

Facilitating Neoantigen Discoveries via combined Transcriptomics-Genomics-Approach for Precision Cancer Vaccine Development

Case Study of Lexogen NGS Services

YGION Biomedical aims to revolutionize cancer treatment by developing **precision cancer vaccines** that leverage a patient's own immune system to specifically target and eliminate cancer cells. This approach requires a deep understanding of the genetic makeup of each individual's tumor and healthy tissue, as it is essential for creating more effective, long-lasting treatments with the ultimate goal of improving the quality of life and long-term outcomes for patients. The challenge is to identify specific tumor-related sequences in individuals that will trigger a potent immune response and are suitable as drug targets, as well as effectively deliver them in a timely manner.

The promise of precision cancer vaccines

In contrast to endogenous cells, cancer cells are prone to accumulating somatic mutations and genomic instability due to their increased proliferation rates and lack of cell cycle control. These mutations can manifest **"neoantigens"** – **cancer-specific aberrant proteins and peptides that the immune system recognizes as "non-self"**. Neoantigens are thus a prime target for cancer immunotherapy.

Cancer vaccines are emerging as a promising approach with the potential to prevent, treat, and even cure certain types of cancer by targeting neoantigens in a personalized approach. Unlike tumor-associated antigens (TAAs), which are commonly overexpressed in cancer but are also present in healthy tissue, targeting neoantigens reduces negative side effects and has the potential to counteract chemoresistance. Neoantigen vaccines represent a cutting-edge advance as they are highly immunogenic, use tumor-specific targets derived from diverse sources, and can generate long-term immune memory against cancer.

While significant progress has been made in identifying, predicting, and screening for neoantigens, several challenges remain before a unique and personalized treatment can be crafted for every patient.

Chances & barriers of precision cancer vaccines

Cancer vaccines are not yet a panacea for all cancer patients, but represent a major step forward in personalized, precision immunotherapy. Ongoing research and clinical trials may reveal the full potential of cancer vaccines in the fight against cancer by harnessing the patient's immune system.

Advantages of precision cancer vaccines

- ✓ Minimal damage to healthy cells due to **targeted immune response**.
- ✓ Potential **long-lasting protection via immune memory**.
- ✓ Increased therapy efficacy due to **synergy with other immunotherapies** and combined therapy.

Challenges of precision cancer vaccines

- ✓ Identification of the right antigens for effective targeting.
- ✓ Tumor heterogeneity and immune evasion mechanisms.
- ✓ Complex custom manufacturing delay start of therapy.
- ✓ Extensive approval and regulatory processes for each individualized anti-cancer vaccine.

A new frontier: Cancer vaccines as a promising pillar of cancer immunotherapies

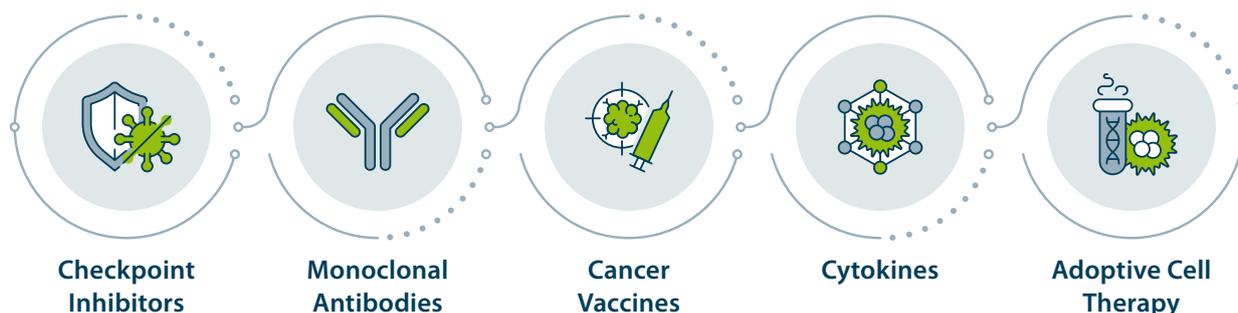


Figure 1 | Overview of different types of cancer immunotherapy. Go to info box on next page for details on all types of cancer immunotherapy.

