





As the discovery and development of novel medicines rapidly evolve, the role of biomarkers in these processes becomes increasingly important. <u>Described by the FDA</u> as a "defined characteristic that is measured as an indicator of normal biological processes, pathogenic processes, or responses to an exposure or intervention," biomarkers are promising tools supporting the preclinical and clinical research of new medicines.

Biomarkers allow researchers and clinicians to define the status of a disease, the human body's response to a disease or modulating agent, and to determine patient populations that may specifically benefit from a certain medication. In short, biomarkers can reflect the physiological, pathological, molecular, or histological state of a living being.

#### How biomarkers can be classified?

Biomarkers can be classified in many different ways. Some are diagnostic, some prognostic, and others pharmacodynamic. While diagnostic biomarkers can help detect and confirm the occurrence of a disease or a disease subtype, pharmacodynamic biomarkers can help to determine whether a therapeutic intervention has triggered the expected therapeutic and physiological response.



Prognostic biomarkers can provide an indication of clinical responses and disease progression. In recent years, for instance, the need for a more patientspecific approach, especially regarding the types of therapies administered by clinicians, has increased.

"Prognostic biomarkers can greatly benefit patients, allowing clinicians to determine in advance what type of drugs are more likely to work for a specific patient population, and avoid those patients who would have no or even toxic responses," explains Joanna Lisztwan, Executive Vice President and Head of Global In Vitro Biology at <u>Evotec</u>. By using biomarkers in clinical trials, companies can effectively select those patients who are more likely to benefit from a novel drug and therefore can more accurately track the drug's efficacy. This greatly increases the efficiency of clinical trials and the possibility of drugs reaching the market faster.



Joanna Lisztwan, Executive Vice President and Head of Global In Vitro Biology at Evotec

"Especially cancer research has greatly benefitted from the genomics revolution," Lisztwan says. "In the last 10-15 years there has been a great emphasis on selecting patient populations based on their genetic backgrounds; and we have seen a lot of very successful results, for example, with kinase inhibitors."

## Understanding the importance of biomarker discovery

In biomarker discovery, researchers differentiate between an unbiased approach and a hypothesis-driven approach. *"In the unbiased approach, there is little to no understanding of the biology or mechanism of action of a given drug,"* explains Maria Pilla, Executive Vice President and Head of Global Preclinical Development at <u>Evotec</u>. "The hypothesisdriven approach, on the other hand, is based on the prediction of what the downstream target might be."

"In order to detect different kinds of biomarkers, one needs to apply a variety of different methods," Lisztwan adds. "At Evotec, for instance, we apply anything from transcriptomics to proteomics and metabolomics. Nowadays, especially with immune-related diseases, cell populations are also used as biomarkers. In this case, we do phenotypic mapping of the various cell populations either within the disease or in response to the drug using multicolorimetric flow cytometry analysis."

This approach allows <u>Evotec's</u> biomarker discovery team to track a large variety of cell membrane receptors in parallel. *"The advantage is that we can rapidly zoom in on specific subpopulations that are impacted by the administered drug. This then allows us to identify what could be a putative biomarker to monitor or track the efficacious response to the drug going forward,"* Lisztwan explains.

### Evotec's secret for successful biomarker discovery

The key to Evotec's success in biomarker discovery and development is the fact that the company considers biomarkers to be an essential component of <u>advancing drug</u> <u>discovery programs</u> and preparing drugs for clinical development.

*"Our clinically-facing view means we want to understand early how to position the* 

drug correctly in the clinic," says Lisztwan. "The fundamental aspect of the drug discovery program is to detect a pharmacodynamic biomarker that will allow us to effectively monitor patients' responses to the drug in the clinic. We also aim to identify patient subpopulations that will be more responsive to a given drug."



Maria Pilla, Executive Vice President and Head of Global Preclinical Development at Evotec

Moreover, <u>Evotec</u> uses technologies for its biomarker discovery platform that are also used in the clinic, allowing them to be applied throughout discovery and development. This translational approach is achieved through stringent communication between the discovery and development teams at Evotec.

"Because we are all working under one roof and we are a unique team, we can really discuss and design the strategies for biomarker identification and assay development to make sure they can support both discovery and development phases in a truly translational way," explains Pilla. "We achieve this translatability, as well as the backtranslation from the clinic, through a close internal cooperation and collaboration with research centers and clinicians."

### Addressing the challenges of biomarker discovery and development

By focusing on translatability, the team at <u>Evotec</u> is addressing one of the key challenges faced by researchers in biomarker discovery and development.

"Typically, there is a suboptimal communication between the discovery and development phases of the R&D process," Pilla explains. "This is because biomarker assays are often developed during the discovery process without anticipating their application in development and clinical phases. In other words, it makes little sense to use a very complex assay in discovery if it will be too difficult to apply in the clinic."

Close communication between discovery and development teams can therefore help to overcome this issue. However, communication shouldn't stop there. The dialogue between the preclinical and clinical world should go both ways, says Pilla. *"It is important to hear from clinicians about what type of biomarkers are worth pursuing in preclinical research."* 

# Using the "under-one-roof" strategy to facilitate success

The continuous dialogue between the <u>discovery and development</u> <u>departments</u> at Evotec allows scientists from all different functions to share their experiences and ensure that they are working towards the same goals. This, as Pilla explains, is particularly important when it comes to designing biomarker assays *"cross-site and cross-business"* to establish translatability from discovery to development.



This close-knit communication supports the company's customers who seek help at all stages of the R&D process. "Although it is often easier to follow an R&D process from the very beginning, we can offer our own experience and support to clients even in the later stages of development," says Pilla. "If, for example, a client wants to move towards clinical trials, we can adjust the biomarker identification platform according to their needs."

Lisztwan adds, "The aim of our biomarker discovery program is to support clients from start to finish. We bring additional input when necessary and discuss issues that might need to be addressed. For instance, if a prognostic biomarker is missing in the project, we deliver proposals for exploratory biomarker and mode-ofaction studies that would help to stratify the patient population."

What about the future of biomarker discovery and development?

As the medical landscape evolves, so does the approach to therapeutic intervention. The approach to drug development is aiming at a faster and lower-risk progression of compounds to the clinic. The use of biomarkers throughout the R&D process can help increase the success rates of drug development programs and result in the accelerated availability of novel therapies on the market.

"In the future, we will move more and more towards translating findings from preclinical research into the clinical world," says Pilla. "Biomarkers will help in choosing a subset of the patient population that is more likely to respond to a given therapy, as well as support human-dose prediction and selection in clinical trials. Hence, therapeutic interventions are moving towards the personalization of medicines, which will revolutionize the way drugs are designed and administered to patients."

Another important point to address in the future is the use of biomarkers for a broader spectrum of diseases. *"A large focus is currently on cancer therapies,"* says Lisztwan. *"However, there is an urgent need in other disease areas to improve stratification of patient populations, identify toxicity early and continue to enhance monitoring of efficacious responses. One area that we at Evotec are heavily investing in is kidney disease. By characterizing the various subtypes present within this very heterogeneous patient population, we aim to provide a means to subclassify and*  identify novel targets and biomarkers in this disease area."

Do you need support with one of your drug discovery projects, working with a team of experts familiar with advancing biomarkers alongside drugs? Or are you in need of a stand-alone biomarker discovery project, for example, in the proteomics space? <u>Get in touch</u> with the experts at Evotec or check out their <u>website</u> for further information!

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