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Abstract 4100

AMP-peptide vaccination against mutant BRAF epitopes promotes lymph node delivery to generate potent, functional T cell immunity

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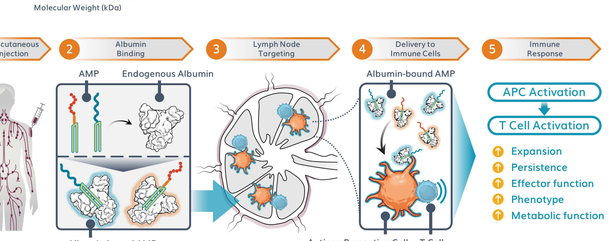
Why Target BRAF with Therapeutic Vaccination?

- BRAF-mutations are **highly prevalent** in melanoma, colorectal and thyroid cancer
  Overall, BRAF mutations exist in 8% of solid tumors, representing approx. 1.5 million cases globally each year [1]
- BRAF mutations are concentrated in **one hotspot** [2-7]
  Up to 97% of BRAF mutations occur at the V600 locus

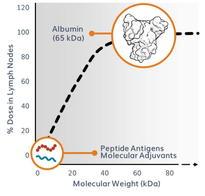


- **Truncal Driver Mutation**
  BRAF mutations occur early in tumorigenesis and are therefore present among all cells within the tumor [7]. Immune escape is unlikely as mBRAF signaling drives tumor survival, and its loss would stop tumor growth.
- **Public Neoantigen**
  Mutant BRAF peptides are not centrally tolerized; cognate TCRs are present in the naïve repertoire [8].
- **Proven Clinical MOA**
  Previously shown that mutant BRAF-specific T cells mediate anti-tumor efficacy [9].

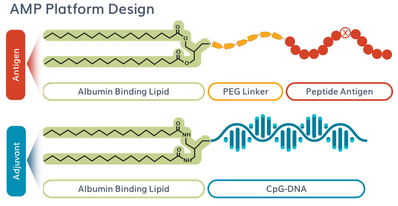
The AMP-Platform Targets Delivery to the Lymph Nodes

- **Smart trafficking to the lymph nodes** after subcutaneous dosing generates immune responses with increased magnitude, function, and durability [10,11].
- **Takes advantage of potent lymph node immune mechanisms**, including activation of innate and adaptive immune cells, antigen-spreading, and improved tumor T cell trafficking / infiltration.
- Mutant BRAF peptides provide **validated antigens** for application of the Amphiphile (AMP) platform.
- Lymph node delivery of potent adjuvants **minimizes systemic exposure to improve safety.**

Lymph Node Biodistribution



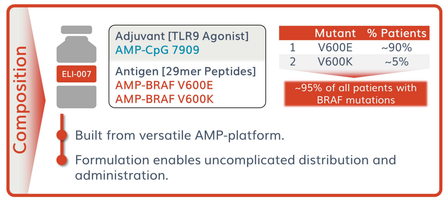
AMP Platform Design



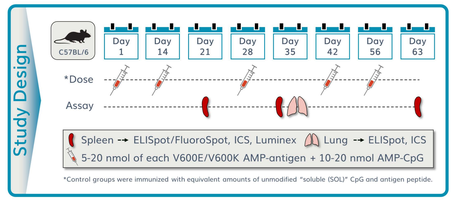
Clinical Experience with the AMP Technology [12,13]

- **ELI-002**, an AMP-vaccine targeting mKRAS, is currently being investigated in clinical trials for treatment of pancreatic and colorectal cancer (**AMPLIFY-201:** NCT04853017 and **AMPLIFY-7P:** NCT05726864).
- **ELI-002** has shown preliminary safety / tolerability, and significant increases in mKRAS T cell responses, associated with reduction / clearance of tumor biomarkers, and reduced risk of progression and death.
- Vaccine candidates targeting mutant p53 or BRAF have been built from the AMP-platform, and utilize the ELI-002 adjuvant, **AMP-CpG**, providing the potential for favorable clinical tolerability and activity.

Off-the-Shelf Formulation

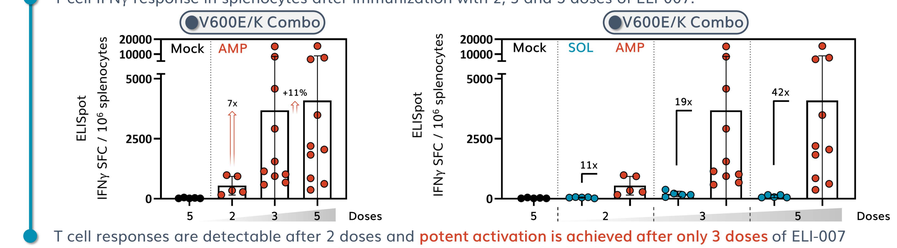


Repeat-Dose Immunization Strategy



Efficient Vaccine Delivery Yields Potent Response after only 3 Doses in Mice

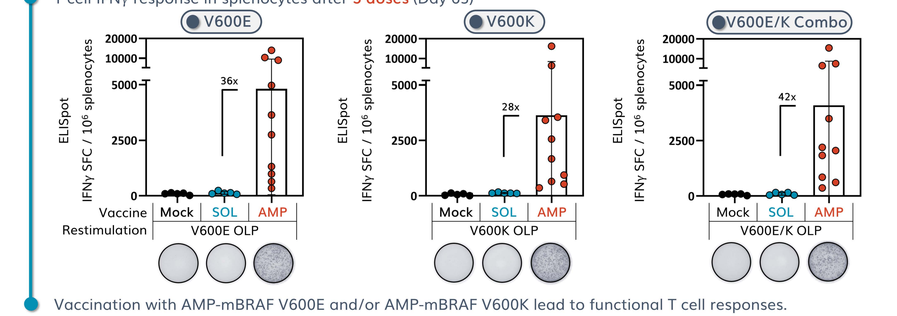
T cell IFNγ response in splenocytes after immunization with 2, 3 and 5 doses of ELI-007.



