Proteomics for Precision Medicine

HOW TO ACCELERATE AND DE-RISK DRUG DEVELOPMENT IN ONCOLOGY

Right Biology, Right Target, Right Biomarkers

White Paper, May 2022

BIOGNOSYS
NEXT GENERATION PROTEOMICS

WHY DOES ONCOLOGY DRUG DEVELOPMENT FAIL?

Fewer than one in 20 new cancer drugs ever make it to market.[1] By enriching the understanding of target biology, proteomics can de-risk the drug development process and increase the likelihood of success.

Despite more than a century of dedicated research, cancer remains one of the leading causes of death.[2] Recent years have seen significant advances in treatment, however, there is still much to be done to ensure that scientific developments result in clinically meaningful improvements. On average, only 3% of oncology drugs ever make it to market[1], and many of those that do make a limited difference to quantity or quality of life for patients.[3,4]

The reasons for these failures can broadly be separated into three categories:

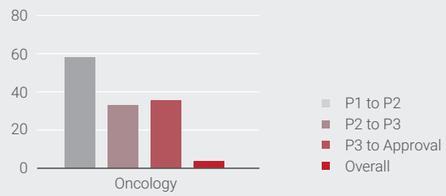
- **Incomplete understanding of underlying biology ('wrong biology'):** Genomic and transcriptomic data does not always reveal the true underlying complexity of cancer, leading to incomplete insights into the biological processes in tumors.
- **Incorrect target ('wrong target'):** Several cancer drugs do not act on their intended target. Analysis of oncology drugs in clinical trials found several cases of efficacy being achieved through off-target effects[5] which can result in toxicity and side effects.
- **Lack of effective biomarkers ('wrong biomarkers'):** A lack of effective biomarkers prevents effective patient identification and stratification, while hampering efforts to monitor treatment response in the clinic.

Although there are initiatives to de-risk the drug development process, continually applying the same tools and approaches is unlikely to lead to innovative, first- or best-in-class targets and transformative progress.

By uncovering the right biology, right target, and right biomarkers, Biognosys' **TrueDiscovery™, TrueTarget™, and TrueSignature™** proteomics platforms can generate the insights needed to support the next generation of cancer diagnostics, therapeutics, and clinical biomarkers.

Biognosys can lead you from the earliest stages of compound characterization through to identifying and validating biomarkers and developing the next generation of game-changing immunotherapies. We make it easy to interpret your data to help you get the insights you need. And our facilities are Good Laboratory Practice (GLP) certified and Good Clinical Practice (GCP) compliant, making us the first global large-scale proteomics service provider able to support you from the beginning to the end of your drug development journey.

(a) Probability of Success of Clinical Trial Phases in Oncology



b) Probability of Success of Clinical trials in Different Therapeutic Areas, Including Oncology and Without Oncology

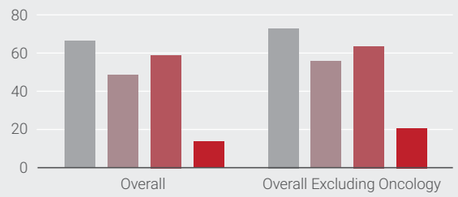


Fig 1. **a) & b).** Source: Chi Heem Wong, Kien Wei Siah, Andrew W Lo. "Estimation of clinical trial success rates and related parameters." Biostatics 20(2): April 2019, Pages 273-286. Published online: 31 January 2018. DOI: 10.1093/biostatics/kxx069

LEVERAGING PROTEOMICS ACROSS THE ONCOLOGY PIPELINE

Biognosys offers a unique suite of proteomics research platforms for every application, from discovery to clinic.

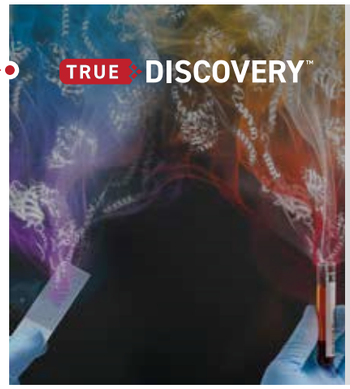
DISCOVERY

PRE-CLINICAL

CLINICAL

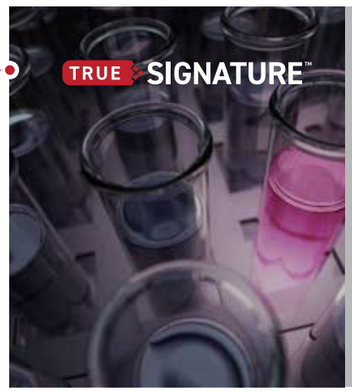
Novel Drug Target Identification and Validation

