UCLA Technology Development Group

IDENTIFICATION OF A PLATFORM FOR T CELL RECEPTOR RECOGNITION OF SPLICE VARIATION NEOANTIGENS IN GLIOBLASTOMA

Case: 2019-693

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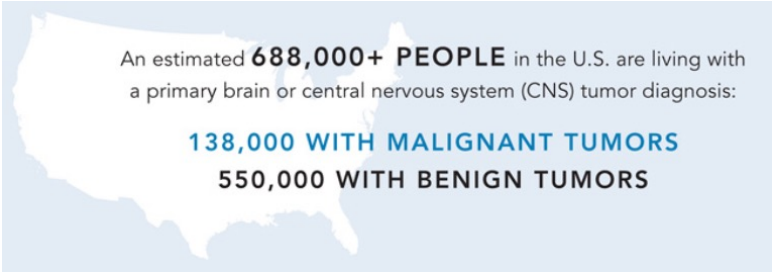
Major research focus centers on understanding the immunology of malignant brain tumors and devising new immune-based therapies to treat these deadly tumors.

Executive Summary

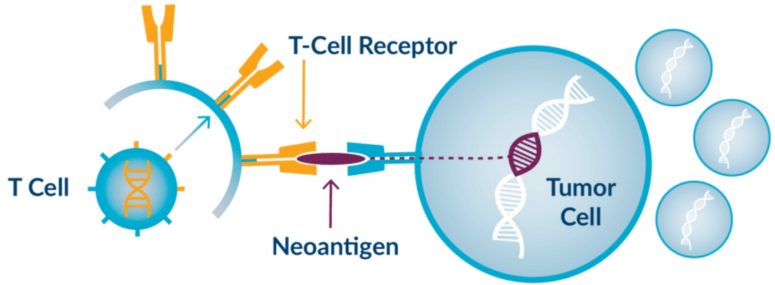
High Level Overview

- Cancer is one of the most common diseases, globally, and is the second leading cause of death after cardiovascular diseases
- Immune cells called T cells recognize foreign protein fragments, called antigens, in order to elicit an immune response
  - Cancer cells produce alternatively spliced RNA, making peptide fragments unique to the cancer cells
  - These protein fragments, called neoantigens, are ideal immunotherapy targets because they are found only in cancer cells
- Knowledge of these alternative RNA splice variation allows for the development of immunotherapies and vaccines.

No current technology can accurately predict and recognize splice variations unique to tumors.



