

Immuno Oncology: Trends and Developments on The Horizon

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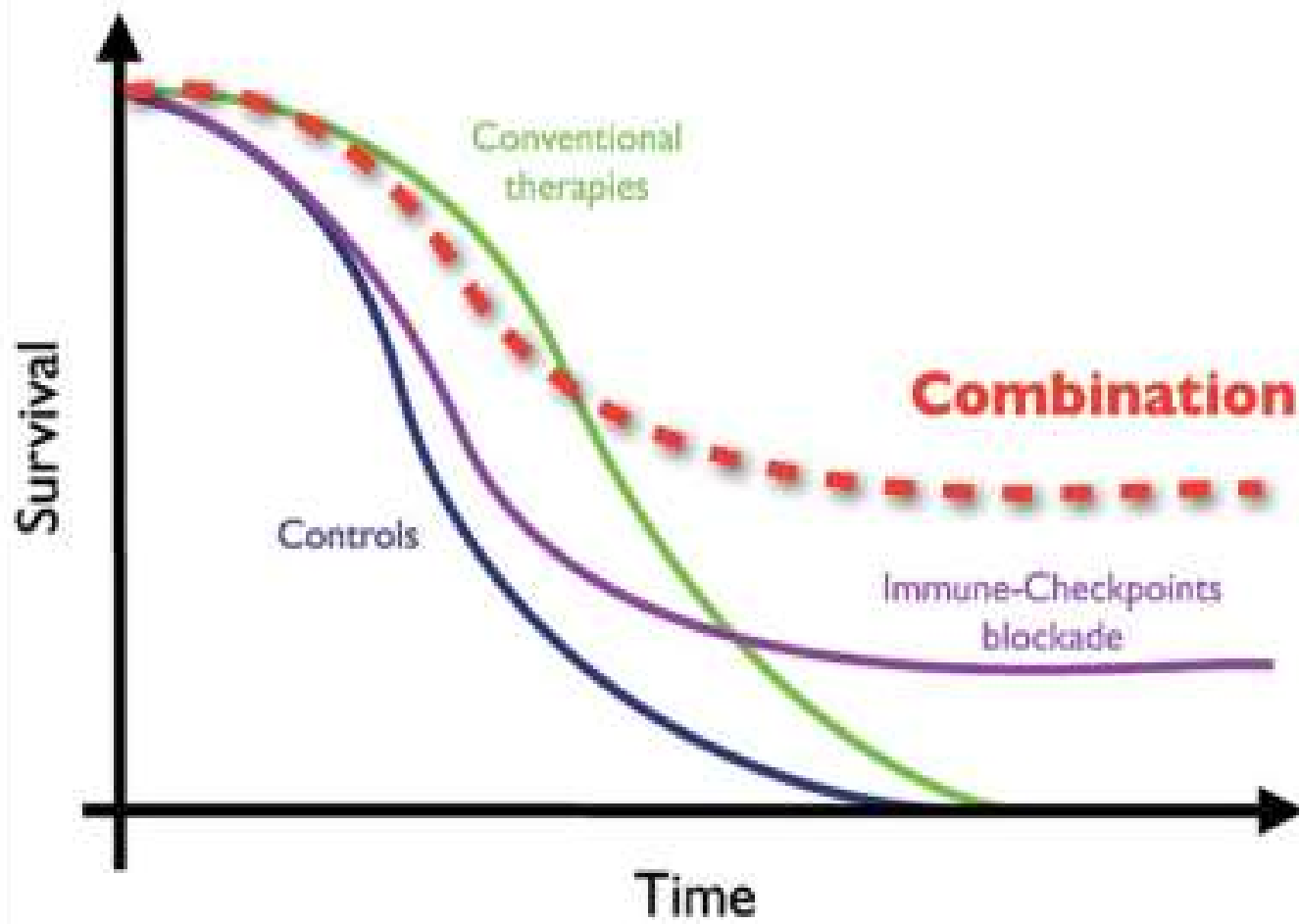
Central European Cooperative Oncology Group (CECOG)