Applications
DRUG TARGET DECONVOLUTION
DRUG TARGET VALIDATION



Unbiased Biological Insights from Tissue and Biofluids

Applications
BIOFLUID BIOMARKER DISCOVERY
TISSUE BIOMARKER DISCOVERY
MECHANISM OF ACTION STUDIES
PHOSPHOPROTEOME PROFILING
IMMUNOPEPTIDOME PROFILING



Custom Panels for Absolute Protein Quantification

Applications
PHARMACODYNAMIC BIOMARKERS
CLINICAL BIOMARKER PANELS

TRUE**DISCOVERY**™: INSIGHTS INTO THE RIGHT BIOLOGY

Biognosys' TrueDiscovery™ platform can identify and quantify proteins in tissue and biofluids, offering unprecedented specificity at scale. Our integrated solutions function across the entire drug development pipeline and can be performed in a GLP-certified and GCP-compliant environment.

The journey to developing a new cancer therapy begins with understanding the underlying biology. To do this, it is helpful to look at the proteome – the ultimate output of the genome – to really understand what is going on inside cells, tissues, and tumors.

Genomics-based approaches, while useful, cannot be relied upon to give a complete picture of cancer biology. This is because genomics and transcriptomics alone cannot determine the presence or expression level of proteins, or provide information about protein function and structure. By contrast, proteomics can quantify and identify all proteins present in a sample, as well as providing functional data in the form of post-translational modifications, structural changes and degradation.

Biognosys' TrueDiscovery platform, powered by our patented Hyper Reaction Monitoring (HRM) mass spectrometry technology, offers unbiased identification and quantification of thousands of proteins from any sample type – cells, tissue and biofluids. We are continually achieving new breakthroughs in depth. Our Tissue Biomarker Discovery service can now quantify 13,800 proteins per tissue or tumor sample, while our Biofluid Biomarker Discovery service can detect 4,200 proteins per sample of plasma and over 11,000 proteins in cerebrospinal fluid (CSF) and urine. TrueDiscovery analyzes thousands of samples simultaneously, making it suitable for a breadth of studies from target-focused precision studies right through to large-scale drug screening.

TrueDiscovery can help you:

- **Profile** the entire proteome, to unprecedented depth and in an unbiased manner
- **Analyze** post-translational modifications and other proteoforms
- **Perform** discovery proteomics on a large scale
- **Generate** reproducible data that are easily transferable to clinical assays
- **Deliver** proteomics in a GLP-certified and GCP-compliant environment

Phenotyping colorectal cancer

Colorectal cancer is highly heterogeneous,[6] with molecular signatures frequently varying between patients. In collaboration with precision oncology experts *Indivumed*, we performed large-scale proteome profiling of colorectal cancer patient biopsies and healthy control tissue to obtain deeper functional insights into the biology of the cancer.[7] We analyzed more than 900 tissue samples in total, using just 5-10 mg of tissue in each case, and profiled more than **7,000 proteins and 20,000 phospho-peptides.**

By integrating this data with Indivumed's multi-omics database, we generated new insights into key molecules and clinically relevant signaling pathways in colorectal cancer. These insights could help to identify new therapeutic targets and advance progress in precision medicine for colorectal cancer.

Beyond pure quantification, our proprietary HRM technology also provides valuable information on mechanism of action across a range of species and sample types. We can offer detailed insights into biological mechanisms inside cells and tissues during tumor development and in response to drugs or other experimental interventions.

We can also provide important functional insights through the analysis of post-translational modifications, which play a critical role in regulating protein and cellular function but cannot be inferred from genomic data alone. For example, our phosphoproteome profiling service offers in-depth, quantitative insights into the kinases, phosphatases, and signaling cascades at work in cancer cells, revealing new targets for drug discovery.

TrueDiscovery provides an unrivaled opportunity to understand cancer biology in new depths, discover novel biomarkers, and establish the mechanism of action.

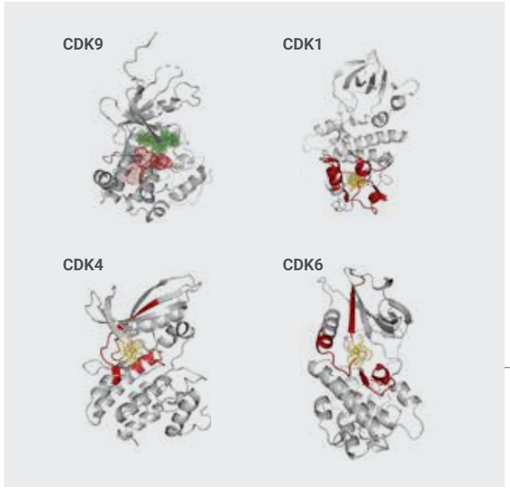
TRUE**TARGET**™: HIT THE RIGHT TARGET

Powered by our patented LiP-MS technology, TrueTarget™ identifies on- and off-target drug binding. This can help identify the mechanism of action and reveal unexpected side effects early on, accelerating and de-risking the drug development process.

