



PRESS RELEASE

Collectis Studies Safety in New CAR Architecture Controlling CAR T-Cell Functions

Publication in *Scientific Reports*, a Nature Publishing Group Journal

January 23, 2017 – New York (N.Y.) – Collectis (Alternext: ALCLS; Nasdaq: CLLS), a biopharmaceutical company focused on developing immunotherapies based on gene edited CAR T-cells (UCART), today announced the publication of a study in [*Scientific Reports*](#), a Nature Publishing Group journal, describing a novel approach to a CAR design with an integrated environmental signal utilizing oxygen concentration to manipulate the CAR T-cell response.

In this report, Alexandre Juillerat, Ph.D. and his collaborators from the Collectis innovation team designed a new CAR architecture that contains an integrated microenvironment sensor. Low oxygen concentration is recognized as a hallmark of the microenvironment of certain solid tumors. The implementation of the novel oxygen sensitive CAR architecture empowers CAR T-cells with the possibility to auto-regulate (switch on or tune-up) their functions in low oxygen (hypoxic) environments.

With the primary purpose of implementing additional levels of safety to the CAR T-cell technologies, in particular to minimize "on-target / off-tumor" effects, this study demonstrated the possibility to use peculiarities of the tumor microenvironment to create self-decision making CAR T-cells with impaired functions at high oxygen concentration. The results showed that this system also possessed the key feature to be prone to quickly return to its off state in the absence of the inducing signal (hypoxia), a characteristic that is of prime interest to protect healthy tissues distant from the tumor site. Beyond this first *in vitro* proof of concept, additional studies are expected to fully assess the therapeutic potential of this approach.

Alexandre Juillerat, Ph.D. Innovation Senior Scientist

Dr. Alexandre Juillerat, Ph.D., graduated in Chemistry from the University of Lausanne, Switzerland. After receiving in 2006 his Ph.D. in protein engineering from the École Polytechnique Fédérale de Lausanne (EPFL, Switzerland), he moved to the laboratory of Structural Immunology at the Institut Pasteur in Paris, France, performing structure-function studies on a major adhesin of *Plasmodium falciparum*. In 2010, he joined the R&D department of Collectis in Paris, France, working on the development and implementation of sequence specific designer nucleases including the transcription activator-like effector nucleases TALEN®. He then joined the Collectis facility based in New York, NY, USA, leading projects associated with the development of the T-cell chimeric antigen receptor (CAR) technology.

An oxygen sensitive self-decision making engineered CAR T-cell

Alexandre Juillerat, Alan Marechal, Jean Marie Filhol, Yannick Valogne, Julien Valton, Aymeric Duclert, Philippe Duchateau and Laurent Poirot

<http://www.nature.com/articles/srep39833>

About Collectis

Collectis is a biopharmaceutical company focused on developing immunotherapies based on gene edited CAR T-cells (UCART). The company's mission is to develop a new generation of cancer therapies based on engineered T-cells. Collectis capitalizes on its 17 years of expertise in genome engineering - based on its flagship TALEN® products and meganucleases and pioneering electroporation PulseAgile technology - to create a new generation of immunotherapies. CAR technologies are designed to target surface antigens expressed on cells. Using its life-science-focused, pioneering genome-engineering technologies, Collectis' goal is to create innovative products in multiple fields and with various target markets. Collectis is listed on the Nasdaq market (ticker: CLLS) and on the NYSE Alternext market (ticker: ALCLS). To find out more about us, visit our website: www.collectis.com

Talking about gene editing? We do it. TALEN® is a registered trademark owned by the Collectis Group.

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