



Yissum Announces the Discovery of a Novel Small Molecule With Potent Anti-Metastatic Activity

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- Yissum Ltd. Tsipi Haitovsky, +972-52-598-9892 Media Liaison tsipih@yissum.co.il Yissum Ltd., the Technology Transfer Company of the Hebrew University of Jerusalem, today announced that scientists from the School of Pharmacy at the Hebrew University of Jerusalem discovered a novel orally available drug that prevents metastasis formation in various types of cancers. The novel drug is a small molecule named cis-ACCP which is a prototype of a family of compounds that may be administered orally and was shown as highly effective in rodents without inducing any adverse side-effects. The development of the drug was a collaborative effort of the laboratories of Prof. Eli Breuer, Prof. Reuven Reich and Prof. Amnon Hoffman, all from the School of Pharmacy at the Hebrew University of Jerusalem. The work was published in the Journal of Medicinal Chemistry (Hoffman et al., electronic publication ahead of print: DOI: 10.1021/jm701087n).

Nava Swersky Sofer, Yissum's President and CEO, stated, "This new class of drugs could potentially change the lives of millions of cancer patients by providing protection from metastasis in the form of a pill. Of course, many years of testing are ahead of us before the drug can reach the patients, but this is the first step."

cis-ACCP, the novel drug, inhibits enzymes called matrix metalloproteinases (MMPs), which are extracellular enzymes known to play a crucial role in physiological tissue remodeling and repair. However, pathological over-expression of MMPs has been associated with a variety of chronic diseases including cancer, arthritis, osteoporosis, multiple sclerosis, arteriosclerosis, congestive heart failure, chronic obstructive pulmonary disease, liver cirrhosis, and others. In cancer, over-expression of MMPs enables the tumorigenic cells to invade other tissues, leading to metastasis formation. In most cases, this is a turning point that renders the tumor untreatable by conventional treatments.

The efficient inhibition of MMPs is therefore an important therapeutic target that has attracted considerable attention within the research community for the last two decades. Yet, in spite of the huge effort devoted to this goal, no clinically useful inhibitor has been developed to date. The main obstacles encountered by scientists trying to develop such inhibitors were high toxicity leading to unacceptable side-effects, and low bioavailability since most of the potential drugs were not soluble in water and hence could not effectively reach the extracellular fluid, where their target proteins are found.

In contrast, cis-ACCP, has a very low toxicity as revealed by preclinical trials on rodents. This is achieved via two important properties of the drug: it inhibits the activity of selected MMPs without inhibiting similar proteins; and due to its hydrophilic (water-soluble) nature, the drug does not enter the cells, but rather stays in the extracellular fluid, where it exerts its effect. In other words, cis-ACCP is self-targeted to its appropriate site of action, namely outside cells, which reduces potential intracellular toxicities.

The preclinical experiments described in the paper also showed that the novel drug prevents cancer cells from invading adjacent tissues (and thus forming metastases), and is effective in treating melanoma (skin cancer) and prostate cancer in rodent model systems. The results showed that cis-ACCP significantly inhibited both tumor growth and metastasis formation.

About the Researchers

Professor Eli Breuer received his academic education at the Hebrew University of Jerusalem and his post doctoral training in the laboratory of Nobel Laureate Herbert C. Brown at Purdue University in Lafayette, Indiana USA. In the past he served as Head of Department of Medicinal Chemistry and later as Director of School of Pharmacy of the Hebrew University of Jerusalem. Breuer was National Representative of Israel in the Division of Chemistry and Human Health of the International Union of Pure & Applied Chemistry (IUPAC) for several years, and is currently a member of the Subcommittee on Medicinal Chemistry and Drug Development of IUPAC.

Professor Amnon Hoffman has over 20 years of experience in the field of pharmacokinetics and pharmacodynamics, with a special interest in the biological aspects of drug delivery systems. Prof. Hoffman is currently the Chairman of the Department of Pharmaceutics and Head of the MSc program in Clinical Pharmacy at The Hebrew University of Jerusalem's School of Pharmacy. He has published over 100 scientific papers and book chapters. He holds 15 patents on novel drug delivery systems, and orally bioavailable peptides. In addition, he is the scientific co-founder of Intec Pharma, a startup company developing a new technology

sustained release drug delivery systems, Gastro-retentive Dosage Form (GDRF).

Professor Reuven Reich received his academic education at the Weizmann Institute of Science, Rehovot and his post doctoral training in the laboratory of Dr. George Martin at National institute of Dental Research, NIH, Bethesda, USA. Professor Reuven Reich has over 20 years of experience in the field of metastasis research and metalloproteinases.

About Yissum

Yissum was founded in 1964 to protect the Hebrew University's intellectual property and commercialise it. \$1 Billion in annual sales are generated by products based on Hebrew University technologies licensed out by Yissum. Ranked among the top technology transfer companies in the world, Yissum has registered 5500 patents covering 1600 inventions; licensed out 480 technologies and spun out 65 companies.

Yissum's business partners span the globe and include companies such as Novartis, Microsoft, Johnson & Johnson, Merck, Intel, Teva and many more. For further information please visit www.yissum.co.il.

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