Target validation is a crucial part of the drug discovery journey. Our proprietary TrueTarget platform offers a unique way of probing drug-target interactions, providing an in-depth characterization of lead candidates to increase confidence in your drug target.

TrueTarget is based upon Limited Proteolysis coupled with Mass Spectrometry (LiP-MS), a technique invented by Professor Paola Picotti at ETH Zurich and co-developed by Biognosys. Unlike other approaches, LiP-MS does not require compound modification or labeling, affinity-based purification, or prior knowledge of the compound's mode of action.

TrueTarget generates unique peptide signatures that reveal drug binding sites at peptide-level resolution across the entire proteome, whether in the intended target or elsewhere. This approach can also be combined with our deep learning algorithms to optimize your drug discovery journey further, identifying and ranking drug target binding sites across species and a wide range of compound classes for rapid target deconvolution and validation.[8]



TrueTarget can help you:

- **Understand** if and where your drug is binding to the expected target
- **Identify** off-target binding and allosteric effects
- **Establish** the mechanism of action
- **Identify** potential issues with specificity and toxicity
- **De-risk** the drug development process
- **Increase** the chances of success in clinical trials and accelerate the journey to market

Target identification of a CDK9 inhibitor

Working together with *AstraZeneca,* we applied TrueTarget to profile a novel inhibitor of CDK9, a cyclin-dependent kinase with essential roles in cancer development.

De-regulation of CDK9, one of the best characterized transcriptional CDKs, leads to a loss of cell cycle control and tumor growth, making it an important therapeutic target. We found that 80% of the top 10 peptide targets of the CDK9 inhibitor were members of the CDK family, with CDK9 confirmed as the strongest target of the inhibitor. Thanks to the peptide-level resolution provided by TrueTarget, we were also able to investigate the exact binding site of the drug. This revealed that the inhibitor binds within the ATP pocket of CDK9, as well as CDK4 and CDK6, consistent with modeling predictions.

Together with other mass spectrometry techniques, these insights helped **define the selectivity and mode of action of the inhibitor,** including mapping the binding sites and identifying off-target effects.[9]

Fig 2. **Representation of LiP data showing the CDK9 inhibitor binding to its target proteins.** CoM = center of mass. Taken from: Hendricks, J.A. et al (2021). Mechanistic Insights into a CDK9 Inhibitor Via Orthogonal Proteomics Methods. ACS Chemical Biology, 17(1), pp.54–67.

TRUE**SIGNATURE**™: DEVELOP THE RIGHT BIOMARKERS

TrueSignature™ provides highly precise and customizable proteomics panels for pharmacodynamic readouts and clinical biomarker monitoring.

Clinical trials that use biomarkers for patient selection are more likely to succeed than trials that don't.[1] You can rely on Biognosys' TrueSignature platform to establish effective biomarkers for your clinical research.

Powered by Parallel Reaction Monitoring mass spectrometry, TrueSignature provides customizable proteomics panels for pharmacodynamic readouts and clinical biomarker monitoring. Your custom TrueSignature panels can be guided by insights from earlier TrueDiscovery studies.

Unlike affinity-based proteomics methods, our mass spectrometry technology doesn't rely on the availability of specific reagents such as antibodies. Panels can also be developed quickly, ready for you to use within a matter of weeks.

TrueSignature can help you:

- **Take insights** from preclinical research all the way through to clinical studies
- **Build** highly precise, customizable protein biomarker panels
- **Simultaneously quantify** up to 100 proteins, including post-translational modifications and other proteoforms
- **Identify and quantify** pharmacodynamic biomarkers for new therapeutics
- **Gather** GCP-compliant data for clinical trials

Pharmacodynamic biomarkers

TrueSignature can be applied to qualitative and quantitative identification of pharmacodynamic biomarkers, which are essential for validating the efficacy and safety of new therapeutics. TrueSignature can speed up the decision-making process in the early stages of drug development and ensure the success of your drug in future clinical trials.

You can customize panels down to amino acid resolution, and panels are also transferable across sample types and species, providing flexibility across the drug development pipeline from preclinical to clinical research.