Basics of Immune Checkpoint Inhibitor Treatment of Cancer

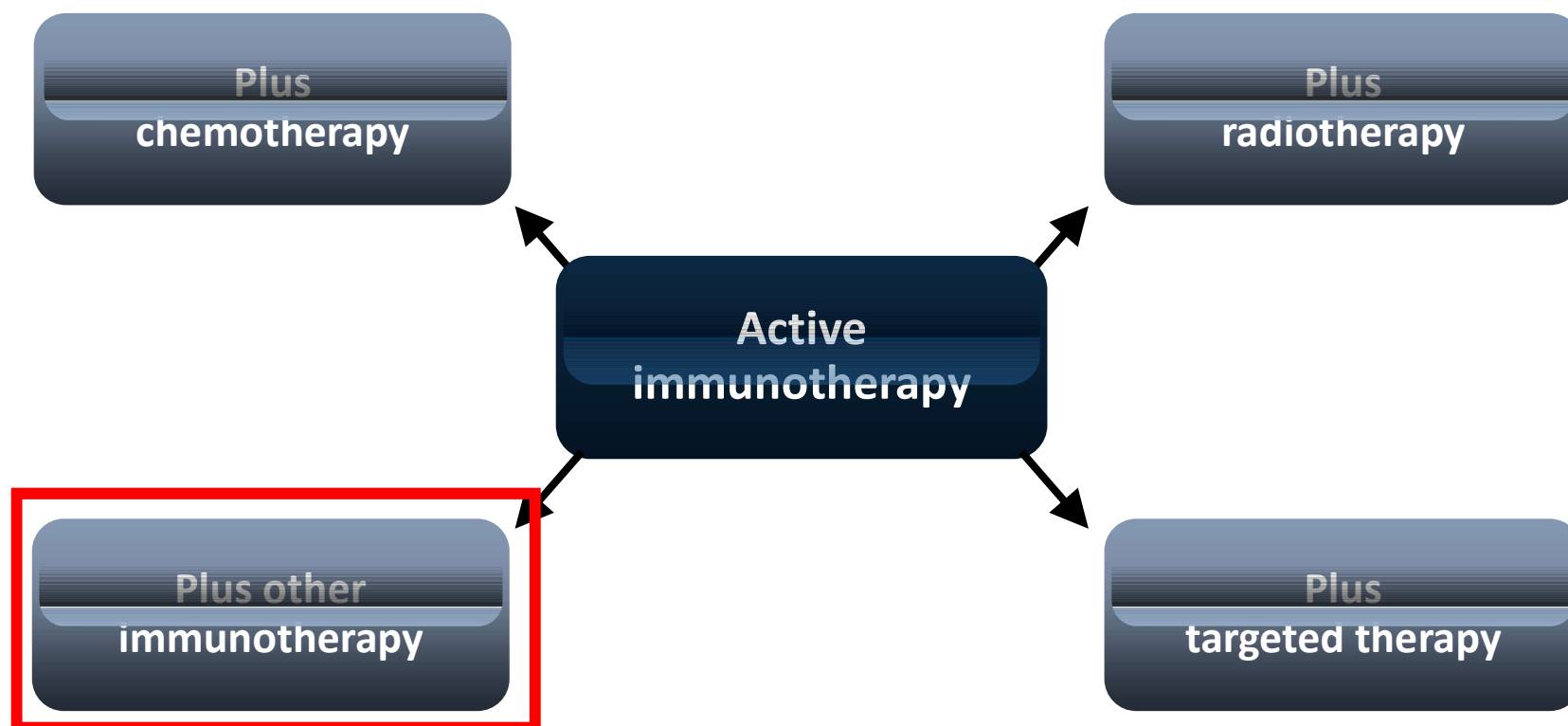
Video

http://players.brightcove.net/2696240571001/VyQDdgBTI_default/index.html?videoId=5230623752001





New Approaches to Build on Active Immunotherapies to Maximize Clinical Benefit



Drake CG. *Ann Oncol.* 2012;23(suppl 8):viii41–viii46; Hannani D, et al. *Cancer J.* 2011;17:351–358; Ménard C, et al. *Cancer Immunol Immunother.* 2008;57:1579–1587; Ribas A, et al. *Curr Opin Immunol.* 2013;25:291–296.