T cell responses are detectable after 2 doses and potent activation is achieved after only 3 doses of ELI-007 yielding a robust IFNγ response in AMP-immunized mice. This can further be potentiated with subsequent doses.

95% of BRAF-driven Cancers Can Potentially Be Addressed With ELI-007

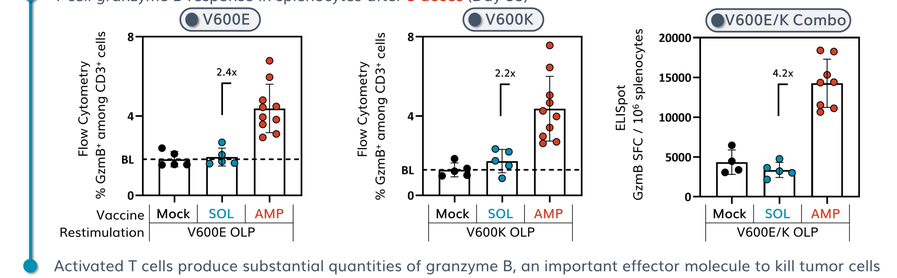
T cell IFNγ response in splenocytes after 5 doses (Day 63)



Vaccination with AMP-mBRAF V600E and/or AMP-mBRAF V600K lead to functional T cell responses.

Vaccine-induced, mBRAF-specific T Cells Show Elevated Cytotoxic Potential

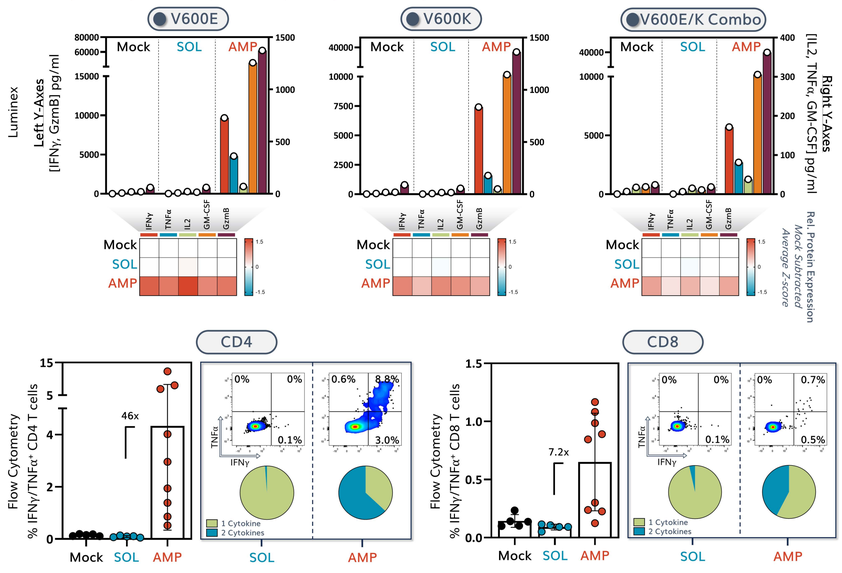
T cell granzyme B response in splenocytes after 3 doses (Day 35)



Activated T cells produce substantial quantities of granzyme B, an important effector molecule to kill tumor cells

ELI-007 Elicits a Comprehensive Polyfunctional T Cell Response

mBRAF-specific cytokine response in splenocytes after repeat immunization with ELI-007

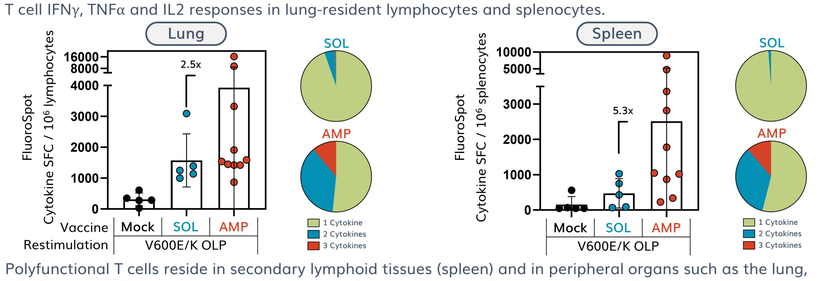


Immunization with ELI-007 induces polyfunctional T cells that produce high levels of IFNγ, TNFα, GM-CSF, IL2, GzmB

Both CD4 and CD8 responses towards the BRAF V600E and V600K antigens are generated.

mBRAF-specific T cells Patrol Potential Metastatic Sites in Peripheral Organs

T cell IFNγ, TNFα and IL2 responses in lung-resident lymphocytes and splenocytes.



Polyfunctional T cells reside in secondary lymphoid tissues (spleen) and in peripheral organs such as the lung, which is one of the predominant sites for metastatic spread in melanoma and colorectal carcinoma.

TAKE HOME MESSAGES

- AMP enhances vaccine potency via targeted lymph node delivery.
- ELI-007 substantially improved T cell responses over soluble comparator vaccines:
  - Polyfunctional T cells that produce T_H1-associated cytokines: IFNγ / TNFα / IL2 / GM-CSF
  - Secretion of Granzyme B, which increases the cytolytic potential of these T cells
- AMP-vaccines have the potential to address a high, unmet medical need for millions of patients with BRAF mutations.
- The AMP-platform technology is simple, rapid and scalable for broad clinical application.

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