
Philogen Announces Publication of a New Study in Collaboration with Google focused on Machine Learning models applied to DNA-Encoded Chemical Library Technology

The collaboration has focused on the use of Google's Machine Learning models combined with Philochem's DNA-Encoded Chemical Libraries

The research activity promises to have a direct impact on the discovery of novel tumor-targeting small organic ligands with broad applicability in a number of different indications

Siena, Italy, March 28, 2023 - 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 new study conducted in collaboration with Google focused on the use of Machine Learning models applied to the screening of DNA-Encoded Chemical Libraries (DELs). Philogen practices DEL technology within its fully-owned Swiss-based Philochem AG subsidiary.

DELs emerged as an efficient and cost-effective ligand discovery tool. The technology allows the rapid selection of specific binders ("Phenotype"), physically connected to unique DNA tags ("Genotype") that work as amplifiable identification barcodes. Philochem has synthesized several DNA-Encoded Chemical Libraries, featuring different designs, that have yielded high affinity and selective binders to a variety of target proteins of pharmaceutical interest.

Results of DEL selection are extremely data-rich, as they may contain enrichment information for billions of compounds on a variety of different targets. In principle, this information can be exploited using computational methods both for the affinity maturation of DEL-derived HIT compounds and for the characterization of binding specificities.

In this collaborative project, Google and Philochem, a fully-owned subsidiary of Philogen, have applied DEL Technology and Instance-Level Deep Learning Modelling to identify tumor-targeting ligands against Carbonic Anhydrase IX (CAIX), a clinically validated marker of hypoxia and of clear cell Renal Cell Carcinoma. The approach yielded binders that showed accumulation on the surface of CAIX-expressing tumor cells in cellular binding assays. The best compound displayed a binding affinity of 5.7 nM and showed preferential tumor accumulation in *in vivo* pre-clinical models of Renal Cell Carcinoma.

The successful translation of LEAD candidates for *in vivo* tumor-targeting applications demonstrates the potential of using machine learning with DEL Technology to advance real world drug discovery.

The results of the study are available as preprint on the BioRxiv website at www.biorxiv.org/content/10.1101/2023.01.25.525453v1.

Dario Neri, Chief Executive Officer of Philogen commented: *"We are excited by the potential of the synergy between DNA-Encoded Chemical Libraries and Artificial Intelligence. The powerful discovery approach that we have developed together with Google should be broadly applicable to additional targets of pharmaceutical interest for the discovery of novel drug prototypes."*

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 focuses on the discovery and development of 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 concept of 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, more stable and better accessible than those expressed directly on the surface of tumor cells. The elaborate expertise in the field of vascular targeting enabled the generation of a strong portfolio with many ongoing projects which are currently 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 which selectively accumulate at the disease sites, (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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