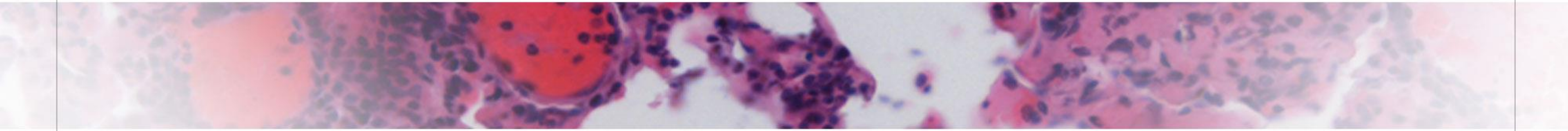
American Society *of* Hematology
Helping hematologists conquer blood diseases worldwide



Dark genome interrogation identifies novel antigens in acute myeloid leukemia – Developing an off-the-shelf vaccine from machine learning to clinic

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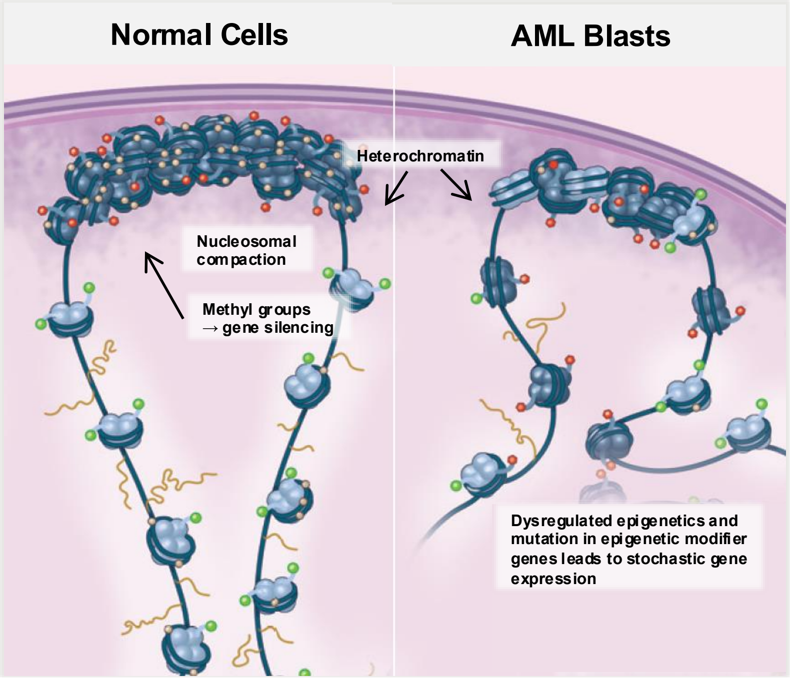
EVAXION

Endogenous retroviruses represents a novel source of therapeutic targets in AML

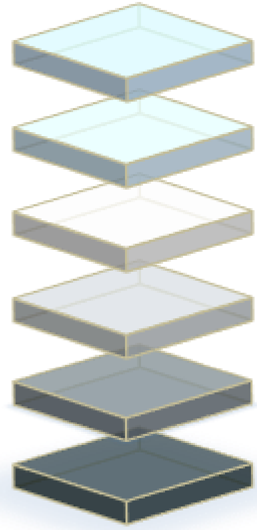
- Durable responses are uncommon in AML patients ineligible for allogeneic SCT, highlighting the need for new therapies
- Epigenetic dysregulation is a hallmark of myeloid malignancy and drives aberrant gene expression
- Epigenetic dysregulation induces AML-specific expression of endogenous retroviruses (ERVs), creating actionable targets
- EVX-04 is an off-the-shelf vaccine designed to target ERV-derived peptides selectively expressed on AML blasts



