LaSalle Universidad
DIRECCIÓN DE INVESTIGACIÓN

Neoantigen Detection Using Transformers and Transfer Learning

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Introduction
- Immunotherapy to Treat Cancer
- Problem

Development
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Review
- Review Results
- Input Encoding
- Transformers
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Immunotherapy to Treat Cancer

Immunotherapy is a type of cancer treatment that helps your immune system fight cancer [1].

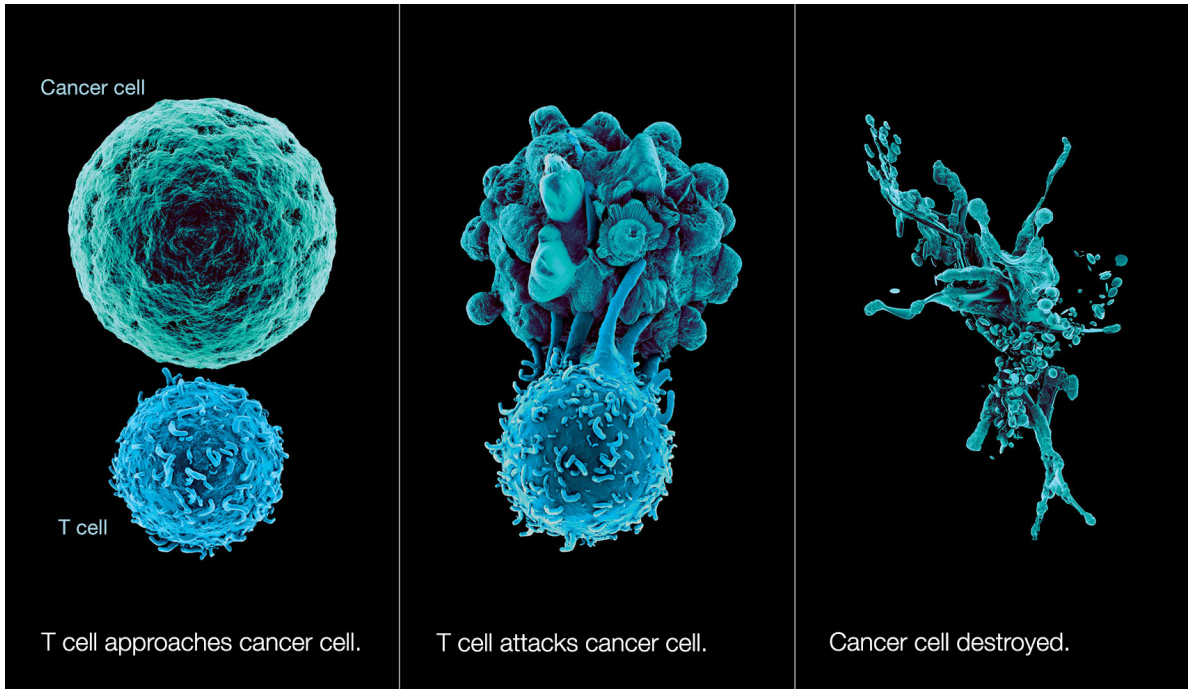

Figure: Example of how a T cell attack a cancer cell [2].

Neoantigen

A new protein that forms on cancer cells when certain mutations occur in tumor DNA. Neoantigens used in vaccines and other types of immunotherapy are being studied in the treatment of many types of cancer [3, 4].

Currently, there is a lot of methods to detect neoantigens; however, only a small number of them manage to stimulate the immune system [5, 6].

