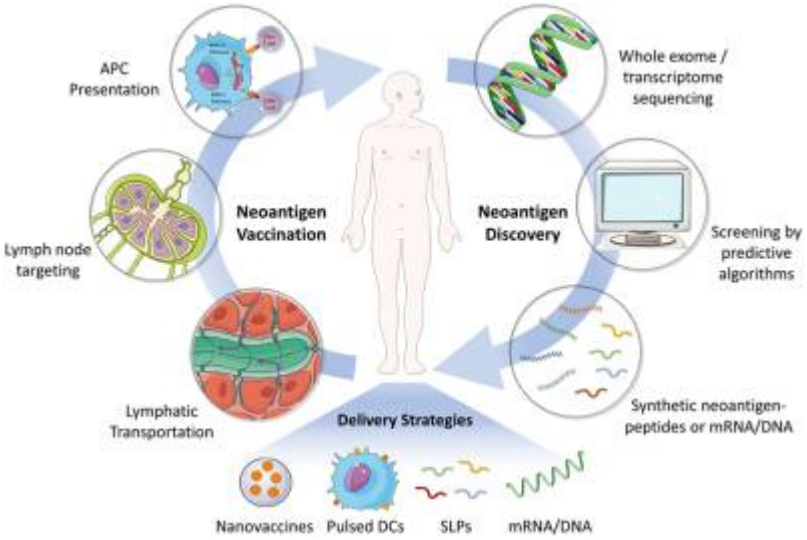
Neoantigen Peptide Vaccines

- Peptide based vesicles for cancer immunotherapy: design, construction and applications
- Intranodal injection of neoantigen-bearing engineered Lactococcus lactis triggers epitope spreading and systemic tumor regressions
- In-depth characterization of vaccine-induced neoantigen-specific T cells in patients with IDH1-mutant glioma undergoing personalized peptide vaccination
- Dendritic cell-derived exosomes induce monocyte antigen-presentation and immune amplification in neoantigen vaccine therapy
- Development of a multi-neoepitope vaccine targeting non-small cell lung cancer through reverse vaccinology and bioinformatics approaches
- Multi-engineered T cell vaccine boosting TCR-T cell therapy enhances anti-tumor function and eradicates heterogeneous solid tumors
- Dual prophylactic and therapeutic potential of iPSC-based vaccines and neoantigen discovery in colorectal cancer
- Strategies for neoantigen screening and immunogenicity validation in cancer immunotherapy (Review)

Neoantigen peptides are derived from unique antigens created by somatic mutations in cancer cells. Neoantigen peptide vaccines are personalized for each patient, targeting specific mutations in their cancer cells. Tumor-Associated Antigen (TAA) Peptide Vaccines: TAAs are proteins overexpressed or uniquely expressed in cancer cells. Peptide vaccines containing TAAs aim to stimulate an immune response against these cancer-specific proteins. Infectious Disease Peptide Vaccines: Peptide vaccines can also target infectious diseases by including peptides derived from pathogens, such as viruses or bacteria, to trigger an immune response.



Neoantigens arise from somatic mutations that differ from wild type antigens and are specific to each individual patient, which provide tumor specific targets for developing personalized cancer vaccines. Decades of work has increasingly shown the potential of targeting neoantigens to generate effective clinical responses. Current clinical trials using neoantigen targeting cancer vaccines, including in combination with checkpoint blockade monoclonal antibodies, have demonstrated potent T-cell responses against those neoantigens accompanied by antitumor effects in patients. Personalized neoantigen vaccines represent a potential new class of cancer immunotherapy [1].

They are exempt from central tolerance, can generate robust immune responses and can function as bona fide antigens that facilitate tumour rejection.

It is a truly personalized therapy because most neoantigens are derived from unique mutations in each tumor genome.

Keskin et al., demonstrated that a strategy that uses multi-epitope, personalized neoantigen vaccination, which has previously been tested in patients with high-risk melanoma, is feasible for tumours such as glioblastoma, which typically have a relatively low mutation load, and an immunologically 'cold' tumour microenvironment.

They used personalized neoantigen-targeting vaccines to immunize patients newly diagnosed with glioblastoma following surgical resection and conventional radiotherapy in a phase 1/Phase 1 B randomized controlled trial. Patients who did not receive dexamethasone-a highly potent corticosteroid that is frequently prescribed to treat cerebral edema in patients with glioblastoma-generated circulating polyfunctional neoantigen-specific CD4+ and CD8+ T cell responses that were enriched in a memory phenotype and showed an increase in the number of tumour-infiltrating T cells. Using single-cell T cell receptor analysis, they provided evidence that neoantigen-specific T cells from the peripheral blood can migrate into an intracranial glioblastoma tumour. Neoantigen-targeting vaccines thus have the potential to favourably alter the immune milieu of glioblastoma [2].

References

1)
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2)
Keskin DB, Anandappa AJ, Sun J, Tirosh I, Mathewson ND, Li S, Oliveira G, Giobbie-Hurder A, Felt K, Gjini E, Shukla SA, Hu Z, Li L, Le PM, Allesøe RL, Richman AR, Kowalczyk MS, Abdelrahman S, Geduldig JE, Charbonneau S, Pelton K, Iorgulescu JB, Elagina L, Zhang W, Olive O, McCluskey C, Olsen LR, Stevens J, Lane WJ, Salazar AM, Daley H, Wen PY, Chiocca EA, Harden M, Lennon NJ, Gabriel S, Getz G, Lander ES, Regev A, Ritz J, Neuberg D, Rodig SJ, Ligon KL, Suvà ML, Wucherpfennig KW, Hacohen N, Fritsch EF, Livak KJ, Ott PA, Wu CJ, Reardon DA. Neoantigen vaccine generates intratumoral T cell responses in phase Ib glioblastoma trial. Nature. 2018 Dec 19. doi: 10.1038/s41586-018-0792-9. [Epub ahead of print] PubMed PMID: 30568305.