Modified from Feinberg, New Eng J Med 2018, DOI: 10.1056/NEJMra1402513

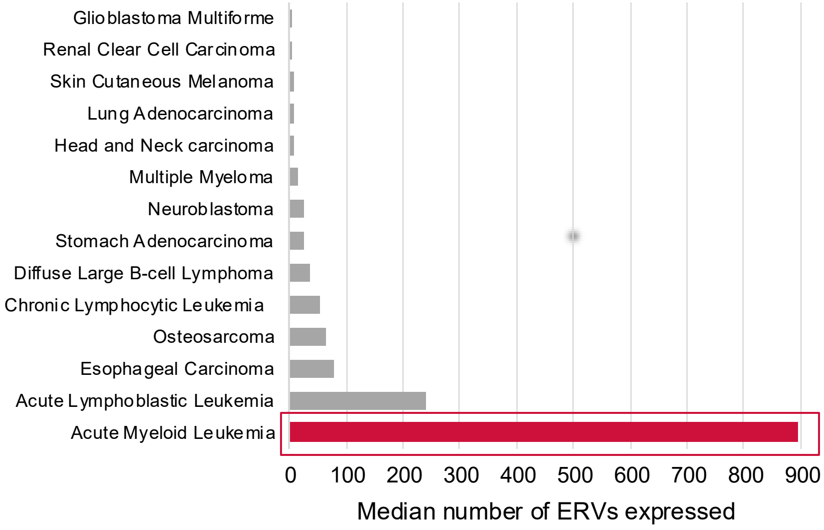
ERVs are highly expressed in AML patients

Patient data sources



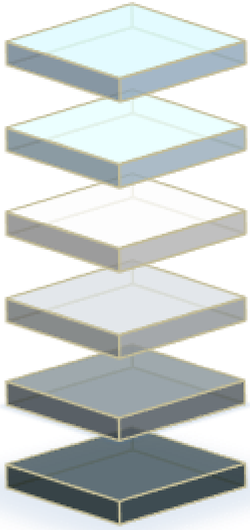
- The Cancer Genome Atlas
- Therapeutically Applicable Research to Generate Effective Treatments
- Cancer Genome Characterization Initiative
- Childhood Cancer Data Initiative
- Multiple Myeloma Research Foundation
- National Human Genome Research Institute

ERV expression across select cancers



ERV expression is shared between AML patients

Patient data sources



- The Cancer Genome Atlas
- Therapeutically Applicable Research to Generate Effective Treatments
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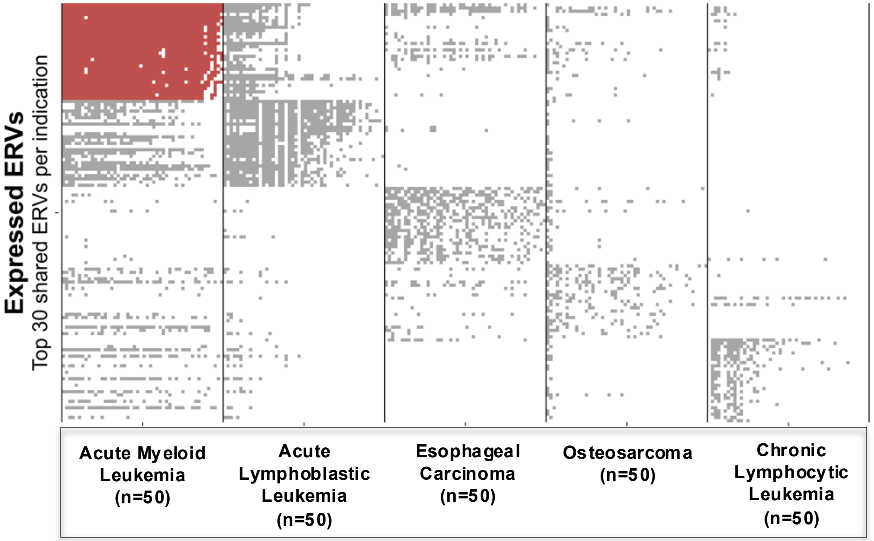
Expression patterns of shared ERVs per indication



AI-Immunology™ drives EVX-04 vaccine design

AI

AI-Immunology™

ERV expression

- 150 TCGA AML patient samples
- Transcriptomic ERV expression
- Translational support using multi-omics

Presentation on MHC

- MHC ligand prediction
- Prevalent alleles in the general population
- Identification of MHC ligand-rich ERV fragments