Clinical biomarker panels

TrueSignature is used by our global biopharma partners to de-risk their clinical research. Our clinical biomarker panels can help you reliably validate and monitor biomarkers to ensure the success of your therapeutic agent. Panels are flexible in size, can be multiplexed, and are customizable across species and indications. Our technology offers unbiased proteomic profiling at unprecedented depth and scale, without the limitations of affinity-based approaches and reagent availability, alongside robust and reliable quantification.

We provide you with reproducible and comparable data across thousands of samples and multiple time points, making TrueSignature ideal for large-scale clinical trials.

Pharmacodynamic biomarkers for protein degradation therapeutics

Clinical-stage biopharma company *Kymera Therapeutics* is developing cutting-edge therapeutics that harness targeted protein degradation pathways to tackle autoimmune conditions, inflammatory diseases, cancer and more.

Building on our long-standing preclinical partnership, we developed custom TrueSignature proteomics panels to provide **a pharmacodynamic readout of protein degradation** in discovery research and clinical studies. These panels allow Kymera to monitor and quantify protein degradation across all stages of their drug development pipeline.

PROTEOMICS FOR BIOMARKER DISCOVERY AND VALIDATION

Our high throughput proteomics workflows can be applied to fresh-frozen or formalin-fixed tissue and tumor samples, blood plasma, and other biofluids, including urine and CSF. Here are just a few examples of our technology in action.

Searching for biomarkers in blood plasma

Blood plasma analysis ('liquid biopsy') offers an easily accessible way of monitoring cancer within the body. Plasma can be sampled at regular intervals, providing an ongoing overview of health and therapeutic response over time. Biognosys has pioneered an industry-leading approach to profiling the proteome, using automated depletion of the most abundant proteins to achieve unprecedented depth, and in a fully unbiased manner.

Identifying tumor agnostic biomarkers

We recently demonstrated the power of our novel plasma proteomics workflow for oncology by analyzing plasma samples from 180 people with lung, breast, colorectal, pancreatic and prostate cancer. We detected over 2,700 proteins and categorized people by cancer type and stage using their plasma protein profiles. We also identified several predictive biomarker candidates, including known biomarkers such as STAT3 in colorectal cancer, as well as biomarkers with novel biological significance.[10]

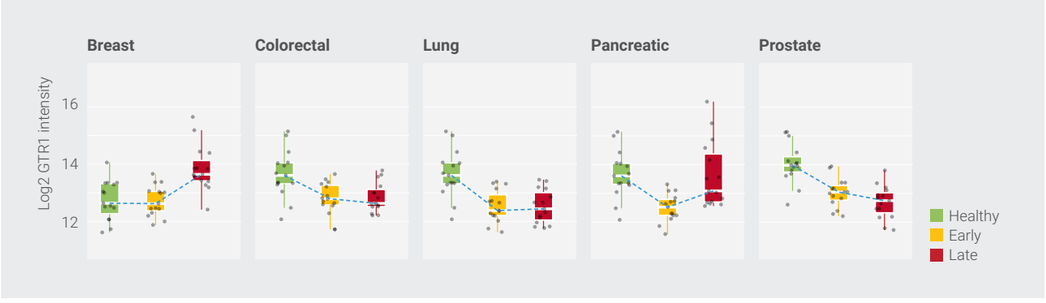
Biomarkers for companion diagnostics

Companion diagnostics provides information essential for the safe and effective use of a drug, for example, identifying which patients are most likely to benefit from a particular drug.[11]

We are combining our discovery proteomics tools with Siemens Healthineers' diagnostic assay development and commercial expertise to help you develop companion diagnostics for your novel therapy.

We can streamline the progress of your companion diagnostic from the initial stages of biomarker discovery right through to assay development and commercialization. Whether applied to early-stage research or patient profiling for clinical trials, our unbiased proteomics solutions are transferable across species and suitable for all stages of the drug development pipeline. Furthermore, our facility is GLP certified and GCP compliant, ensuring that any preclinical or clinical data you collect has the quality and traceability required by regulators for market authorization.

Fig 3. **Stage Classification Across Cancer Types.** In our cross-tumor biomarker study, GTR1 was differentially abundant across all cancers and could be used to predict stage. a) Boxplot visualization of log-transformed GTR1 quantities across stage and cancer type. Taken from: Tognetti, M. et al (2021) Biomarker Candidates for Tumors Identified from Deep-Profiled Plasma Stem Predominantly from the Low Abundant Area. bioRxiv. DOI: https://doi.org/10.1101/2021.10.05.463153



DEEP INSIGHTS IN IMMUNO-ONCOLOGY

Immunotherapy has revolutionized the way we treat cancer: a more targeted form of treatment that has generated survival benefits for a range of patients. Proteomics is advancing immunotherapy even further by identifying new therapeutic targets and matching the right immunotherapy to the right patient.