Immuno Oncology: Examples of Partners for Combination \geq 2017

- Combination Checkpoint Blockade
- Checkpoint-Blockade plus
 - Immune-Stimulatory Agents
 - Metabolic Modulators
 - Other Immune Modulators
 - Macrophage Inhibitors
 - Injectable Therapies
 - Cancer Vaccines
 - Adoptive Cell Transfer



Combination of Immune Checkpoint Inhibition and Vaccines

Efficacy for combined PD-1 inhibitor and cancer vaccine in HPV-16-positive cancer

A reduction in T-cell activity via tumour-mediated CTLA-4 and PD-1 signalling may contribute to the disappointing lack of success experienced with tumour vaccines in the clinic.¹ The introduction of checkpoint inhibitors as cancer treatments has led to a growing interest in cancer vaccines in combination with these new agents.

In a presentation yesterday, Professor Bonnie Glisson from MD Anderson Cancer Center, Houston, TX, USA, reported data from a phase II trial demonstrating the promising efficacy of a combination of nivolumab and the human papillomavirus (HPV)-16 vaccine, ISA 101, in 24 patients with recurrent, incurable HPV-16-positive cancer (Abstract 11360).

The trial met its primary endpoint, achieving an overall response rate (ORR) of 33%.



"The ORR of 36% in 22 patients with oropharyngeal cancer compares favourably with the 16% achieved with nivolumab monotherapy in similar patients in CheckMate 141," said Professor Glisson. At a median follow-up of 8.6 months, the median overall survival had not been reached.

"These data suggest that anti-PD-1 therapy can enhance the effects of cancer vaccines by counteracting the immunosuppressive tumour microenvironment, and the findings should be confirmed in a larger, randomised trial," observed Professor Glisson.

1. Ali OA, et al. Cancer Immunol Res 2016;4:95-100

Immuno Oncology

- **Revolutionary Change in Treatment Paradigm of Malignancies**
- **Currently, we are witnessing ONLY the End of the Beginning**