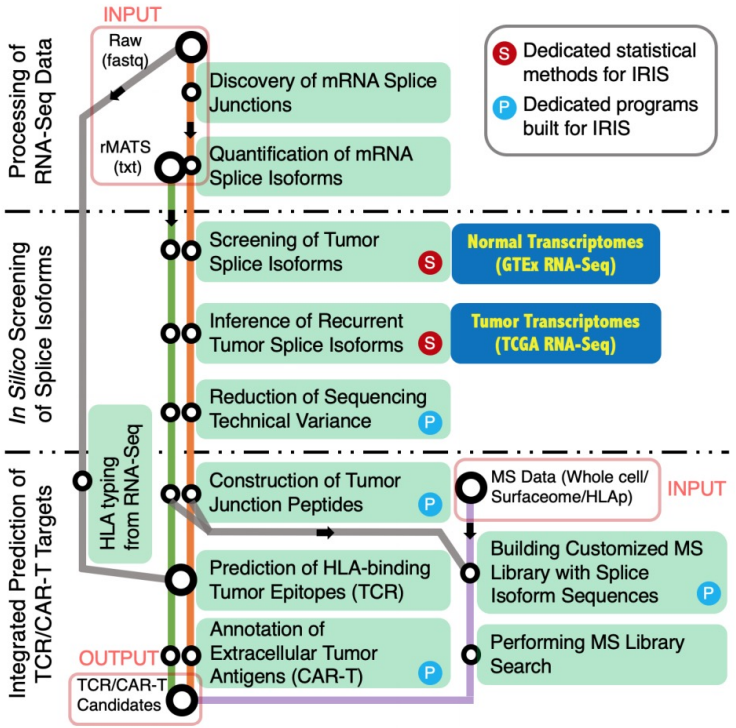
Tumor Specific Antigen Recognition



IRIS Innovates in Neoantigen Identification

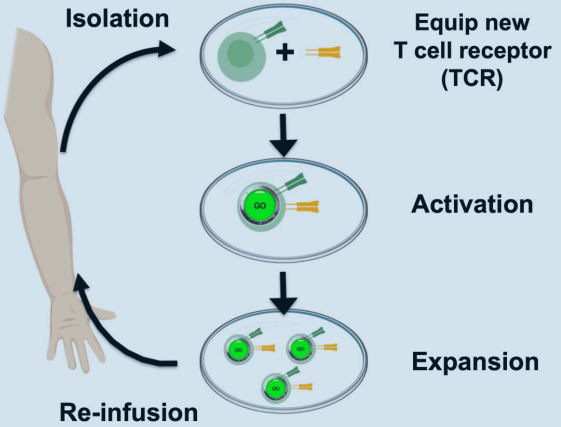
- UCLA researchers have created a platform for the screening and identification of alternative mRNA splice variants unique to brain cancer
- This platform is called **IRIS**: **I**soform peptides from **R**NA splicing for **I**mmunotherapy target **S**creening
- IRIS is capable of screening multiple patient samples simultaneously in ‘group mode’ or can be performed in ‘personalized mode’ to identify targets for a specific patient sample
- IRIS predictions have been validated by tumor-infiltrating lymphocytes, which recognized the predicted splice variant peptides.

IRIS Discovery Platform



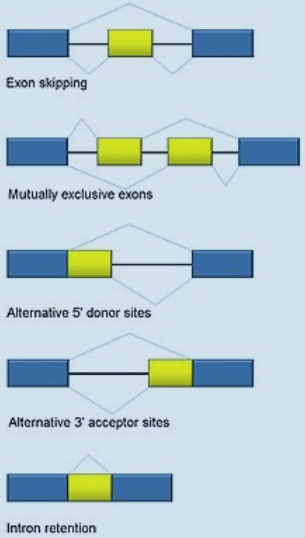
Potential Applications of IRIS

TCR and CAR-T therapies for cancer



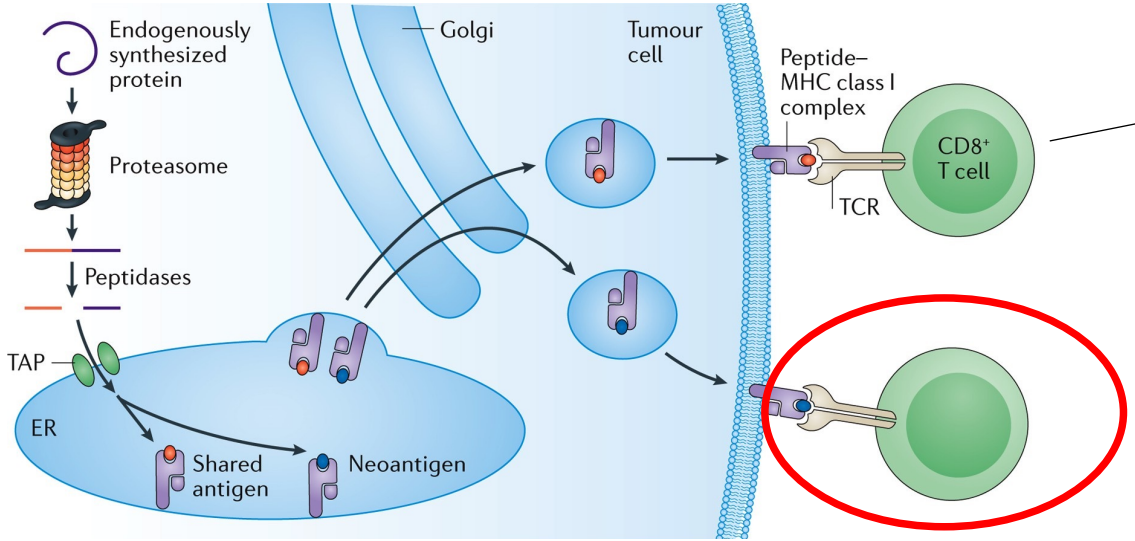
Neo-epitope peptide vaccines for the treatment of cancer