So far, we have outlined some of the major pitfalls of drug development in oncology: understanding the underlying biology of cancer, identifying the correct therapeutic target, and finding informative biomarkers for patient stratification and monitoring.

All of these challenges – **right biology, right target, and right biomarkers** – come together in the fast-developing field of immuno-oncology.

Immunotherapy has been revolutionary for cancer treatment, generating survival benefits across several cancer types.[12,13,14] However, significant challenges remain. Many patients do not respond to existing immunotherapies, highlighting the need to find better biomarkers to stratify patients. And while these treatments can be curative for those who do respond, there are others for whom the transformative effects of immunotherapy do not last. There can also be significant side effects, which can limit the utility of immunotherapy.

A deeper understanding of the underlying biology of cancer and how this interacts with the immune system and tissue microenvironment is essential to identify new ways to improve the effectiveness and durability of immunotherapy.

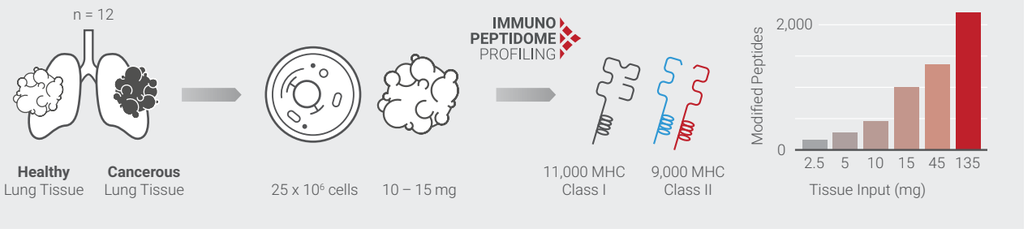
Immunopeptide profiling for next-generation immunotherapy

Immunopeptidomics is the profiling of the small fragments of proteins presented on the surface of cells by Major Histocompatibility Complex (MHC) or Human Leukocyte Antigen (HLA) receptors, which act as signals to orchestrate the activity of the immune system.

Mass spectrometry is the only technology that can reliably quantify and identify immunopeptides in biological samples at scale. Biognosys' immunopeptidome profiling service is a semi-automated mass spectrometry workflow that can robustly identify immunopeptides from small amounts of cultured cells and tissue samples.

Immunopeptidomics has the potential to accelerate the development of the next generation of immunotherapies in oncology through the detection of neoantigens, immunopeptides that reflect tumor-specific mutations. Immunopeptidome analysis can also be used for patient profiling, revealing more about the role of the immune system in tumorigenesis and potential therapeutic targets. Our immunopeptidome profiling pipeline can reliably identify and quantify 10,000 MHC Class I and 10,000 Class II immunopeptides in just 15 mg of tissue, making it suitable for high-throughput, large-scale preclinical and clinical applications as well as smaller research studies.

Fig 4. **High Throughput Immunopeptidomics From Needle-size Biopsies.** We measured a cohort of 12 cancerous and matched healthy lung biopsies, identifying 11,000 MHC Class I and 9,000 MHC Class II immunopeptides from as little as 15 mg tissue.



CASE STUDIES

Here is a selection of case studies that highlight the potential of Biognosys proteomics workflows in oncology research. Proteomics is a powerful tool for understanding the underlying biology and discovering actionable biomarkers to speed up and de-risk the oncology pipeline.

Predicting treatment response in pancreatic cancer

Pancreatic ductal adenocarcinoma (PDAC) is the most common form of pancreatic cancer, a disease with a five-year survival rate of around 11%.[18] There is an urgent need for new therapeutics and precision medicine biomarkers in PDAC, to better understand which patients would be most likely to benefit from which treatments.

As part of the Phase II PRINCE trial led by the Parker Institute for Cancer Immunotherapy (PICI),[19] Biognosys' unbiased mass spectrometry proteomics workflow was used to investigate the effects of two immunotherapies for PDAC: nivolumab and sotigalimab, in combination with chemotherapy.

We found that patients treated with nivolumab had higher levels of proteins associated with type II interferon response, immune cell migration and T cell activation, and reduced levels of immunomodulatory proteins. By contrast, patients treated with sotigalimab had higher levels of proteins associated with mature antigen-presenting cells (APCs) and the activation of CD4+ T cells, B cells, and monocytes.

We therefore showed that these two immunotherapies generate unique immune responses. With further development, these biomarker signatures could help to identify PDAC patients who may benefit most from particular drug combinations.

Understanding the side effects of immunotherapy

In research presented at the 2021 American Association for Cancer Research congress, we discovered proteomic signatures associated with immune-related adverse events (irAEs) in people receiving PD-1 checkpoint inhibitors for non-small cell lung cancer (NSCLC).

