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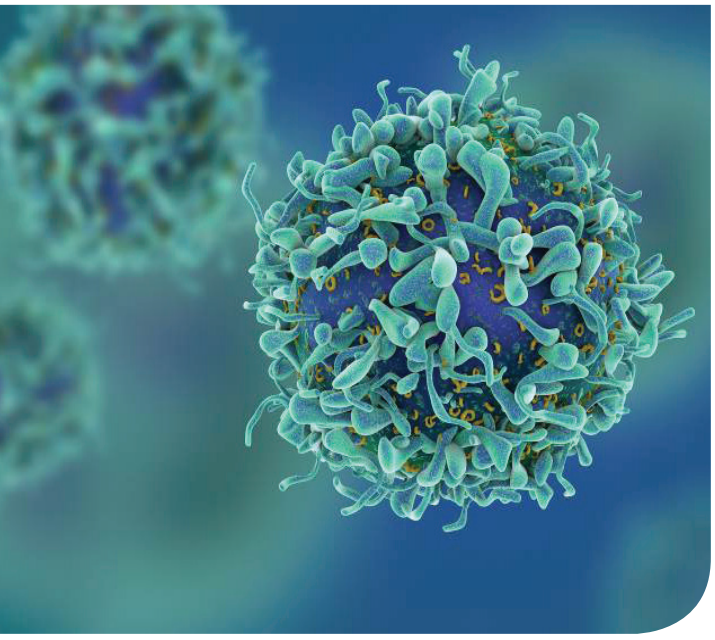

Shedding light on phenotypic drug discovery to advance oncology efforts

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Tumour cells are extremely effective at exploiting and evading human biology for the unfortunate benefit of disease progression. Consequently, developing therapeutics for oncology requires a similar approach to fighting cancer itself—investigators must use multifaceted, creative, and comprehensive strategies. Use of target-based and broader – or phenotypic – approaches are not mutually exclusive. Both can, and should, be incorporated at all stages of the drug discovery continuum to best meet the challenges inherent in this therapeutic space.

One key challenge in oncology is the complexity of the host tumour microenvironment (TME). Cancerous cells of all types do not propagate in isolation, but as part of an intricate, hierarchical interaction of support tissue, vasculature, and immune cells that together form the TME. Tumour shape is also diverse; tumours are not flat, but three-dimensional, with gradients of oxygenation, nutrition, and pH. Complex human biology thus contributes to the difficulty in broadly predicting drug candidate behaviour based on single analyte data. This is where phenotypic drug discovery shines. With a comprehensive, human disease model and cell-based strategy, one can gain actionable insights for candidate efficacy, toxicity, mechanism of action and more, on multiple pathways simultaneously.

Eurofins Discovery's OncoPanel and ImmunoSignal services, together with BioMAP Phenotypic Profiling and Screening services, comprise the Eurofins Discovery Phenotypic Centre of Excellence. Since 2000, this team of scientific and operational experts has advanced candidate pipelines for nearly 500 clients. With technical capabilities centrally located, the team is well positioned to provide greater impact, with cross-platform collaborations and tailored services.

OncoPanel allows profiling of test agents and combinations across a range of cancer types, guiding patient population selection and stratification. With over 300 2D and 100 3D cancer cell line models, including epigenetic, kinase, and gene-focused panels, thorough candidate assessment is possible. ImmunoSignal offers test agent profiling using a suite of assays to evaluate effects on immune cell and Toll-like receptor function. BioMAP services consist of quality-assured human primary cell systems to model specific disease states, analytics powered by the BioMAP Reference Database to provide actionable insights, and expert interpretation of compound activities on translationally relevant biomarker readouts. BioMAP Oncology Panels enable scientists to assess effects of drug candidates in human TME models and BioMAP Combo ELECT services facilitate determination of combination therapy outcomes in any individual system. Eurofins Discovery Phenotypic Services client reports inform on pipeline progression, key opinion leader reports, and investigational new drug applications. For more information, visit *www.eurofinsdiscoveryservices.com*