Identification of novel splice-variants in disease



IRIS Exhibits Considerable Advantages

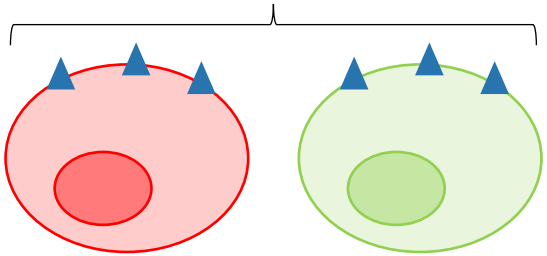
IRIS utilizes neoantigens for immunotherapeutic targeting, reducing off-target toxicities



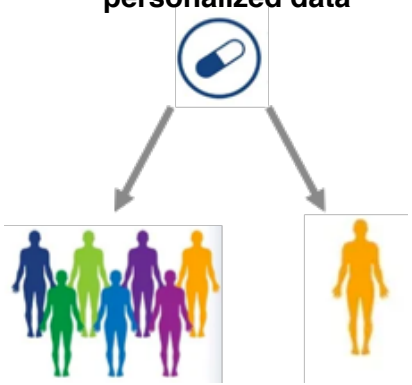
Neoantigen Not Found in Healthy Cells

- Reduced Toxicities
- Reduced Immune Tolerance

Conserved Antigens

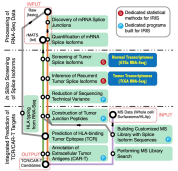


IRIS can be applied to group data or personalized data

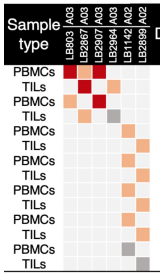


Developmental Timeline of Technology

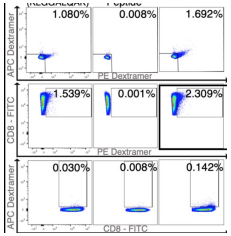
Aug. 2018: Initial Conception



IRIS pipeline developed for identifying neoantigens in brain cancer

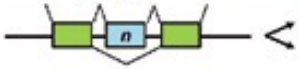


7 of 8 candidates were recognized by human glioma patient T cells

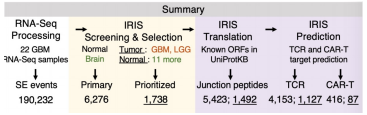


Top candidate selected to determine patient clonotyping

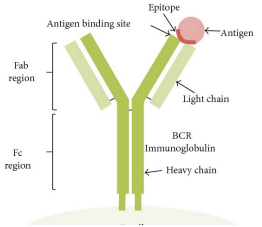
Bioinformatics tools developed to identify cancer-specific splicing changes



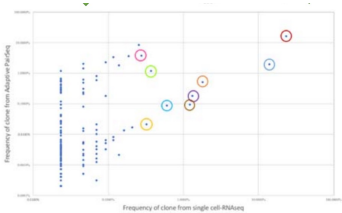
22 glioma patient samples used to generate candidate epitope list