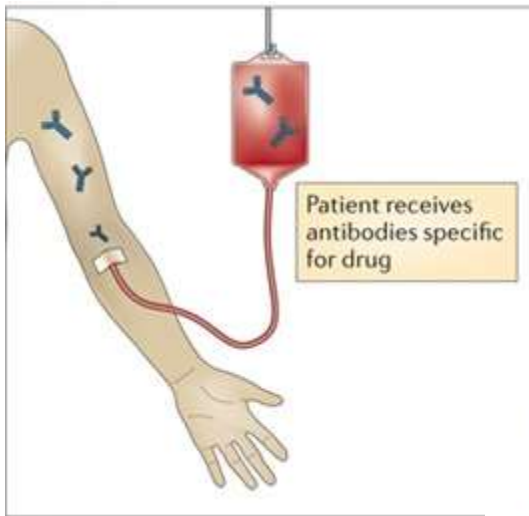


The future of vaccines against cancer

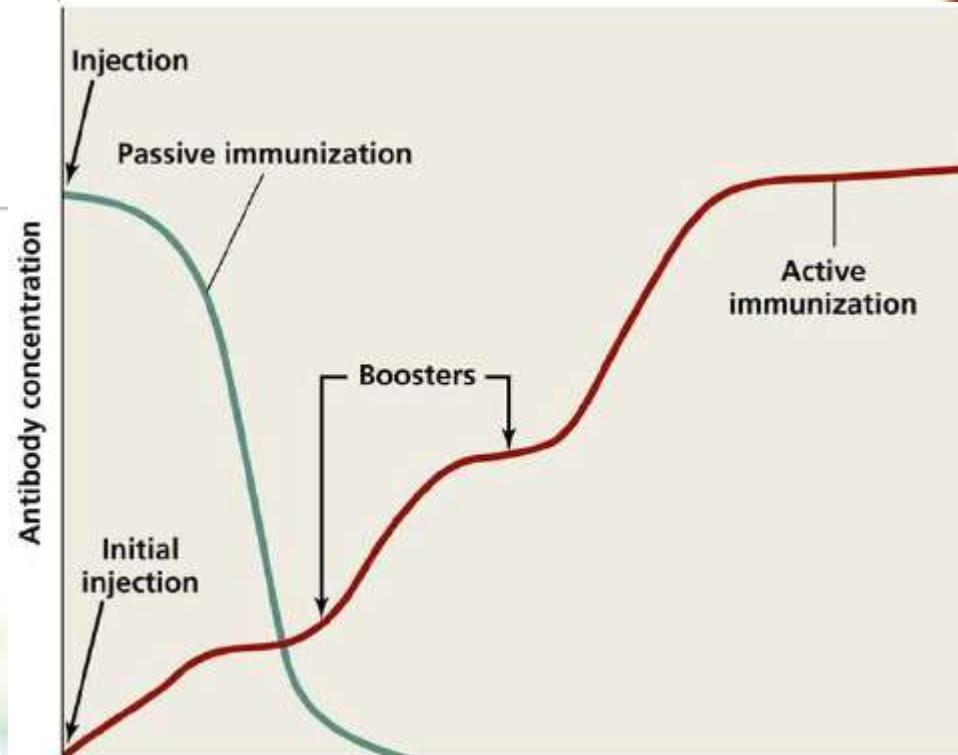
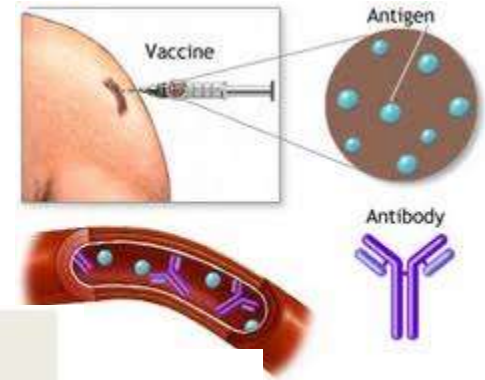
Univ. Prof. Dr. Ursula Wiedermann
Institute of Specific Prophylaxis & Tropical Medicine
Medical University of Vienna, Austria, Europe

Why go for Active Immunization against cancer ?

