Esperite's business unit develops therapy for Crohn's disease perianal fistulas

Published on October 21, 2016 at 2:08 AM

Esperite's business unit The Cell Factory, in collaboration with Women's and Children's Health Department of the University of Padua and the Padua University Hospital have started a translational project on extracellular vesicles (including exosomes) first in man use in treatment of Crohn's disease perianal fistulas. Inflammatory bowel disease (IBD) affects approximately 0.5% of the western countries population and this number is rapidly increasing. There are over 0.5 million people in the US and over 1 million in Europe with Crohn's disease, with over 10 new cases per 100.000 people every year. The annual cost of therapy exceeds 5 billion USD in the US only (CDC). Up to 50% of Crohn's disease patients are affected with difficult to treat perianal fistulas, and 75% require surgery (CDC).

Esperite's business unit The Cell Factory in collaboration with Women's and Children's Health Department of the University of Padua and the Padua University Hospital are developing therapies for inflammatory bowel disease (IBD) using extracellular vesicles (EVs). The first target is Crohn's disease perianal fistulas in adults. A first in man study using EVs including exosomes for treatment of Crohn's disease perianal fistula will start in 2017.

Inflammatory bowel disease (IBD) encompasses a spectrum of diseases affecting gastrointestinal tract. The most common are Crohn's disease and ulcerative colitis. IBD is a chronic and often recurring inflammation of the intestines with unknown cause and limited treatment options. In the most severe cases of Crohn's disease, the patients suffer from perianal fistulas that significantly affects normal activity and may lead to complications such an increased risk of cancer and life-threating systemic inflammation. In Europe current treatment of Crohn's disease is focused on anti-TNF-alpha therapy whereas anti-integrin biologics are an alternative available in the US. Unfortunately, perianal fistulas often do not respond to these systemic treatments. Several clinical trials are ongoing to target perianal fistulas using allogenic mesenchymal stem cells (MSCs) with very positive results.

Our approach is focused on using extracellular vesicles (including exosomes) derived from mesenchymal stem cells (MSCs) for the first time in the treatment of inflammation responsible for Crohn's disease perianal fistulas.

Esperite has acquired the full rights of a broad patent family enabling MSC-derived extracellular vesicles use in treatment of all autoimmune, chronic and acute inflammatory diseases. EVs including exosomes are nanometre-size, natural biological particles secreted by different types of cells in vivo and in vitro. They contain proteins, growth factors, mRNA and other molecules responsible for the therapeutic effect of MSCs. In addition, EVs have several advantages over allogenic MSCs e.g.: up to 10-times lower production costs, no risk of uncontrolled proliferation and differentiation, lower risk of immune response and easy and safe delivery into different tissues and organs in vivo. High stability allows for easy transport and storage of the "ready-to-use" products. All these features make the EVs a viable alternative to allogenic stem cell therapies in the near future.

Anti-inflammatory effects of EVs have been demonstrated in multiple preclinical studies in vitro and in vivo. The research team led by Professor Maurizio Muraca has demonstrated initially at Bambino Gesù Children's Hospital in Rome and now at the University of Padua in Italy, significant efficacy of MSC-derived EVs in treatment of IBD in animal models. Currently, Esperite's The Cell Factory and the University of Padua are performing in vivo experiments in animals using clinical grade EVs to confirm their safety, efficacy, bio-distribution and to explain the mode of action prior to clinical translation expected in 2017.

The scientific and medical rationale of using MSC-derived EVs in treatment of IBD and Crohn's disease is based on very positive preclinical and clinical results with allogenic MSCs. A growing body of evidence is suggesting that MSC secretory properties are responsible for their therapeutic effect. In addition, to date there is no convincing evidence that injected MSCs reach the injury site and survive for any significant time in the body. As a consequence, short-term survival of allogenic MSCs in vivo may limit EV secretion and therefore the amount of therapeutically active substance delivered in situ. Considering this, we expect that delivery of concentrated MSC-derived EVs directly to the site of injury would result in greater therapeutic effect when compared to allogenic MSC therapies. Local administration is safer for patients, and easier for medical personnel.

The extracellular vesicles including exosomes are produced at The Cell Factory, Esperite's business unit focused on

R&D and regenerative medicine. The Cell Factory produces ultra-pure EVs under GLP/GMP conditions, using proprietary technology for expansion of MSCs in fully defined media with no use of animal-derived components. Stem cells are expanded using a stirring bioreactor system. The Cell Factory's proprietary, closed cell culture system produces high purity EVs using pharmaceutical-quality sequential filtration. The system can be easily scaled up reducing production costs and improving footprint and process efficiency. EV products can be manufactured with this technology at least 10x more efficiently and more cheaply when comparing to allogenic MSC equivalent products.

Esperite is looking for partners to support the development of extracellular vesicle therapeutics.

Prof. Maurizio Muraca commented:

> The positive results obtained in recent clinical trials with MSCs represent a promising background for the therapeutic use of MSC-derived EVs. In addition, it is well known that MSCs are characterized by an inconstant behavior, due both to inter-donor variability and to possible unpredictable responses of transplanted cells, determined by the recipient's environment. At variance with their cells of origin, EVs are carrying specific signals which can be pre-determined during the production process. We thus expect their therapeutic effect to be more reproducible and less prone to the influence of the recipient's environment.

Source:
http://www.esperite.com/