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Improving cancer treatment with molecular diagnostics – *From patient molecular profiling to liquid biopsy*

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Eurofins Clinical Diagnostics supports the pharmaceutical industry with specialty diagnostics tests to identify those patients who can best benefit from a particular treatment. Molecular diagnostics tests inform the physician on the patient's molecular profile, aiding in drug recommendation and dosage adjustment in a personalised manner. The main advantages of molecular profiling include not only an increase in drug efficiency thanks to targeting the right patients but also better drug safety profiles, i.e. fewer adverse side effects and lower toxicity, which greatly benefit patients. Some successful examples in cancer treatment where Eurofins is involved are: FLT3 gene profiling to guide acute myeloid leukemia (AML) treatment, and BCR-ABL fusion gene molecular profiling for Acute Lymphoblastic Leukemia (ALL) treatment.

Another important innovation in molecular diagnostics applied to oncology is the use of liquid biopsy. Once a patient is suspected to have cancer, a confirmatory diagnosis by tissue biopsy will follow. If cancer diagnosis is confirmed, tumour molecular characterisation will be the next step to provide the full picture of the clinical situation. This service, provided by Eurofins Clinical Diagnostics, enables oncologists to make an informed decision on the best treatment for each individual patient. It is recommended for the patient to be monitored by using liquid biopsy, an innovative test developed at Eurofins and that follows on cancer driver mutations in tumour cell-free DNA. As the test is non-invasive, i.e. only a blood draw is required; it can be performed periodically without discomfort for the patient. Depending on the patient's response to the treatment, i.e. changes in cancer driver mutations, modifications of drug dosage and schedule can be recommended.

Eurofins Clinical Diagnostics offers tissue and liquid biopsy testing for precision therapy and dynamic monitoring of cancer patients and is involved in several clinical trials with pharmaceutical companies to improve cancer patient outcomes thanks to more personalised treatments. One of those important trials where Eurofins is currently participating involves a new Tyrosine Kinase Inhibitor (TKI) combined with Letrozole for the treatment of breast cancer. For more information visit: *www.eurofins.com/clinical-diagnostics/clinical-diagnostics-services/oncology/*

Eurofins provides one-stop solution for biocidal products authorisation

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Biocidal Products are substances or mixtures used to "control" any harmful organism by other means than just physical or mechanical action. Some examples are antimicrobials, anti-fouling, preservatives, rodenticides, insecticides, and repellents. Since they are widely used in households, hospitals, industry, and institutional areas, and they might be harmful towards humans and the environment, their marketing is highly regulated.

Biocidal Product authorisation is disciplined by the European Regulation (EU) 528/2012. It is quite a long and complex path, that usually requires the collaboration between a consultancy team and a number of analytical laboratories (chemical, microbiological for antimicrobials and preservatives, toxicological, and eco-toxicological).

Eurofins BioPharma Product Testing Italy provides clients with a ONE STOP SOLUTION for Biocidal Products Authorisations. Eurofins' consultancy team creates the best testing strategies that enables clients to save time and resources. The chemical laboratory manages all chemical physical analyses. The microbiological laboratory takes care of all efficacy testing on antimicrobials and preservatives.

The toxicological laboratory performs all the *in vitro* toxicological tests with the eco-toxicological lab to support requests of aquatic testing or biodegradability. And the project management team ensures the project meets its timelines and works in close cooperation with the consultancy team who, as study monitor, revises data and corrects the strategy when necessary.

Once all analytical data are collected, the consultancy team can prepare the human health and environmental risk assessment, the product authorisation report, and the IUCLID dossier.

In addition to the preparation of dossiers for biocidal products, the consultancy team constantly monitors the developments of the regulatory issues, assuring an exhaustive fulfillment of clients' designated obligations as a producer.

