

## Symphogen A/S

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# Immaculate therapeutic antibody discovery

**Harnessing its antibody discovery platform Symplex, Symphogen has developed a fully integrated approach to discovering and developing next-generation antibody therapeutics.**

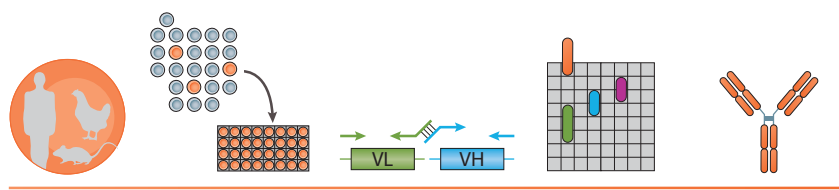
Traditional antibody discovery procedures are often limited by the number of unique full-length antibodies that can be expressed and tested functionally or may deliver lead molecules that require additional molecular optimization. Symphogen's antibody technology overcomes these issues by using natural immune responses to build massive target-specific, full-length antibody repertoires.

Symphogen's state-of-the-art antibody discovery platform, Symplex, enables millions of B cells from the natural immune responses of animals and humans to be prepared and sorted (according to a set of carefully selected markers) in order to focus on the B cells that produce target-specific antibodies. A proprietary single-cell polymerase chain reaction-based method then clones the antibodies from each of these cells while maintaining the natural pairing of the heavy and light chains. The subsequent approach is fully recombinant, the repertoire can be made in any isotype or multiple isotypes in parallel and, because the repertoire is immortalized, it can be screened again and again. Symphogen has optimized the procedure for multiple species including humans, mice, rats and chickens (Fig. 1).

"Our Symplex platform delivers very large, high-quality, target-specific repertoires that can be screened very early for functional activity which increase the likelihood of finding antibodies with ultra-rare functional properties," said Mikkel Pedersen, Symphogen's senior VP of research. "Not only are we able to find antibodies with unique function against conserved epitopes and difficult targets, we can secure species crossreactivity and obtain early functional data on full-length mAbs [monoclonal antibodies]."

Using optimized procedures, the entire repertoire of full-length, target-specific antibodies are expressed, purified and screened in parallel for binding, affinity, function, immunogenicity and early quality attributes. Coupled with next-generation sequencing, this high-dimensional analysis provides detailed information for each of the thousands of antigen-specific antibodies, from which unique leads that have an optimal set of properties can be rapidly selected. Potential critical features of the lead candidates are taken into consideration very early in the development path; thus, once development starts on the lead, no sequence optimization is needed.

"Our highly efficient antibody discovery and research platform, supported by comprehensive early development capabilities, enables the construction of huge high-quality antibody repertoires, the identification of rare functional antibodies and their preclinical development on aggressive timelines," said Pedersen. "We can move from immunization to unique drug lead with a desired set of properties in just 18 months and from lead over preclinical



## Harvesting

Harvesting of tissues, preparation of B cells and in vivo mAb optimization

## Cell sorting

Single cell sorting of rare isotype-switched, affinity-matured antibody-producing B cells

## Repertoire generation

PCR performed on each B cell. Variable regions grafted onto selected human isotype(s)

## High-throughput screening

Entire repertoire expressed in micro-scale. Parallel upfront screening for binding (Hu, Mo and Cy) and function

## Lead selection and validation

Expression and purification of all antigen-specific mAbs. Early validation, affinity determination and epitope binning

**Fig. 1 | Symphogen's antibody discovery platform.** This state-of-the-art technology provides immunization to lead in 18 months. Cy, cynomolgus macaque; Hu, human; mAb, monoclonal antibody; Mo, mouse; PCR, polymerase chain reaction.

development to IND [investigational new drug] in an additional 18 months. We have filed five INDs in the past three years—an exceptional achievement made possible by the unique way we run projects."

## Focusing on immuno-oncology

Although its technology platform can be used for various indications, most of Symphogen's research and development (R&D) activities are currently focused on identifying antibodies against novel targets to mobilize the immune system to fight tumors. The company is currently building a strong immuno-oncology pipeline of best-in-class or first-in-class antibody-based drug candidates. These include antibodies directed at FLT3, AXL and CD40 with the purpose of mobilizing and activating dendritic cells. "Despite being a key cell type for mounting an antitumor immune response against 'cold' tumors, the promise of dendritic cells has largely been underexplored to date," explained Pedersen. "To realize the potential of this cell type, we are developing antibody-based approaches for deploying and enhancing the activity of dendritic cells—an innovation that has great potential for use in combination regimens and for treating tumors that fail to respond to checkpoint inhibitors."

The company has additional antibody-based programs aimed at first-in-class targets for marshaling other types of immune cell in the fight against tumor cells.

## Partnering approach

Symphogen is currently collaborating with Servier Pharmaceuticals covering six separate programs within immuno-oncology, three of which are in

clinical development. They include the unique programmed cell death 1 (PD1)-targeting antibody Sym021, the first chicken-derived mouse cross-reactive antibody to enter clinical development; Sym022, a novel LAG3-targeting antibody that shows enhanced anticancer activity in combination with anti-PD1 antibody therapy; and Sym023, a unique anti-TIM3 antibody with a novel mode of action.

Symphogen is open to working with different types of collaborator, including those keen to harness its antibody platform to deliver high-quality leads, or more strategic partnerships to fully utilize its unique, effective and fully integrated R&D platform capable of end-to-end drug development. "We believe we have one of the best antibody discovery platforms in the world that rapidly delivers unique, highly differentiated, therapeutic antibodies and that has application across multiple indications and targets including those that are highly conserved," said Pedersen. "When it comes to cancer, our heritage of identifying and developing combination therapies positions us at the core of future treatments, enabling new and improved options for patients."

## Contact

Mikkel Wandahl Pedersen,  
Senior VP of Research  
Symphogen A/S  
Ballerup, Denmark  
Tel: +45 8838 2450  
Email: mwp@symphogen.com