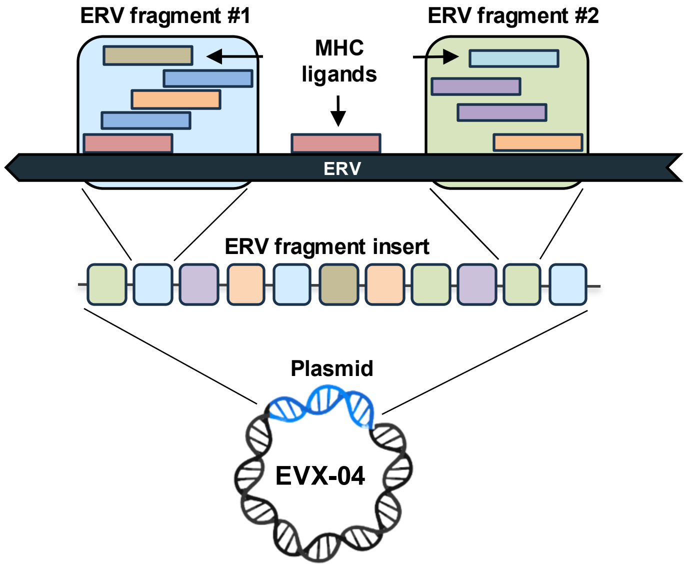
No off-target expression

- ERV expression in healthy tissues
- Prevention of off-target hits and central tolerance
- Filtering of immuno-suppressive domains

EVX-04

AI-Immunology™ selects the optimal set of MHC ligand-rich ERV fragments to include in EVX-04

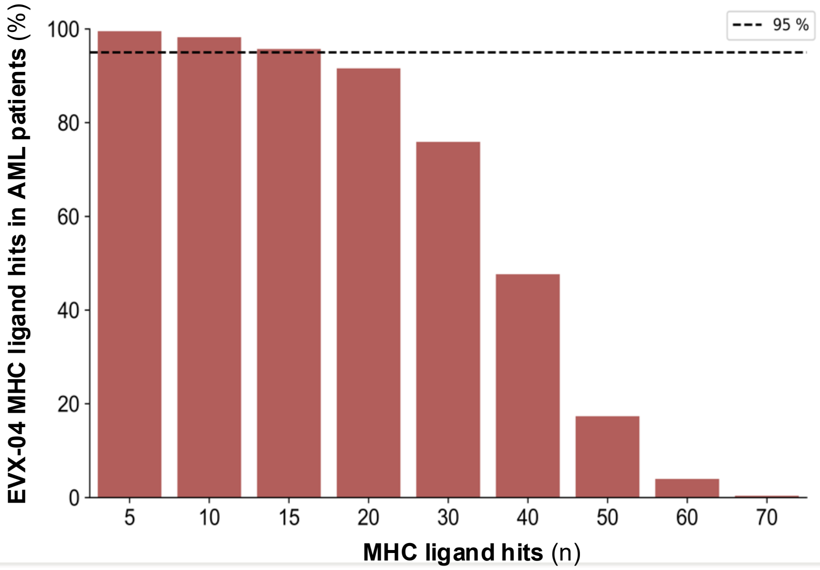
AI-Immunology™ designed EVX-04 vaccine



- AI-Immunology™ identifies 5 million ERV fragments and corresponding MHC ligands
- An optimization process selects ERV fragments with MHC ligands that covers all AML patients
- EVX-04 consists of 16 ERV fragments inserted into a DNA plasmid

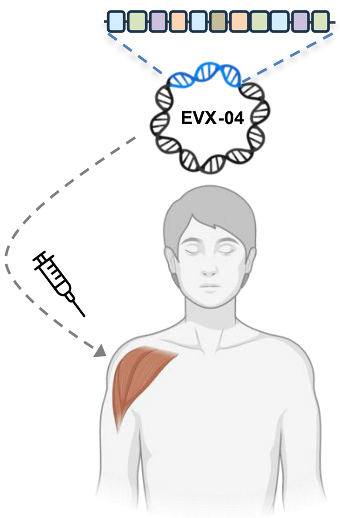
EVX-04 contains multiple ERV-derived MHC ligands to maximize AML patient coverage