Difference between passive immunotherapy and active vaccination



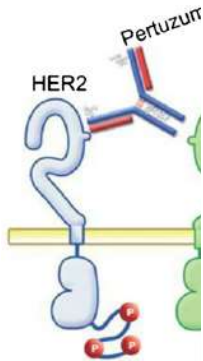
Specificity	Memory
Yes	No



Specificity	Memory
Yes	Yes



Action of monoclonal antibodies Herceptin and/or Perjeta



Trastuzumab reduces the growth signal

- By binding to HER2 and preventing dimerization



Trastuzumab flags tumor cells for ADCC

- By binding to HER2 and the FC receptors of immune cells

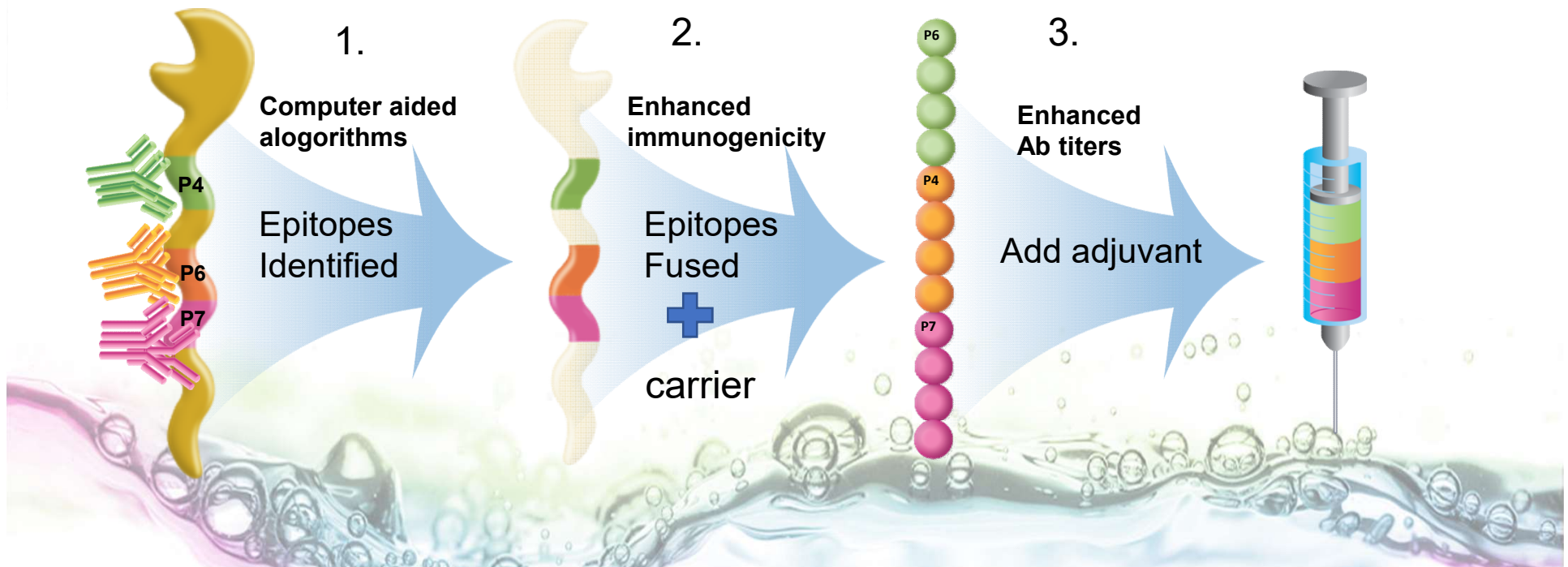
BUT:

Action and efficacy depends on continuous application of the monoclonal antibodies