Antimicrobials and preservatives have further support due to the presence in the consultancy team of a CEN/TC 216 Expert and CEN/TC216/WG3 Convenor who can provide clients with the best advice on how to address the product efficacy. For more information visit: *www.Eurofins.com/bpt*

CRISPR/Cas – the system that revolutionises gene editing

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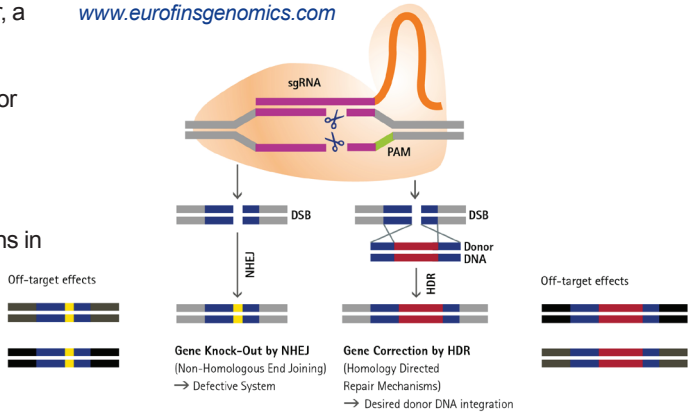
The CRISPR/Cas system is a self-defense mechanism of bacteria and archaea to fend off exogenous DNA. The ground-breaking article in *Science* in 2012 by Emmanuelle Charpentier, Jennifer Doudna et al. described the use of the CRISPR/Cas system as a molecular genetics tool. Since then, many researchers and companies have taken advantage of this new and easy technology to genetically modify organisms.

The mechanism behind the "molecular scissors" is the introduction of a double-stranded DNA cut at a predetermined target sequence by the Cas enzyme. The resulting double-strand break is detected by the cell's own DNA repair processes and subsequently fixed; however, a 10 to 15 bp insertion or deletion is typically introduced.

The development of modified Cas9 enzymes and the discovery of other Cas enzymes broadens the options for gene editing. Combined with the use of specifically designed guide RNAs, it is now possible to not only introduce targeted insertions and deletions but also to introduce certain mutations and entire gene constructs.

Recently, the CRISPR/Cas9 system was used in humans in a clinical setting. A patient who suffered from beta-thalassemia was treated with modified stem cells. Specifically, the patient's own hematopoietic stem cells were modified ex vivo using CRISPR/Cas9 and then re-infused into the patient's bloodstream. An equivalent treatment is already planned for sickle cell disease.

This new approach of cell-based therapies inevitably requires a multitude of novel genomics products but also novel testing. Eurofins Genomics provides many solutions, from cloning oligos, single guide RNAs to donor DNAs in the form of synthetic genes. The success of a gene edit can be determined by Sanger sequencing, fragment length analysis, or next generation sequencing. Eurofins' solutions are provided for research purposes, patient testing within clinical trials, and lost release testing of CRISPR modified primary cells amongst others. For more information, visit: *www.eurofinsgenomics.com*



Self Emulsifying Drug Delivery Systems as a formulation strategy to improve oral bioavailability

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The majority of new chemical entities show limited aqueous solubility. The oral delivery of these compounds presents a major challenge due to low bioavailability. Several formulation strategies are applied to improve the solubility, including salt formation, particle size reduction, solid dispersions and complexation. Especially when lymphatic absorption is targeted, lipid-based formulations like Self Emulsifying Drug Delivery Systems (SEDDS) are more appropriate.

