragments that target the regulators of ovulation. The artificial intelligence technology developed by this biotech firm enables the digitisation of antibody discovery, accelerating and securing this critical step.

Best antibodies will be selected in vitro by UNIMORE, where they will be tested using human ovarian cells. This working package is fundamental to ensure the functionality of antibodies in humans and relies on the expertise of its Unit of Endocrinology in hormonal regulation of the reproductive functions.

The antibody fragments thus optimised will then be tested *in vivo* in mice by administering synthetic non-inflammatory mRNA coding for this new class of biologics. This will trigger the production of antibody fragments by the mouse's muscle fibres, their secretion into the blood and finally their action on the ovaries. This technology, called NANOTAXI®, will thus make it possible to avoid the bioproduction of antibody fragments, which is cumbersome, expensive and lengthy. The most promising antibody fragments will then be tested non-invasively in ewes.³

¹ Università degli studi di Modena e Reggio Emilia

² Associated with the MAbImprove LabEx dedicated to therapeutic antibodies.

³ By the platforms operated by the Val de Loire INRAE Research Centre at the L'Orfrasière Animal Physiology Experimental Unit and Pixanim (INRAE Université François-Rabelais and Tours University Hospital).

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About...

INRAE - Created on January 1, 2020, the French National Research Institute for Agriculture, Food, and Environment (INRAE) is a major player in research and innovation. INRAE carries out targeted research and resulted from the merger of INRA and IRSTEA. It is a community of 12,000 people with 268 research, experimental research, and support units located in 18 regional centres throughout France. Internationally, INRAE is among the top research organisations in the agricultural and food sciences, plant and animal sciences, as well as in ecology and environmental science. It is the world's leading research organisation specialising in agriculture, food and the environment. INRAE's goal is to be a key player in the transitions necessary to address major global challenges. Faced with a growing world population, climate change, resource scarcity, and declining biodiversity, the institute is developing solutions that involve multiperformance agriculture, high-quality food, and the sustainable management of resources and ecosystems.

www.inrae.fr/en

IN-CELL-ART (ICA), which is headquartered in Nantes (France) is a biopharmaceutical company specializing in the preclinical and pharmaceutical development of nanocarriers named NANOTAXI® for nucleic acids. Its founder and research team, which includes a Nobel Laureate, have designed new classes of vectors that are organized on a nanometric scale, which enables them to cross the cell barrier efficiently and safely. ICA NANOTAXI® technology displays unique properties for development of mRNA and DNA vaccines and for production of non-immunogenic antibodies from within the body following NANOTAXI® delivery of mRNA or DNA encoding this novel class of biologic agents. IN-CELL-ART is a privately held company, which was founded in 2005, laureate in 2012 and 2013 of the Fast 50 Deloitte award, and in 2013 of Territoires Innovation Pays de la Loire Awards (France).

www.incellart.com

UNIMORE participates with the Unit of Endocrinology headquartered at the Sant'Agostino-Estense Hospital of Modena (Italy). It is a translational research team with recognized basic and clinical international experts that have consolidated over time scientific bases in the field of reproductive physiopathology. The UNIMORE Unit is an established excellence with highly technological equipment to study signals delivered by hormones at the intracellular level. Skilled researchers work at UNIMORE in a stimulating environment where they can express

their potential at the highest levels by applying highly innovative nanotechnological approaches to health problems with high social impact.

www.unimore.it

MAbSilico is a TechBio company developing and commercializing Al-based software for antibody discovery and development. The software platform can be used for any antibody format, for therapeutic and biomarker purposes. Only requiring the antibodies sequences and the target name, MAbSilico software supports biologists to select, after simulation and modeling in minutes, the best antibody candidate. The Al-based solutions are on the shelf and have been validated with biological assays through a formal approach. For antibody selection MAbBinning allows the prediction of the pairwise competition within a collection of antibodies against a given target, and the prediction of the epitopes of antibodies. The 3D structure of the target or a close homolog is required. MAbTope can be for the characterization to perform the modeling of the epitope of an antibody on its target. The customer receives the epitope, the paratope and 3D models of the partners interaction.

www.mabsilico.com