EVX-04 is predicted to contain at least 15 MHC ligand hits in 95% of AML patients

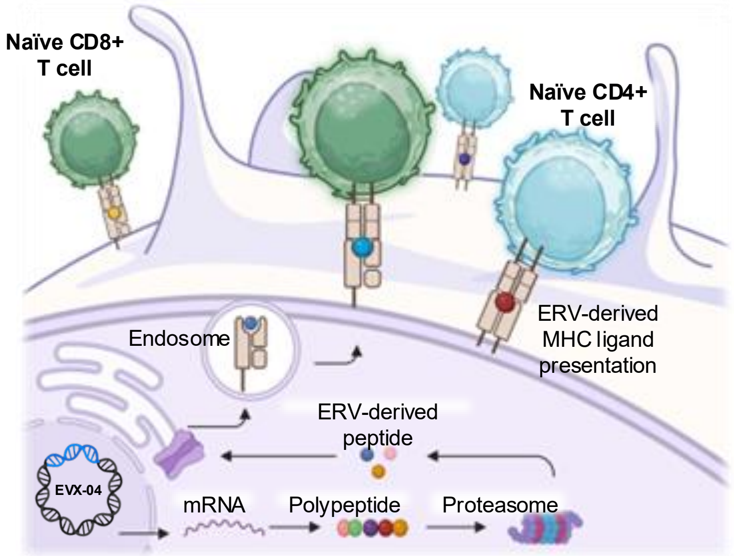


EVX-04 targets AML through T cell mediated immunity

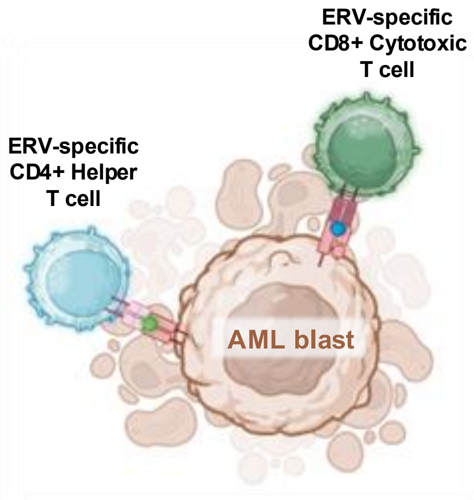
EVX-04 is administered intramuscularly



CD4+ and CD8+ T cells are primed by antigen presenting cells to recognize the EVX-04 ERV targets