Healthy patient T cells show very low recognition of epitopes



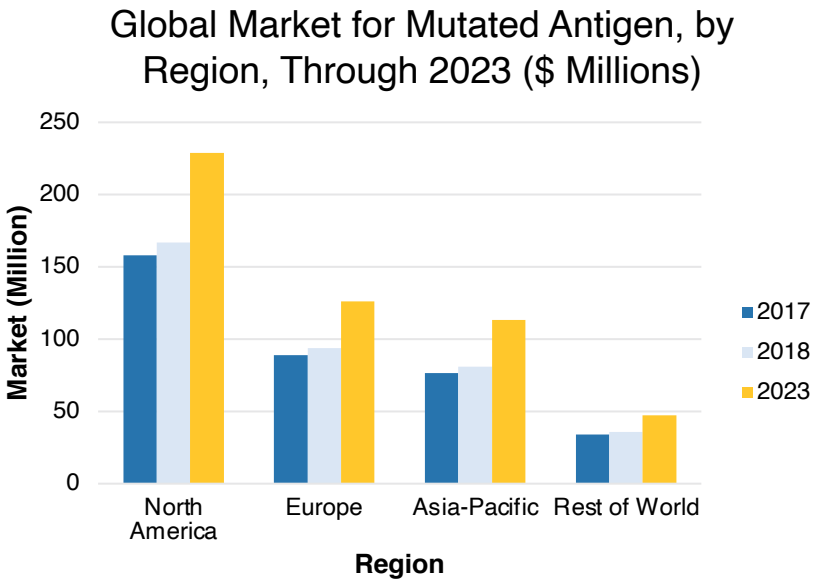
A few TCR clones dominate in recognition of the neoantigen



Market Opportunity

Market Overview: Global tumor-specific antigen market experiencing strong growth

BCC research report **BIO184A**



The global tumor-specific antigen market was $1.8 billion in 2018.

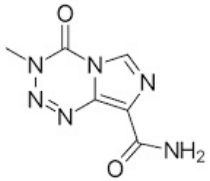
- Projected growth to **$2.4 billion by 2023.**
- Compound Annual Growth Rate **(CAGR) of 6.2% by 2023.**

The mutated antigen market, which consists of neoantigen immunotherapies, shows the largest market area in North America.

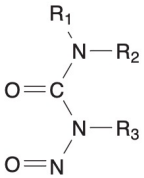
- CAGR of mutated antigen market is 6.5%.
- High growth is expected across all regions.

Competition in Glioblastoma Therapy

Chemotherapeutics (Systemic Application)



Temozolomide

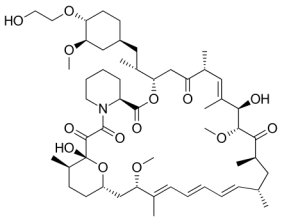


Nitrosourea

Disadvantages

Targeted Therapeutics (Signaling Pathways)

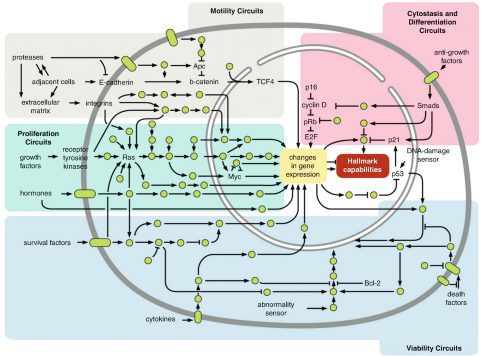
bevacizumab
100 MG/4 ML INJECTION FOR IV USE