Immunotherapy for Cancer
Personalized Vaccines

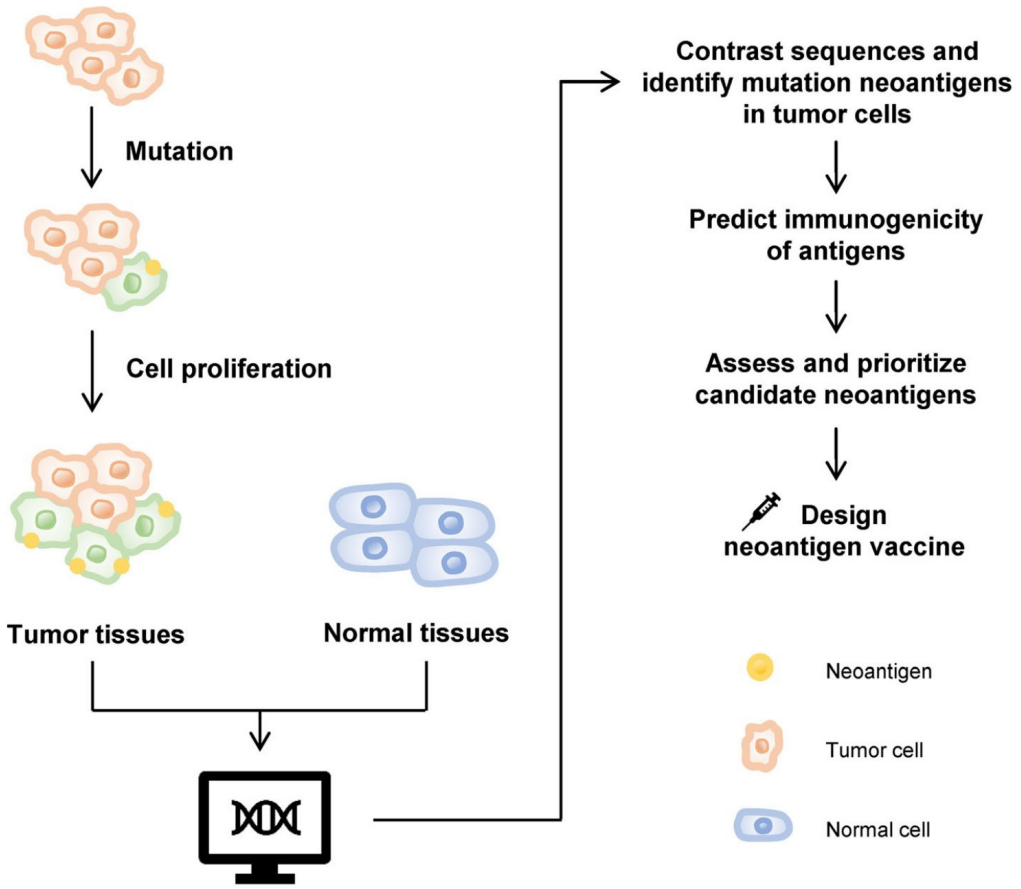

Figure: Personalized vaccines process for Cancer [7].

