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Philogen
innovating targeting

Philogen announces the publication of a new study in the European Journal of Nuclear Medicine and Molecular Imaging

The study describes the discovery of GCPIII as the protein responsible for the accumulation of conventional PSMA targeting agents in healthy organs

This discovery will assist in the development of small molecule therapeutics which can overcome the limitations of first-generation PSMA ligands

Philogen S.p.A., a clinical-stage biotechnology company focused on the development of innovative antibody and small molecule ligands, announces the publication of a study in the peer-reviewed journal "European Journal of Nuclear Medicine and Molecular Imaging" describing the identification of Glutamate CarboxyPeptidase III (GCP III) as the protein responsible for the undesired side effects of conventional PSMA targeting agents approved for the treatment of metastatic prostate cancer.

The study was conducted by scientists at Philochem AG, the wholly-owned Swiss subsidiary company of Philogen. The paper can be accessed on the European Journal of Nuclear Medicine and Molecular Imaging website at the following link.

PSMA is a tumor-associated antigen which is highly expressed in prostate cancer. Radioligand therapeutics based on conventional PSMA targeting agents show survival benefit in patients with metastatic prostate cancer, but typically suffered from xerostomia (i.e., dry mouth) and other adverse effects due to the accumulation of the drug in salivary glands and kidneys. Scientists at Philochem identified a closely related isozyme of PSMA, called Glutamate CarboxyPeptidase III (GCPIII), as responsible for the off-target accumulation of PSMA targeting agents in these two healthy organs. Fluorescence polarization experiments highlighted the cross-reactivity of the drug binding both to PSMA (its target) and to GCPIII (so-called anti-target), with high affinity. The hypothesis was corroborated by immunofluorescence analyses, confirming a strong expression of GCPIII in human specimens of salivary glands and kidney. Based on these results, Philochem proposes the membranous expression of GCPIII in kidney and salivary glands as the cause of the off-target accumulation of PSMA targeting ligands in these organs.

The reported achievements could lead to the rational design of novel selective PSMA inhibitors that do not cross-react with GCPIII, enabling the discovery of a novel class of PSMA-targeting radioligand therapeutics with improved performance.

Dario Neri, Chief Executive Officer of Philogen commented: "*This study illustrates the mechanism of accumulation of PSMA-targeted drugs in salivary glands and kidney of patients. This knowledge is already helping scientists at Philochem to develop small molecule therapeutics which can overcome limitations of first generation PSMA ligands*."

Philogen Group Description

Philogen is an Italian-Swiss company active in the biotechnology sector, specialized in the research and development of pharmaceutical products for the treatment of highly lethal diseases. The Group mainly discovers and develops targeted anticancer drugs, exploiting high-affinity ligands for tumor markers (also called tumor antigens). These ligands - human monoclonal antibodies or small organic molecules - are identified using Antibody Phage Display Libraries and DNA-Encoded Chemical Library technologies.

The Group's main therapeutic strategy for the treatment of these diseases is represented by the so-called tumor targeting. This approach is based on the use of ligands capable of selectively delivering very potent therapeutic active ingredients (such as pro-inflammatory cytokines) to the tumor mass, sparing healthy tissues. Over the years, Philogen has mainly developed monoclonal antibody-based ligands that are specific for antigens expressed in tumor-associated blood vessels, but not expressed in blood vessels associated with healthy tissues. These antigens are usually more abundant and more stable than those expressed directly on the surface of tumor cells. This approach, so called vascular targeting, is used for most of the projects pursued by the Group.

The Group's objective is to generate, develop and market innovative products for the treatment of diseases for which medical science has not yet identified satisfactory therapies. This is achieved by exploiting (i) proprietary technologies for the isolation of ligands that react with antigens present in certain diseases, (ii) experience in the development of products targeted at the tissues affected by the disease, (iii) experience in drug manufacturing and development, and (iv) an extensive portfolio of patents and intellectual property rights.

Although the Group's drugs are primarily oncology applications, the targeting approach is also potentially applicable to other diseases, such as certain chronic inflammatory diseases.

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