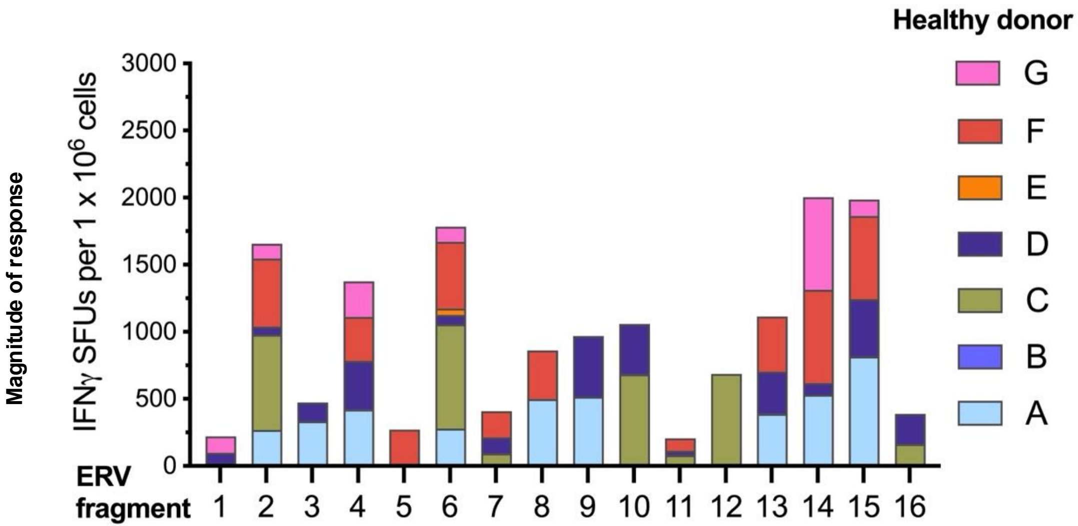


ERV-specific CD4+ and CD8+ T cells recognize and eliminate AML blasts



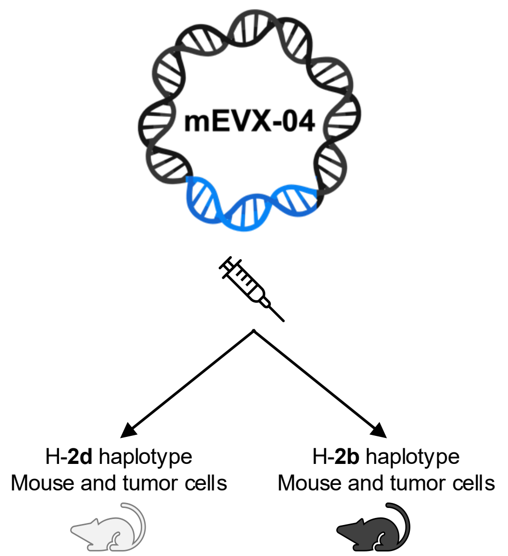
EVX-04 ERV fragments elicit potent responses *in vitro*

ERV-specific T-cell responses observed for all EVX-04 fragments

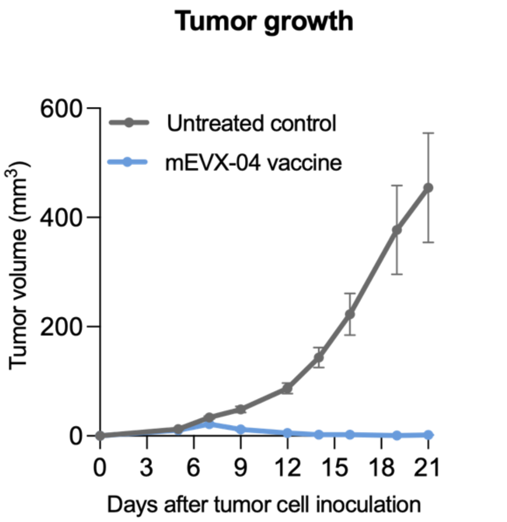


Murine EVX-04 prevents tumor growth *in vivo*

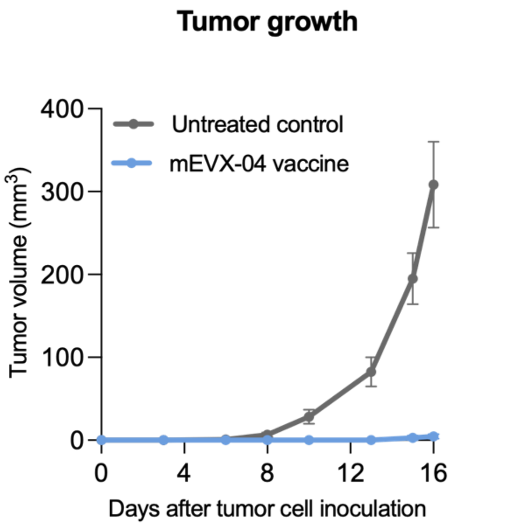
EVX-04 surrogate containing shared colon carcinoma and melanoma ERV fragments



Murine colon carcinoma model
(BALB/c, H-**2d** haplotype)



Murine melanoma model
(C57BL/6, H-**2b** haplotype)



Conclusion

- Evaxion's AI-Immunology— platform designed EVX-04, an off-the-shelf AML vaccine targeting ERVs
- With inclusion of 16 ERV fragments, EVX-04 allows for broad coverage of the AML population
- EVX-04 induces ERV-specific T cells and anti-tumor immunity in vitro and in vivo
- A first-in-human study of EVX-04 in combination with azacitidine and venetoclax in frontline AML is in preparation