We performed deep proteome profiling on plasma samples from NSCLC patients before therapy and 8-weeks after treatment initiation. We found **82 proteins associated with irAEs.** We also identified 13 proteins that were associated with low-grade toxicity, which is linked to better overall response and higher survival benefit from immunotherapy, including **two with prognostic value.**

We also performed functional analysis, revealing a network of five proteins involved in immune, inflammatory, vesicle transport, and acute phase related responses. These insights could lead to new biomarkers to help clinicians better predict and manage toxicity during immunotherapy.[20]

Immunopeptidome profiling in lung cancer

We recently demonstrated the power of our immunopeptidomics workflow in lung cancer, generating MHC immunopeptide profiles from needle biopsies of 12 lung cancer and matched healthy tissue samples.[21]

On average, we were able to identify more than 11,000 Class I and more than 9,000 Class II immunopeptides from each sample. Around 3,000 of the identified Class I immunopeptides were upregulated in the lung cancer samples, with significant enrichment of proteins related to lung cancer development including:

- **MMP11,** an important remodeller of the cancer microenvironment and potential therapeutic target in lung cancer
- **CHEK,** a cell cycle checkpoint kinase
- **TNC,** an extracellular membrane protein that is upregulated during neovascularization
- **SET,** a proto-oncogene that is highly overexpressed in lung tumors

NOVEL INSIGHTS TO ACCELERATE YOUR ONCOLOGY RESEARCH

Mass spectrometry proteomics is an essential part of the oncology drug development toolkit, from early quantification and mechanism of action studies (TrueDiscovery™) through to studies of on- and off-target binding (TrueTarget™) and developing biomarker panels for pharmacodynamic readouts and endpoint evaluation in clinical trials (TrueSignature™).

As the first global proteomics service provider to be GLP certified for preclinical studies and GCP compliant for clinical trials, we are the proteomics provider of choice for pharmaceutical companies and biotechnology companies across the world.

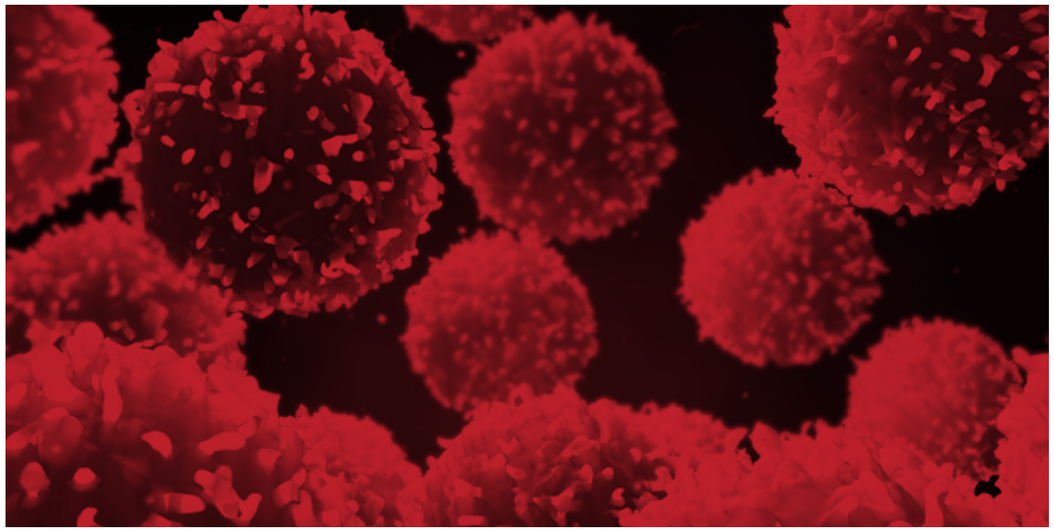
We work with more than 800 customers worldwide, including 19 of the top 20 pharma companies, helping them to apply cutting-edge proteomics across their drug development pipeline and deliver life-changing medicines to the patients who need them.

By integrating quantitative proteomics with other omics technologies at scale, we can offer you a newly detailed picture of cancer biology and unrivaled insights into how best to target the disease at every stage.

Our unbiased, proteome-wide approach offers unique opportunities to discover and validate true first-in-class targets, widening and accelerating your oncology pipeline. As the field advances further, the applications and benefits of proteomics for oncology research will only continue to expand.

At Biognosys, we make integrating proteomics into your research and development pipeline easy and convenient. Our team of expert scientists offers advice every step of the way, providing easy-to-understand data reports that highlight key biological insights, de-risking and accelerating your journey from hit to lead to clinical trial.