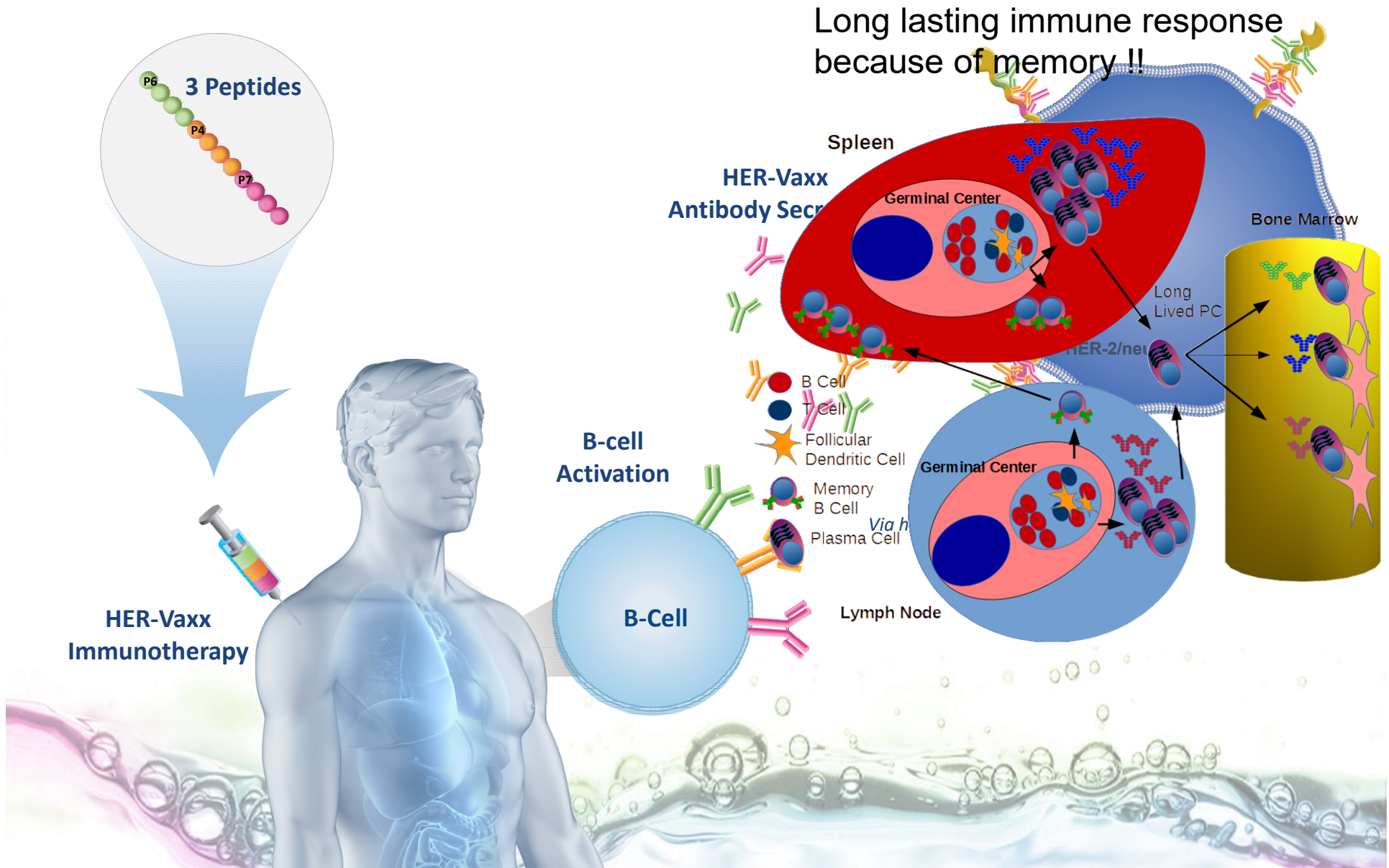
Tumor cell

HER-Vaxx: Vaccine better than monoclonal antibodies

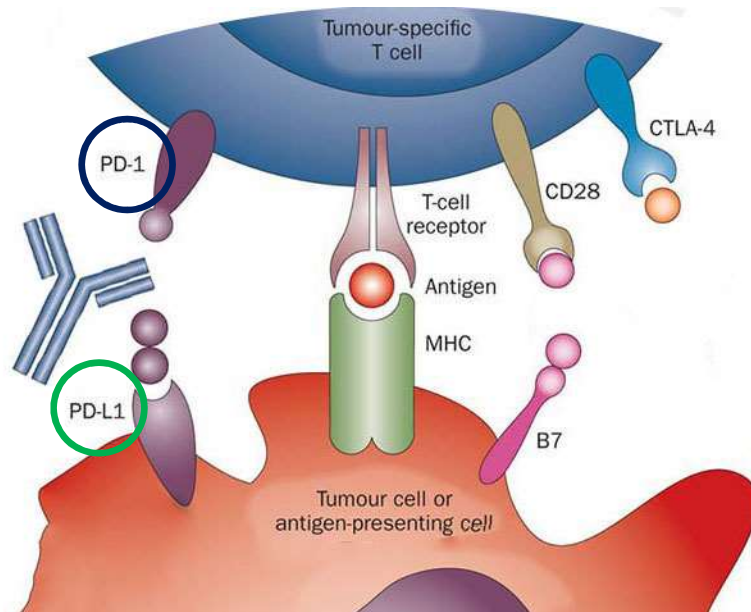
- Advanced B-cell vaccine designed to **stimulate a patient's own immune system** to repeatedly attack the cancer
- Stimulates a patient's B cells to produce **polyclonal antibodies** that target cells with overexpressing HER-2 receptors on their surface
- HER-Vaxx consists (1) **of three fused peptides from the HER-2 receptor** conjugated to (2) **a carrier** plus (3) an **adjuvant**



