

UIB and Lipopharma's scientists discover a third basic and critical requirement to transform a normal cell into a cancer cell.

- ▲ *Low sphingomyelin levels are found in cancer cells and promote their proliferation.*
- ▲ *A new compound that normalizes sphingomyelin levels, 2-hydroxyoleic acid, constitutes a potent and non-toxic treatment against cancer.*

Palma de Mallorca, December 6th 2011. Prof. Dr. Pablo Escriba, main promoter of Lipopharma, and his team of researchers at the **University of the Balearic Islands** (Spain) have discovered a new basic requirement to transform a normal cell into a cancer cell: the presence of very **low membrane levels of sphingomyelin**, a major phospholipid in the membrane of normal human cell membranes.

Until now it was known that the requirements for a normal cell to undergo tumorigenic transformation are: (1) activation of proto-oncogenes to oncogenes that produce altered proteins that accelerate cancer cell growth, and (2) inactivation of proteins produced by tumor suppressor genes (which normally act as repressors of this proliferation).

The type and number of oncogenes and tumor suppressor genes altered in a given cancer varies from cancer to cancer and from patient to patient. However, the new discovery shows that 100% of all human cancer cells studied until now exhibit low sphingomyelin levels. The work, that has been published today in the *Proceedings of the National Academy of Sciences of the USA*, highlights the relevance of this phenomenon, which could be connected with impairment of proliferation signals that occur at the membrane. Thus, sphingomyelin hampers the binding of certain oncogene products and shortcuts the proliferation signals sent to the cell nucleus to activate cancer cell division.

In normal cells, high sphingomyelin levels reduce the proliferative capacity of the cell, so that restoration of this situation in cancer cells would be a potential means to treat cancer. In fact, this study shows that the synthetic fatty acid, 2-hydroxyoleic acid, activates the enzyme **sphingomyelin synthase (SMS)** and restores membrane sphingomyelin to those levels found in normal cells. Not only is this compound the first SMS activator known but also a potent inhibitor of tumor growth. In fact, 2-hydroxyoleic acid has been designated orphan drug for the treatment of glioma (a type of severe brain cancer) by the European Medicines Agency, and clinical studies in patients will soon start to test its efficacy. In addition, these results further demonstrate that low sphingomyelin is the third basic requirement (in addition to oncogene activity and tumor suppressor gene product inactivation) to induce cancer and that this phenomenon is more important than the other requirements, as cancer cells reduce their proliferative capacity upon sphingomyelin restoration. Finally, this study will also open a new field in anticancer drug discovery, as **SMS can be considered a new drug target in oncology and 2-hydroxyoleic acid the first specific and potent regulator of its activity**.

Contact:

Lipopharma

Ctra. Valldemossa, Km. 7,4. ParcBIT. Edif. 17. 2nd. C-8. E07121 – Palma de Mallorca. Spain.

Tel. (+34) 971 439 886 :: Email: info@lipopharma.com :: www.lipopharma.com

ADDITIONAL INFORMATION

About Minerval®

Minerval® (2-hydroxyoleic acid) is a novel synthetic lipid that regulates the membrane lipid structure and composition of glioma cancer cells (including a marked increase in Sphingomyelin levels), inducing a translocation of **Ras** to the cytosol and subsequently inactivating the **MAPK** signalling pathway, which is found to be altered in almost 90% of adult glioblastomas. This deregulation of the MAPK pathway by Minerval® induces **differentiation** and **selective autophagy** in cancer cells but not in normal cells.

Minerval® is currently being tested for treatment of several types of cancer, most of them with very poor therapeutic prognosis, including lung cancer, malignant brain tumours, pancreatic cancer, leukemia, prostate cancer, colorectal cancer or breast cancer. Available preclinical results indicate that Minerval could become the first ever effective treatment for some of the most aggressive types of cancer such as of non-small cell lung cancer (NSCLC), glioma or pancreatic cancer. Minerval couples its powerful anticancer effect with absence of toxicity at therapeutic doses and its oral administration leads to a very attractive profile in cancer treatment. Moreover, as **Dr. Pablo V. Escribá**, inventor of Minerval®, Professor of Cell Biology at the UIB, co-founder and main scientific promoter of Lipopharma points out "having a mechanism of action (MOA) totally different to most drugs currently used in oncology, brings a new hope in a very stringent research area, where advances have been very modest in the last decades for patients suffering from this deadly types of cancer. The novel MOA adds value as an agent that can be applied either as mono-therapy or in combination with other drugs". Lipopharma is preparing the first clinical trials in humans for the treatment of glioma to start in Q1 2012 and expects to have this compound in the market for treatment of glioma by 2014. Minerval® was designed by Dr. Escribá and his team of scientists at the Department of Biology of the University of the Balearic Islands and later licensed to Lipopharma for its oncology indications.

About MLT

Membrane-Lipid Therapy (MLT) derives from a highly specialized scientific knowledge developed by Lipopharma's scientists and consists on the design of structure-based molecules that regulate the structure and functions of the membrane lipids, instead of targeting cellular proteins. This innovative know-how is Lipopharma's main expertise and lays on new discoveries made by Lipopharma's scientists related to the role of membrane lipids and membrane lipid structure on the regulation of localization and activity of membrane signalling proteins. This new therapeutic approach (MLT) constitutes a "disruptive innovation" which we believe will radically change the way diseases are fought, due to its exceptional combination of very high efficacy and lack of side effects.

About Lipopharma

Lipopharma is an innovative biopharmaceutical company based in Palma de Mallorca (Spain), spun off from the University of the Balearic Islands, that specializes in the rational design and clinical development of pharmaceutical/nutraceutical products aimed at the prevention and treatment of human pathologies. The design of molecules is based on structure-function principles according to the unique MLT know-how developed by Lipopharma's scientific team. Lipopharma is also developing a portfolio of new products based on the MLT with potential applications in fields such as neurodegenerative diseases, inflammation or cancer. More detailed information on Lipopharma's pipeline can be found at the company's website (www.lipopharma.com)

Disclaimer

Except for historical information, this press release may contain forward-looking statements, which reflect the companies' current expectations regarding future events. These forward looking statements involve risk and uncertainties, which may cause but are not limited to, changing market conditions, the successful and timely completion of clinical studies, the establishment of corporate alliances, the impact of competitive products and pricing, new product development, uncertainties related to the regulatory approval process and other financial, technical or market risks. All forward-looking statements are qualified in their entirety by this cautionary statement and Lipopharma Therapeutics SL does not undertake any obligation to revise or update this press release to reflect events or circumstances after the date hereof