



PRESS RELEASE

Collectis Announces a New CAR Architecture Controlling CAR T-Cell Functions

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

New York, January 11, 2016 – Collectis (Alternext: ALCLS – Nasdaq: CLLS) today announced the publication of a study in *Scientific Reports*, a Nature Publishing Group journal, describing the design and development of a new CAR architecture with an integrated switch-on system that permits control over CAR T-cell functions. This integrated switch-on system offers the advantages of controllable CAR T-cells for safety while allowing for the possibility of multiple cytotoxicity cycles using a small molecule drug.

The possibility to control spatially and temporally the CAR T activity is very desirable to mitigate potential unwanted risks, such as cytokine-release syndrome¹ (CRS) and the “on-target, off-tumor” effect². To date, few strategies are available and mostly rely on suicide mechanisms that ultimately lead to a complete eradication of the engineered T-cells, thus resulting in a premature end of the treatment. Consequently, implementing non-lethal, spatio-temporal control of gene edited CAR T-cells represents an important advancement in improving the CAR T-cell technology.

In this report, Alexandre Juillerat, Ph.D., and his collaborators engineered a system directly integrated within the CAR architecture. In particular, they showed that such system turns a CAR T-cell from an off-state to an on-state upon addition of a small molecule, inducing the cytolytic properties of the gene edited T-cell. Overall, this non-lethal system not only offers the advantage of a temporal control of activation to mitigate the risk of CAR-induced toxicities but also enables opportunities for spatial activation of the engineered CAR T-cells using local targeted drug delivery.

Alexandre Juillerat, Ph.D. Innovation Senior Scientist

Dr. Alexandre Juillerat, Ph.D., graduated in Chemistry of 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.

¹ CAR T-cell therapy can cause several worrisome side effects, including the cytokine-release syndrome. The infused T-cells release cytokines, which are chemical messengers that help the T-cells carry out their duties. With cytokine-release syndrome, there is a rapid and massive release of cytokines into the bloodstream, which can lead to dangerously high fevers and precipitous drops in blood pressure.

² Off-tumor/on-target toxicities are the recognition of normal tissues expressing the tumor-associated antigen.

Design of chimeric antigen receptors with integrated controllable transient functions

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

<http://www.nature.com/articles/srep18950>

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 16 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 S.A. is listed on the Nasdaq Global 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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