Everolimus

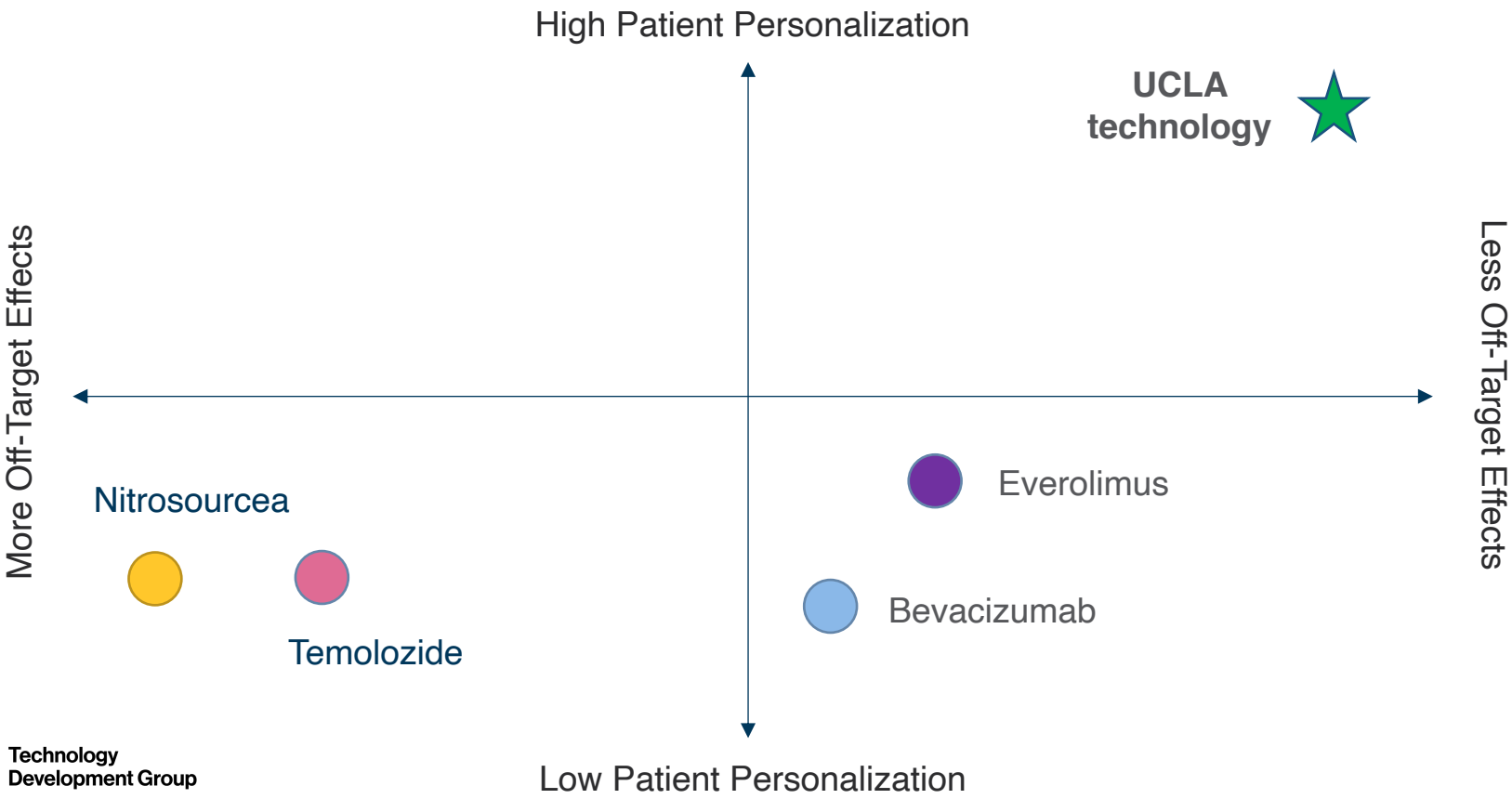
Disadvantages

Complex Signaling Pathways

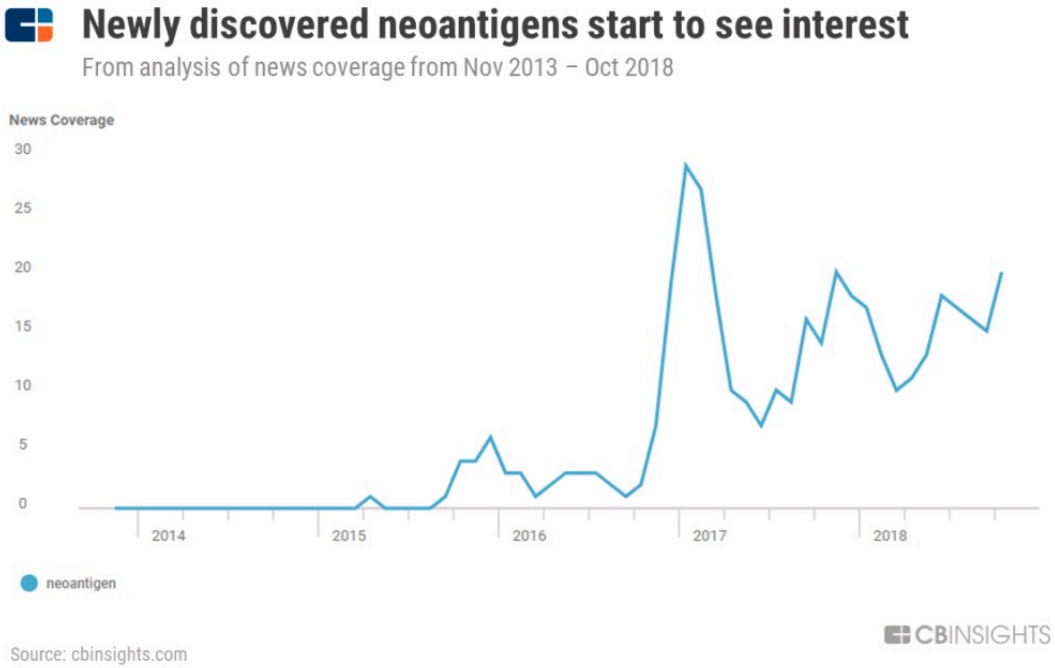


Many pathways overlap in healthy cells

Competition Analysis



Market Stakeholder Profiles in Tumor-Specific Antigens Market



Currently, neoantigen-based technologies are very new.

Major players in developing these therapies include:

- BioNTech
- Genentech
- Genocea Biosciences
- Neon Therapeutics
- Gristone Oncology
- Agenus
- Adaptive Biotechnologies

Commercialization Potential

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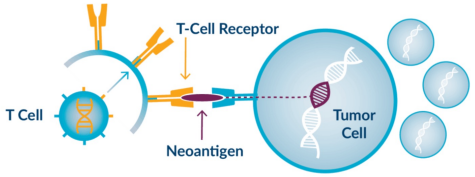
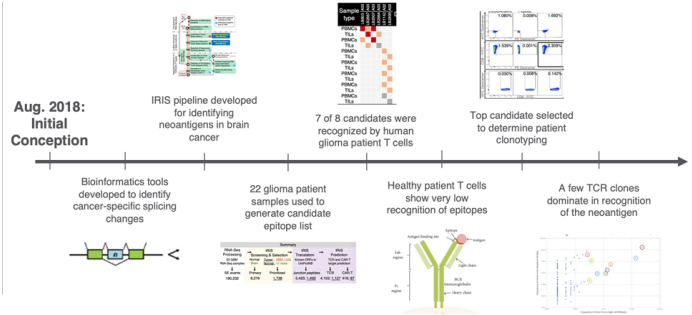
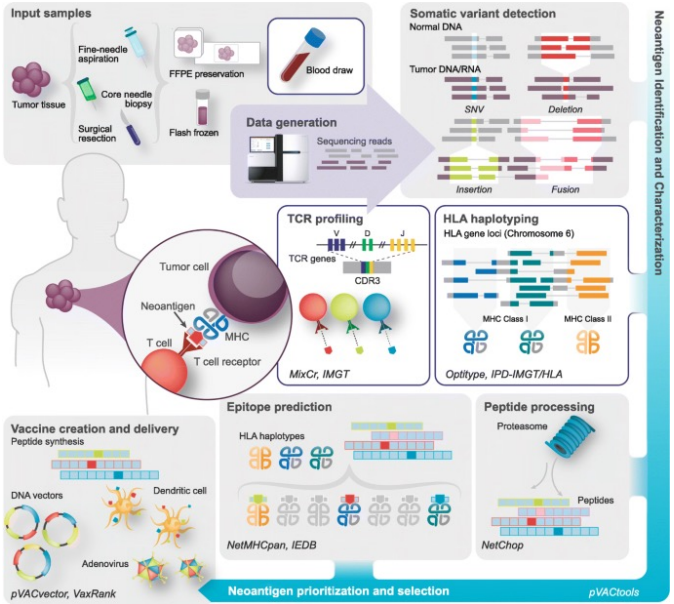


Neoantigens are being widely recognized as potential targets for next generation cancer therapeutics. However, current methods to identify neoantigens requires many patient samples, that are not readily accessible. Instead, IRIS allows minimal patient sample material, while providing accurate targets

Methodology has been validated on clinical samples



Multiple Platforms for Neoantigen Discovery focus on common mutations



IRIS gives the ability to identify neoantigens based on splice variants and has been used to develop a novel T Cell Receptor Therapy for Brain Cancer

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Thank You

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