



Esperite (ESP) acquires patent to use MSC-derived exosomes for broad applications in immunology

The patent from Bambino Gesù Paediatric Hospital OPBG (Rome, Italy) will enable development of more effective and accessible therapies for a broad spectrum of inflammatory and autoimmune diseases including type 1 diabetes, arthritis and multiple sclerosis

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Esperite (Euronext: ESP) has acquired the full rights of a broad international patent enabling MSC-derived exosomes use in treatment of inflammatory and autoimmune diseases. Esperite is positioned now to spearhead advances in treatment for graft versus host disease (GvHD) after solid organ and cell transplantations, Crohn's disease, arthritis, multiple sclerosis, cystic fibrosis, stroke, traumatic brain and spinal cord injury, newborn encephalopathy, and type 1 diabetes among others. This exosome technology will permit development of more effective, safer and affordable therapies as an alternative to allogeneic MSCs.

Exosomes play important roles in cell-cell communication, regulating the cellular processes in vivo and mediate interactions of immune cells. It has been demonstrated that MSC-derived exosomes have more specific interactions with immune system cells, especially with B lymphocytes, when comparing to the origin cells (MSC). Exosomes presented a dose-dependent effect on inhibiting predominantly B lymphocytes. This will allow regulating more precisely the immune system response using exosomes in multiple clinical applications. Immunosuppressive and immunomodulatory effect of exosomes could be enhanced by special culture conditions of MSC and by addition of binding molecules to the exomes, for example annexins.

Exosomes can have clinical applications as biological markers to give prognoses for various diseases, including the detection of cancer, and for the delivery of drugs to very specific targets reducing necessary doses and preventing off-target side effects. The patent covers the pharmaceutical compositions consisting or comprising exosomes to target anti-inflammatory drugs to specific tissues.

The Cell Factory, Esperite's R&D Division for regenerative medicine, has broadened its bioproduction platform and patent portfolio with the exosome manufacturing technology for a broad application in regenerative medicine therapeutics. Exosome production is based on The Cell Factory's proprietary technology platform for clinical grade production of MSC. The Cell Factory developed the MSC expansion method, in compliance with GMP guidelines and ATMP regulations, using neither animal nor human originated products, sera or feeders during the entire process of storage and bioproduction. This ensures a high purity of MSC and their secretome, including exosomes. Production can be easily scaled-up in 3D cell cultures bioreactors for high-throughput manufacturing.

The exosomes high stability allows for easy transport and storage of the "ready-to-use" products. Exosomes can be cryopreserved in a very small volume without cryoprotectants, and can be used immediately after thawing without washing, which is very important for routine use at hospitals. Exosomes properties will allow non-invasive routes of administration and application by the patients at home. It is expected that exosomes will become a vital alternative for allogenic stem cell therapies in the near future.

Exosomes are nanometre-size vesicles (microvesicles) 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 stem cells. Exosomes can be easily and safely delivered into different tissues and organs in vivo. Exosomes have no HLA markers reducing the immune response and making them a universal vector for drug delivery. Therefore, it is expected that clinical trials and registration process will be fast for the medicinal products containing exosomes.

Billions-worth market of stem cell therapies mainly use stromal/mesenchymal stem cells (MSC), with over 500 MSC clinical trials worldwide. In most of the applications, the immunomodulatory and trophic capabilities of MSC are utilized. It has been demonstrated that exosomes secreted by MSC have similar immunomodulatory potential as the origin cells and can be used instead of MSC in therapy. Esperite's acquired patent covers exosome applications in treatment of all autoimmune, chronic and acute inflammatory diseases: rheumatoid arthritis, inflammation of connective and vascular tissues (rheumatology), autoimmune inflammatory disease, systemic vasculitis, giant cell arteritis, Wegener's granulomatosis, Henoch-Schonlein purpura, central nervous system vasculitis, cryoglobulinaemia, multiplex mononeuritis, Takayasu's arteritis, Burger's disease, intestinal chronic inflammatory diseases, Crohn's diseases and ulcerative colitis, autoimmune haemolytic anaemia, Addison's diseases, Type 1 diabetes and adult late-onset autoimmune diabetes, recurrent autoimmune diabetes in long standing diabetic patients after receiving islet or pancreas transplantation, systemic lupus erythematosus, dermatomyositis, scleroderma, Sjogren's syndrome, multiple sclerosis, chronic autoimmune hepatitis, primary biliary cirrhosis, psoriasis, alopecia areata, vitiligo, Good-pasture's syndrome, Guillain-Barré's syndrome, chronic glomerulonephritis, dermatitis and

eczema, Reiter's syndrome, reactive arthritis, cystic fibrosis, sinusitis, chronic bronchitis, periodontal disease and diverticulosis among others.

Another important application of exosomes is prevention of transplant rejection of cells, tissues, organs and in gene therapy. Exosomes injection will reduce immune response and will stimulate development of immune tolerance. Ready-to-use exosomes will be very attractive medicinal product for multiple injections with no need of hospitalisation and therefore more accessible for patients compared to cell infusions.

Application of exosomes in acute inflammatory diseases is of special importance in neurology. For example, "off-the-shelf" exosomes can be immediately used in brain stroke patients, traumatic brain and spinal cord injury and newborn encephalopathy to reduce neuroinflammation and prevent damage of neurons.

The Ospedale Pediatrico Bambino Gesù OPBG (Rome, Italy) is the largest paediatric Hospital and research center in Europe, providing over 1.550.000 healthcare services each year to children and adolescents from all over the world.

Marcin Jurga, R&D Manager of The Cell Factory: "The regenerative medicine field requires multiple tools to provide effective therapies for different unmet medical needs. Therapeutic potential of mesenchymal/stromal cells has been well demonstrated in several clinical trials. Exosomes offer even more flexibility in design of new therapies, production of bioactive artificial tissues and implants, and non-invasive delivery methods. This technology will provide safer and more affordable treatments for patients."

Frederic Amar, CEO of ESPERITE group: "Esperite is pioneering new technologies in regenerative medicine to improve the way we address human diseases. We are delivering on our commitment to transform healthcare standards. The exosome technology will enable new therapeutic approaches, more accessible and affordable. Esperite confirms its role as the leading force in regenerative medicine"

About ESPERITE

ESPERITE Group, listed at Euronext Amsterdam and Paris, is a leading international company in regenerative and predictive medicine established in 2000.

To learn more about the *ESPERITE* Group, or to book an interview with CEO Frederic Amar: [+31 575 548 998](tel:+31575548998) - ir@esperite.com or visit the websites at www.esperite.com and www.genoma.com.