Immunotherapy for Cancer

Personalized Vaccines

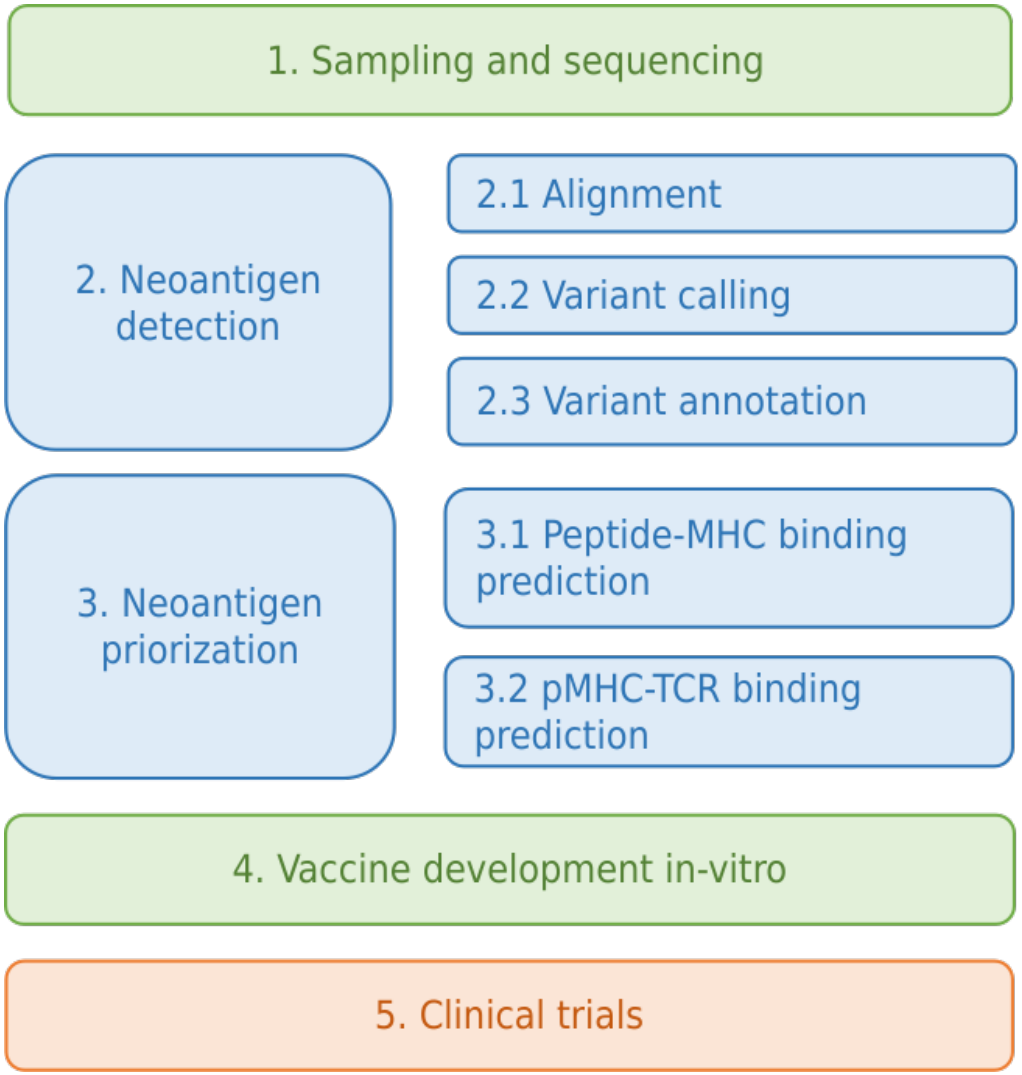

Figure: Personalized vaccines process for Cancer.