To find out what proteomics can do for you, get in touch today to speak with one of the experts at **biognosys.com.**



References

1. **Wong, C.H., Siah, K.W. and Lo, A.W. (2018)** Corrigendum: Estimation of clinical trial success rates and related parameters. Biostatistics, 20(2), pp.366–366.
2. **World Health Organization (2022)** Cancer. Who.int. Available online at: https://www.who.int/news-room/fact-sheets/detail/cancer. [Accessed 9 March 2022]
3. **Davis, C., Naci, H., Gurpinar, E., Poplavska, E., Pinto, A. and Aggarwal, A. (2017)** Availability of evidence of benefits on overall survival and quality of life of cancer drugs approved by European Medicines Agency: retrospective cohort study of drug approvals 2009-13. BMJ, [online] p.j4530.
4. **Kim, C. and Prasad, V. (2015)** Cancer Drugs Approved on the Basis of a Surrogate End Point and Subsequent Overall Survival. JAMA Internal Medicine, 175(12), p.1992.
5. **Lin, A., Giuliano, C.J., Palladino, A., John, K.M., Abramowicz, C., Yuan, M.L., Sausville, E.L., Lukow, D.A., Liu, L., Chait, A.R., Galluzzo, Z.C., Tucker, C. and Sheltzer, J.M. (2019)** Off-target toxicity is a common mechanism of action of cancer drugs undergoing clinical trials. Science translational medicine, 11(509).
6. **Buikhuisen, J.Y., Torang, A. and Medema, J.P. (2020)** Exploring and modelling colon cancer inter-tumour heterogeneity: opportunities and challenges. Oncogenesis, 9(7).
7. **Vowinckel, J., Corwin, T., Woodsmith, J., Treiber, T., Bruderer, R., Reiter, L., von Leitner, E.-C., Novy, K., Juhl, H. and Rinner, O. (2021)** Proteome and phospho-proteome profiling for deeper phenotype characterization of colorectal cancer heterogeneity. Journal of Clinical Oncology, 39(15_suppl), pp.e15536–e15536.
8. **Piazza, I., Beaton, N., Bruderer, R., Knobloch, T., Barbisan, C., Chandat, L., Sudau, A., Siepe, I., Rinner, O., de Souza, N., Picotti, P. and Reiter, L. (2020)** A machine learning-based chemoproteomic approach to identify drug targets and binding sites in complex proteomes. Nature Communications, 11(1), p.4200.
9. **Hendricks, J.A., Beaton, N., Chernobrovkin, A., Miele, E., Hamza, G.M., Ricchiuto, P., Tomlinson, R.C., Friman, T., Borenstain, C., Barlaam, B., Hande, S., Lamb, M.L., De Savi, C., Davies, R., Main, M., Hellner, J., Beeler, K., Feng, Y., Bruderer, R. and Reiter, L. (2021)** Mechanistic Insights into a CDK9 Inhibitor Via Orthogonal Proteomics Methods. ACS Chemical Biology, 17(1), pp.54–67.
10. **Tognetti, M., Sklodowski, K., Müller, S., Kamber, D., Muntel, J., Brudeer, R. and Reiter, L. (2021)** Biomarker Candidates for Tumors Identified from Deep-Profiled Plasma Stem Predominantly from the Low Abundant Area. bioRxiv 10.05.463153; doi: https://doi.org/10.1101/2021.10.05.463153
11. **FDA (2019)** Companion Diagnostics. Available online at: https://www.fda.gov/medical-devices/in-vitro-diagnostics/companion-diagnostics [Accessed 16 March 2022].
12. **Garon, E.B., Hellmann, M.D., Rizvi, N.A., Carcereny, E., Leighl, N.B., Ahn, M.-J., Eder, J.P., Balmanoukian, A.S., Aggarwal, C., Horn, L., Patnaik, A., Gubens, M., Ramalingam, S.S., Felip, E., Goldman, J.W., Scalzo, C., Jensen, E., Kush, D.A. and Hui, R. (2019)** Five-Year Overall Survival for Patients With Advanced Non Small-Cell Lung Cancer Treated With Pembrolizumab: Results From the Phase I KEYNOTE-001 Study. Journal of Clinical Oncology, 37(28), pp.2518–2527.
13. **Wolchok, J.D., Chiarion-Sileni, V., Gonzalez, R., Grob, J.-J., Rutkowski, P., Lao, C.D., Cowey, C.L., Schadendorf, D., Wagstaff, J., Dummer, R., Ferrucci, P.F., Smylie, M., Butler, M.O., Hill, A.G., Marquez-Rodas, I., Haanen, J.B.A.G., Bas, T., van Dijck, W., Larkin, J. and Hodi, F.S. (2021).** CheckMate 067: 6.5-year outcomes in patients (pts) with advanced melanoma. Journal of Clinical Oncology, 39(15_suppl), pp.9506–9506.
14. **Yang, F., Markovic, S.N., Molina, J.R., Halfdanarson, T.R., Pagliaro, L.C., Chintakuntlawar, A.V., Li, R., Wei, J., Wang, L., Liu, B., Nowakowski, G.S., Wang, M.L. and Wang, Y. (2020)** Association of Sex, Age, and Eastern Cooperative Oncology Group Performance Status With Survival Benefit of Cancer Immunotherapy in Randomized Clinical Trials. JAMA Network Open, 3(8), p.e2012534.
15. **Onoi, K., Chihara, Y., Uchino, J., Shimamoto, T., Morimoto, Y., Iwasaku, M., Kaneko, Y., Yamada, T., & Takayama, K. (2020)** Immune Checkpoint Inhibitors for Lung Cancer Treatment: A Review. Journal of clinical medicine, 9(5), 1362. https://doi.org/10.3390/jcm9051362
16. **Ramos-Casals, M., Brahmer, J.R., Callahan, M.K. et al** Immune-related adverse events of checkpoint inhibitors. Nat Rev Dis Primers 6, 38 (2020). https://doi.org/10.1038/s41572-020-0160-6
17. **Zhou, X., Yao, Z., Yang, H. et al** Are immune-related adverse events associated with the efficacy of immune checkpoint inhibitors in patients with cancer? A systematic review and meta-analysis. BMC Med 18, 87 (2020). https://doi.org/10.1186/s12916-020-01549-2
18. **American Cancer Society (2022)** Survival Rates for Pancreatic Cancer. Available online at: https://www.cancer.org/content/dam/CRC/PDF/Public/8780.00.pdf [Accessed 5 April 2022]
19. **Maurer, D., Yu, J.X., Sklodowski, K., Tognetti, M., Reiter, L., Bruderer, R., Vowinckel, J., Pfeiffer, S., O'Hara, M., O'Reilly, E., Wolff, R., Wainberg, Z., Ko, A., Rahm, O., Fisher, G., Lyman, J., Cabanski, C., Gherardini, P.F., O'Donnell-Tormey, J. and LaVallee, T. (2021)** 343 Multiomic biomarker signatures identify subsets of patients who may benefit from either nivolumab or sotigalimab in combination with chemotherapy in metastatic pancreatic cancer. Journal for ImmunoTherapy of Cancer, 9(Suppl 2), pp.A370–A370.
20. **Sklodowski, K., Dozio, V., Poli, R., Lanzós, A., Lopez-Lastra, S., Beeler, K., and Romano, E. AACR 2021** Abstract #1615 https://www.abstractsonline.com/pp8/#!/9325/presentation/2716
21. **Shapiro, I., Raess, L., Tognetti, M., Temu, T., Bernhardt, O., Feng, Y., Bruderer, R. and Reiter, L. AACR 2022** Abstract #1374/5 https://www.abstractsonline.com/pp8/#!/10517/presentation/13916