SEDDS are isotropic mixtures of drugs, lipids, and surfactants, potentially with one or more hydrophilic co-solvents or co-emulsifiers. Following their oral intake, the digestive motility of the stomach and intestine provide the agitation necessary for self-emulsification into a fine oil-in-water emulsion. A distinction is made between SEDDS and self micro-emulsifying drug delivery systems (SMEDDS) or self nano-emulsifying drug delivery systems (SNEDDS), on the basis that the latter have a smaller droplet size and are visibly transparent instead of opalescent. SEDDS present the drug in a dissolved form, avoiding the rate-limiting dissolution step, and the small droplet size provides a large interfacial area for drug absorption. Surfactants help to solubilise the lipophilic drug compound and avoid precipitation of the drug in the gastro-intestinal lumen. SEDDS are applied either for indications where a quick onset of action is required or for sustained delivery by the addition of polymers.

Eurofins Amatsigroup (CDMO) offers the design and formulation of SEDDS based on pre-formulation solubility and phase-diagram studies to identify the most efficient self-emulsifying region. Ultimately, SEDDS are formulated as an oral solution in vials or gelatin capsules or are transformed into granules, pellets, or powders for filling in hard capsules or for tablet production. Liquid SEDDS can be converted into solid SEDDS by adsorption on solid carriers using conventional technologies like spray drying, granulation, and melt extrusion. To conclude, SEDDS are a unique and industrially feasible approach to overcome the problem of low oral bioavailability associated with lipophilic drugs. For more information visit: *www.eurofins.com/cdmo*

Eurofins Lancaster Labs' newly opened largest building expansion is Lean and Green

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Every inch of Lancaster's 168,000 ft^2 new building addition is designed with a LEAN concept to help analysts work smarter, not harder. The five-story state-of-the-art testing facility also began with firm roots in Green and Sustainability motives. And continually emerging technologies in the industry served as the impetus to expand and onboard next generation instrumentation and analytical techniques. To that, this new expansion along with renovations to existing labs broaden and enhance testing services such as Gene Therapy with expanded BSL2 capacity, Antibody Drug Conjugates (ADCs), Extractables and Leachables for both pharmaceutical and medical device products, Microbiology Sterile & Non-sterile and medical device products, and Method Development and Testing for small molecule products. This 13th expansion in the company's nearly 60-year history adds 50% more capacity to Lancaster's existing 330,000 square foot facility for a total of more than 1/2 million square feet.

Lean improves the client experience – During the architectural planning of all new additions or renovations of existing laboratories, facility engineers and designers engaged and collaborated with analysts performing the testing to determine the optimal work flow. Streamlining operations from sample administration/pickup to glassware and chemical storage to instrumentation – all parts of the workflow are optimised through a Lean process to improve quality and TAT for clients.

Green is good for the environment and bottom line – What began as a grass-roots employee Green Team several years ago to find ways to reduce waste, water, and energy usage, has blossomed to a formal Sustainability Programme. This programme has become vital to the company's recycling and conservation designs to the facility and surrounding campus. Some of the new building's Green design features include: magnetic driven chillers that require 30-50% less energy than other chiller plants, 100% capture of roof water for reuse of building chiller plants, 100% LED light package, white PVC roof to reflect heat away from the building, building vertical allows for four acres of usable space on a one-acre footprint, utilisation of condensing hot water boilers, use of point source exhaust to reduce the number of hoods/ Ventilated Balance Enclosures (VBEs), increased usage of VBEs instead of hoods to reduce exhaust from the building, exhaust heat recovery on exhaust fans to pre-heat the make-up air for the lab areas.

The "IT" factor for data quality – In addition to expanding and improving the physical lab designs, Eurofins Lancaster Laboratories invests significantly in IT infrastructure and security-supporting systems. As part of Eurofins BioPharma Product Testing, the largest network of harmonised GMP product testing laboratories worldwide with four facilities in the U.S. and 31 throughout Europe and Asia Pacific, all facilities in this integrated network have the same LEAN systems, customised proprietary Laboratory Information Management System (LIMS), and harmonised quality systems in place. Likely some of the company's strongest differentiators in continually driving down TAT and improving data quality has been through its innovative Electronic Lab Notebook system and secure online data access tool LabAccess.com. For more information visit: *www.Eurofins.com/bpt*

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