pMHC binding prediction

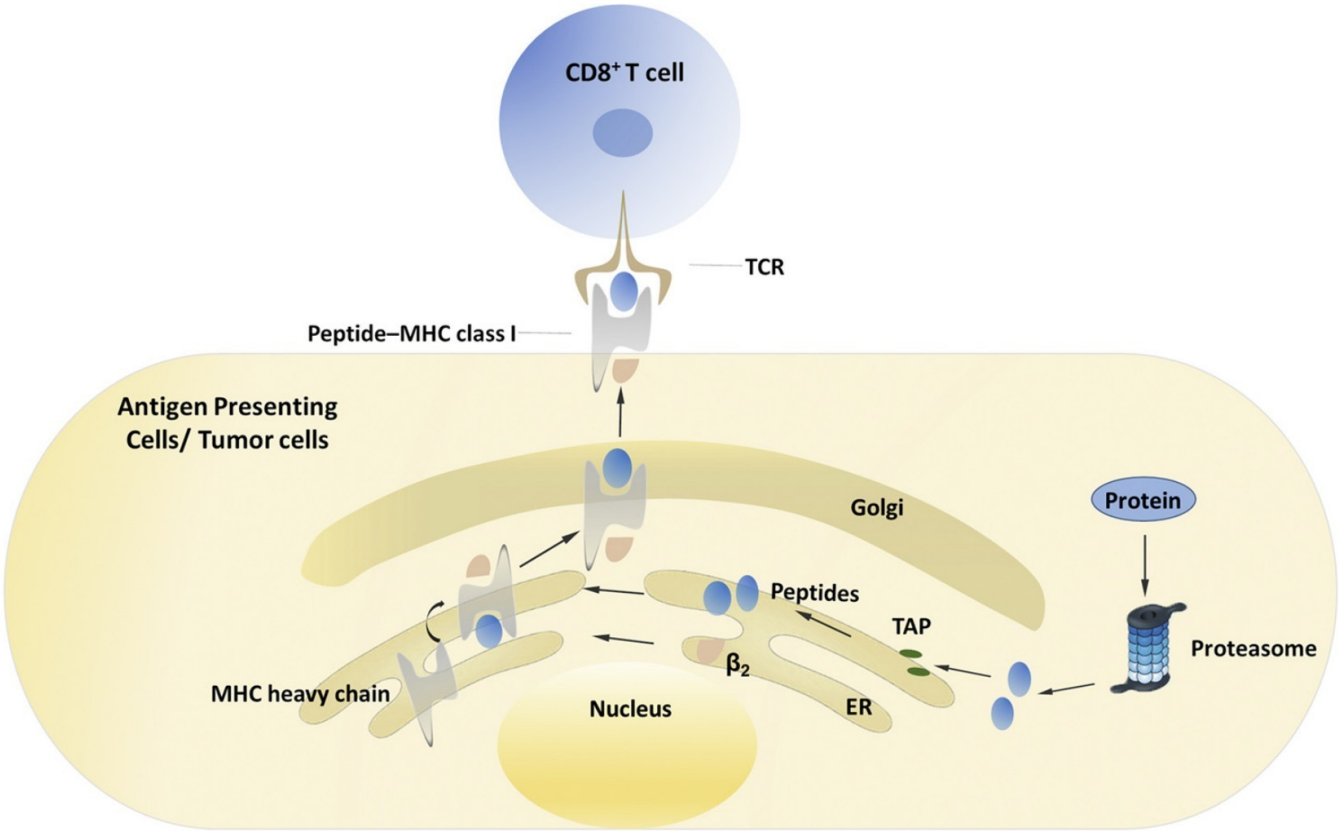

Figure: pMHC presentation process in MHC class I [8].

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Problem
Peptide-MHC Binding Prediction

Less than 5% of detected neoantigens (peptides binded to MHC) succeed in activating the immune system [9].

This is a **binary classification problem**. A peptide could be represented like: $p = \{A, ..., Q\}$ and a MHC like: $q = \{A, N, ..., Q, E\}$. Finally, we need to know the probability of affinity between p and q (pMHC)