KEY TAKEAWAYS

- Oncology drug development fails due to poor understanding of the underlying biology of cancer *(wrong biology)*, insufficient target validation *(wrong target)*, and a lack of effective biomarkers for patient stratification *(wrong biomarkers)*.
- There is an urgent need for new approaches to de-risk the oncology drug development pipeline and increase the likelihood of clinical trial success.
- Next-generation proteomics can fill this gap by providing fresh insights into cancer biology at unprecedented scale and depth.
- Biognosys provides unbiased proteome-wide profiling of cells, tissue, blood plasma, and other biofluids. Our proteomics technologies accelerate and validate each stage of the drug discovery and development pipeline:

  TrueDiscovery™ - Understand the right biology
  TrueTarget™ - Hit the right target
  TrueSignature™ - Develop the right biomarkers

- Biognosys also provides large-scale immunopeptide profiling to support the development of next generation personalized immunotherapies.
- Rapid advances, including integration with other omics technologies and clinical data, are rapidly making proteomics an indispensable tool in the drug development pipeline.

At Biognosys, we believe that deep proteome insights hold the key to breakthrough discoveries that transform science for better lives. We make the proteome actionable to empower research, drug development, and clinical decision-making with our versatile portfolio of mass spectrometry-based proteomics research services, software, and kits. These solutions provide a multi-dimensional view of protein expression, function, and structure in all biological species and sample types.

Contact us at **services@biognosys.com** to discuss your specific study needs with one of our scientific consultants.

biognosys.com

BIOGNOSYS
NEXT GENERATION PROTEOMICS