The role of RNA sequencing in precision oncology and cancer immunotherapy

RNA sequencing (RNA-Seq) is a **cornerstone technology in precision oncology and cancer immunotherapy**, offering unprecedented resolution into gene expression and tumor heterogeneity. It facilitates the **discovery of molecular mechanisms, signaling pathways, and a wide range of biomarkers** (coding and non-coding) associated with tumor progression and therapeutic resistance. This capacity to provide mechanistic insights and identify predictive biomarkers has established RNA-Seq as the **gold-standard method for modern cancer research and drug development**, a topic explored in our article "[How RNA Sequencing is Revolutionizing Cancer Research: Bringing Precision Medicine to Cancer Patients](#)" and constantly applied and supported in numerous customer projects at Lexogen.



Figure 2 | Lexogen NGS Services provides customizable end-to-end sequencing services and tailored bioinformatics solutions.

Accelerate neoantigen identification with an expert NGS sequencing service partner

Partnering with experienced sequencing service providers and CROs can significantly increase assay speed and accelerate neoantigen discovery. A fast discovery is crucial to ensure patients can be treated in a timely manner, to increase treatment success, and ensure the highest possible quality of life during cancer care.

At **Lexogen NGS Services**, we have successfully realized projects in precision medicine and aided in the development of numerous promising personalized therapies. With **YGION Biomedical** we are pursuing a long-term partnership. Beyond that, Lexogen NGS Services has an **outstanding track record for processing of challenging samples types for RNA-Seq, DNA-Seq, and single-cell analysis** including:

- ✓ various cell lines and primary cells,
- ✓ tissues,
- ✓ FFPE samples,
- ✓ whole blood samples,
- ✓ serum, plasma, and other biofluids,
- ✓ PBMCs,
- ✓ extracellular vesicles, etc.

Lexogen provides **customizable sequencing services and tailored bioinformatics solutions** to pharmaceutical and biotech companies, academic institutions, and researchers worldwide. Our end-to-end services, paired with project planning and consultation, is fully flexible and also allows customers to start at any step. From extraction to data analysis and reporting – we adapt to fit your individual needs.

Improving neoantigen prediction by integrating DNA and RNA sequencing

Combining DNA- and RNA-Seq offers a powerful approach to neoantigen discovery by creating a more comprehensive and effective list of potential targets for personalized cancer vaccines. While DNA-Seq identifies a broad range of mutations, RNA-Seq confirms which of these are actively expressed and thus more likely to be presented to the immune system. This integrated method allows to **select neoantigens with higher immunogenic potential and biological relevance, significantly improving the design and efficacy of immunotherapies**. Generating high-quality transcriptomic and genomic data is critical for effective neoantigen prediction and precision medicine. However, the patient-derived samples used, e.g., tumor and FFPE tissue or biofluids, often pose significant challenges and require a specialized approach to ensure meaningful and reliable data for downstream analysis.

Cancer immunotherapy offers a major breakthrough in cancer therapy and comprises several distinct approaches that leverage the body's immune system to fight cancer. **DNA- and RNA-Seq are routinely used for development, characterization, efficacy studies and mode-of-action confirmation** of cancer immunotherapy using:

- **Checkpoint inhibitors** release blockages on T cells, so these can effectively attack cancer cells again.
- **Monoclonal antibodies** bind specific epitopes on cancer cells and engage the immune system.
- **Cancer vaccines** introduce tumor antigens to stimulate the immune system to eliminate cancer cells.
- **Cytokines** like interferons and interleukins enhance the natural immune reaction.
- **Adoptive cell therapy** isolates immune cells, engineers them *ex vivo* and reintroduces the modified cells for a stronger response.

Interested in working with Lexogen NGS Services?
Scan the code and consult with us!

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