Problem

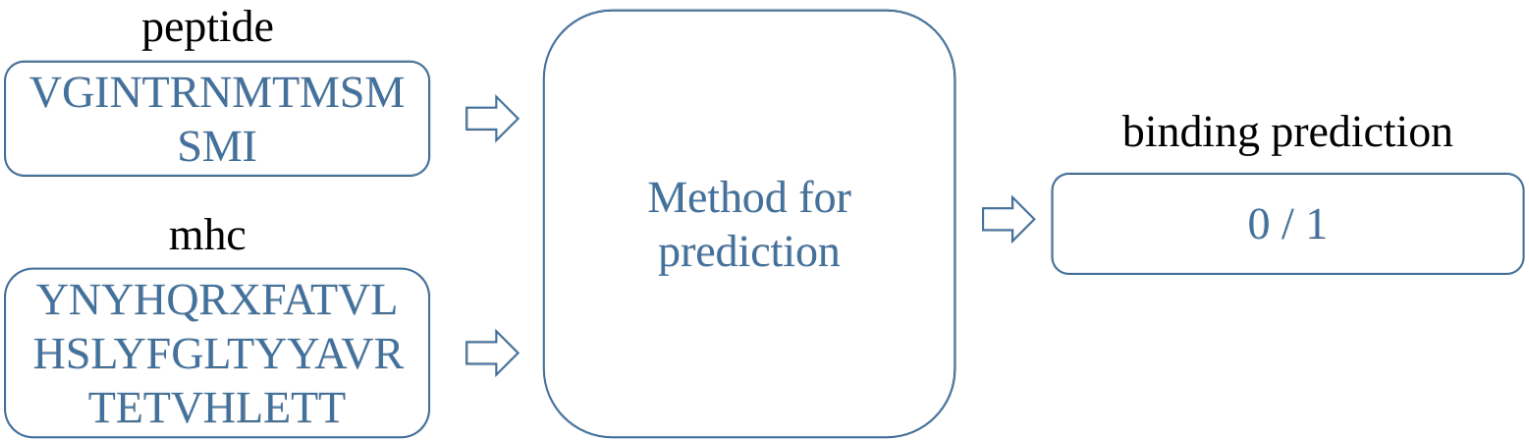

Figure: pMHC binding prediction problem.

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Projects

Name	State	Task
Principales estrategias y métodos basados en deep learning para la detección de neo antígenos en el marco del desarrollo de vacunas personalizadas en la inmunoterapia del cáncer	Finished	Review
Desarrollo de una Aplicación Web para la Detección de Neoantígenos en el Marco de Desarrollo de Vacunas Personalizadas para Tratar el Cáncer	In progress	pMHC binding prediction
NeoArgos-tools: Un Pipeline de Detección In-silico de Neoantígenos de Cáncer para el Desarrollo de Vacunas Personalizadas	Not started	Pipeline development

Projects
Review

"Principales estrategias y métodos basados en deep learning para la detección de neo antígenos en el marco del desarrollo de vacunas personalizadas en la inmunoterapia del cáncer"

Team

- Vicente Machaca Arceda (ULaSalle).
- Valeria Goyzueta (ULaSalle).
- Yván Tupac (UCSP).
- Maria Cruz (UCSP).

Publications

- Deep Learning and Transformers in MHC-Peptide Binding and Presentation Towards Personalized Vaccines in Cancer Immunology: A Brief Review
- Neoantigen Detection Using Transformers and Transfer Learning in the Cancer Immunology Context.

Projects
pMHC binding prediction

"Desarrollo de una Aplicación Web para la Detección de Neoantígenos en el Marco de Desarrollo de Vacunas Personalizadas para Tratar el Cáncer "

Team

- Vicente Machaca Arceda (ULaSalle).
- Richart Escobedo Quispe (ULaSalle).
- Jose Grados (ULaSalle).
- Krystian Kurt (ULaSalle).

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Results

We analyzed papers' titles, and then a small subset of **54 papers were selected**.

Table: Number of papers found in databases according to search string.

Year	Research papers
2018	46
2019	72
2020	86
2021	61
2022	58
Total	**323**

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Input Encoding
One-hot

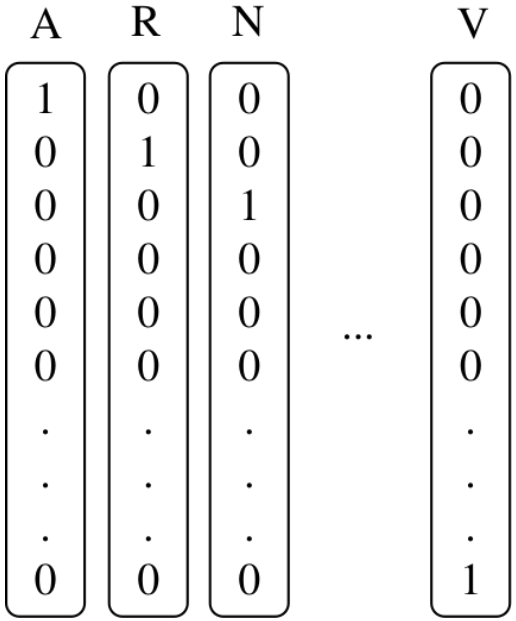

Figure: pMHC presentation process in MHC class I [8].

Input Encoding
BLOSUM

Table: BLOSUM62 matrix. Normally, it is used to represent amino acids numerically. Each amino acid is represented by a row.

	C	S	T	P	A	G	N	D	E	Q	H	R	K	M	I	L	V	F	Y	W
C	0																			
S	-1	4																		
T	-1	1	5																	
P	-3	-1	-1	7																
A	0	1	0	-1	4															
G	-3	0	-2	-2	0	6														
N	-3	-1	0	-2	-2	0	6													
D	-3	1	-1	-1	-2	-1	1	6												
E	-4	0	-1	-1	-1	-2	0	2	5											
Q	-3	0	-1	-1	-1	-2	0	0	2	5										
H	-3	0	-2	-2	-2	-2	1	-1	0	0	8									
R	-3	-1	-1	-2	-1	-2	0	-2	0	1	0	5								
K	-3	-1	-1	-1	-1	-2	0	-1	1	1	-1	2	5							
M	-1	0	-1	-2	-1	-3	-2	-3	-2	0	-2	-1	-1	5						
I	-1	-2	-1	-3	-1	-1	-4	-3	-3	-3	-3	-3	-3	1	4					
L	-1	-2	-1	-3	-1	-4	-3	-4	-3	-2	-3	-2	-2	2	2	4				
V	-1	-2	0	-2	0	-3	-3	-3	-2	-2	-3	-3	-2	1	3	1	4			
F	-2	-2	-2	-4	-2	-3	-3	-3	-3	-3	-1	-3	-3	0	0	0	-1	6		
Y	-2	-2	-2	-3	-2	-3	-2	-3	-2	-1	2	-2	-2	-1	-1	-1	-1	3	7	
W	-2	-3	-2	-4	-3	-2	-4	-4	-3	-2	-2	-3	-3	-1-	-3	-2	-3	1	2	11

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Transformers

The **Transformer Neural Network** is a novel architecture that aims to solve sequence-to-sequence tasks while handling long-range dependencies with ease. It was proposed in the paper “Attention Is All You Need” [35].

Bidirectional Encoder Representations from Transformers (BERT) [36] is a recent paper published by researchers at Google AI Language. It has caused a stir in the Machine Learning community by presenting state-of-the-art results in a wide variety of NLP tasks,

Table: List of pre-trained BERT models.

Model	Parameters	Layers
TAPE	92M	12
ProtBert	420M	30
ESM1	43M, 85M y 670M	6, 12, and 34
ESM1-b	650M	33
ESM2	8M, 35M, 150M, 650M, 3B, 15B	6, 12, 30, 33, 36, and 48

Transformers

Table: Transformers used for pMHC binding and presentation prediction.

Year	Name	Model
2022[37]	**HLAB**	BERT from ProtBert pre-trained model followed by a BiLSTM with attention mechanism.
2022[38]	MHC RoBERTa	RoBERTa pre-trained and followed by 12 multi-head SA and a FC layers, it outperformed NetMHCPan 3.0.
2022[39]	**TransPHLA**	It used SA mechanism based on four blocks, it slightly outperformed NetMHCpan4.1 and is faster making predictions.
2021[40]	ImmunoBERT	BERT from TAPE pre-trained followed by a linear layer. Authors claimed that N-terminal and C-terminals are highly relevant after analysis with SHAP and LIME.
2021[41]	BERTMHC	BERT from TAPE pre-trained followed by a linear layer. It outperformed NetMHCIIpan3.2 and PUFFIN.

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Limitations

They ignored Posttranslational modifications (PTMs) such as phosphorylation, glycosylation, and deamidation, which influence the specificity of MHC binding and presentation and several aspects of the biology underlying pMHC presentation are poorly understood. Furthermore, to get accurate results for neoantigen detection, we need to integrate pMHC-TCR studies.

Another limitations are related to high computing requirements for training BERT architectures. For instance, the biggest ESM2 model has 15 billion parameters.

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Future works

Future work could include the use of transfer learning from ESM1-b [44] and ESM2 [45].

Moreover, there is pHLA3D, a dataset of 3D structures of the alpha/beta chains and peptides of MHC-I proteins; it opens new perspectives for studying pMHC prediction.

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Questions?