HER-Vaxx: Mechanism Of Action



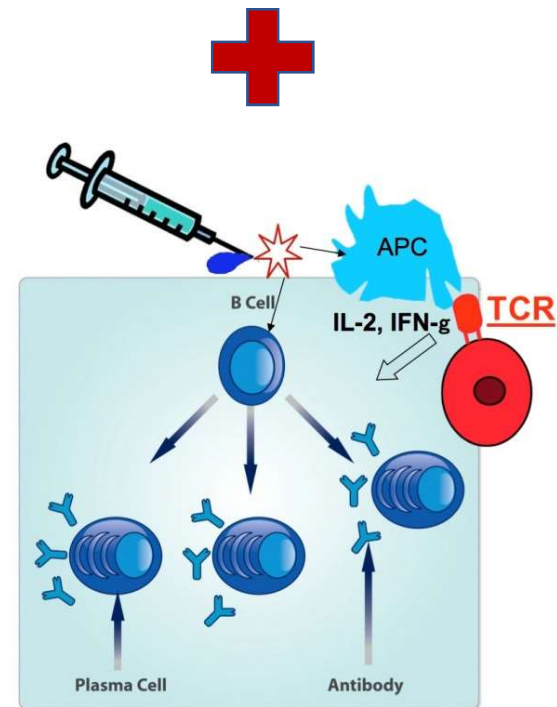
Immune-checkpoint antibodies combined with cancer vaccines



PD-1: Programmed cell Death 1

PD-L1: PD-1 ligand

CTLA-4 etc.



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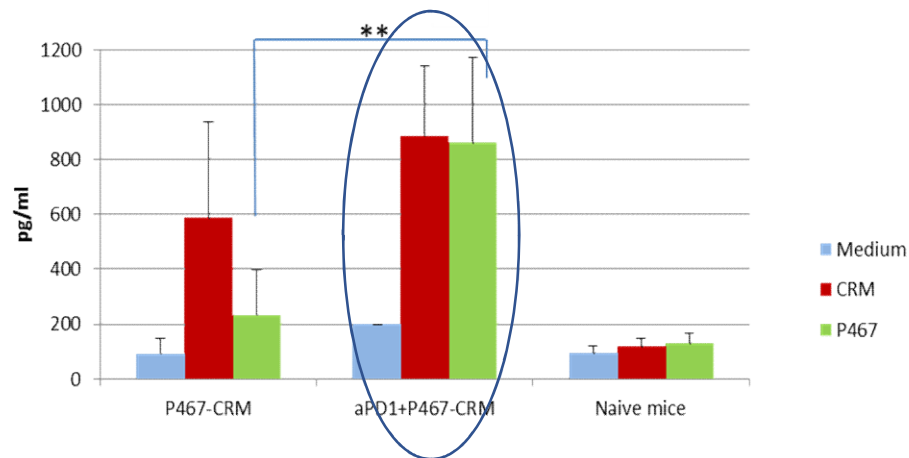
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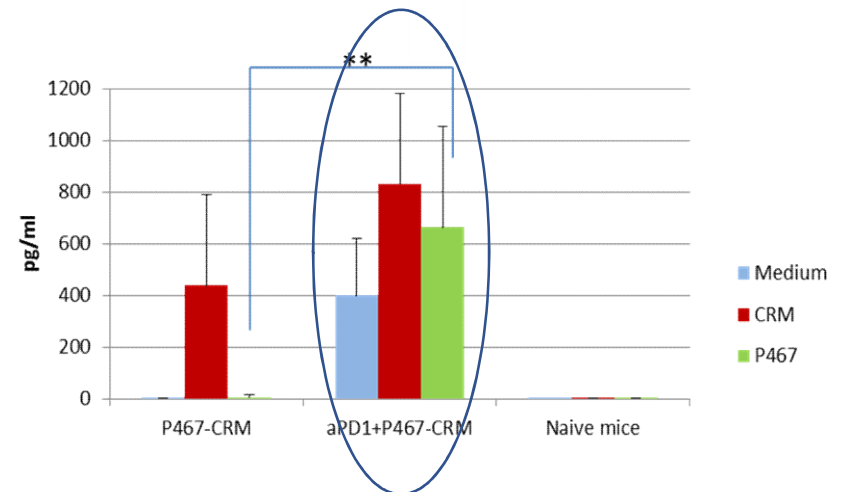
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HerVaxx and PD1 monoclonal antibody leads to enhanced anti-Her-2 responses at the cellular level

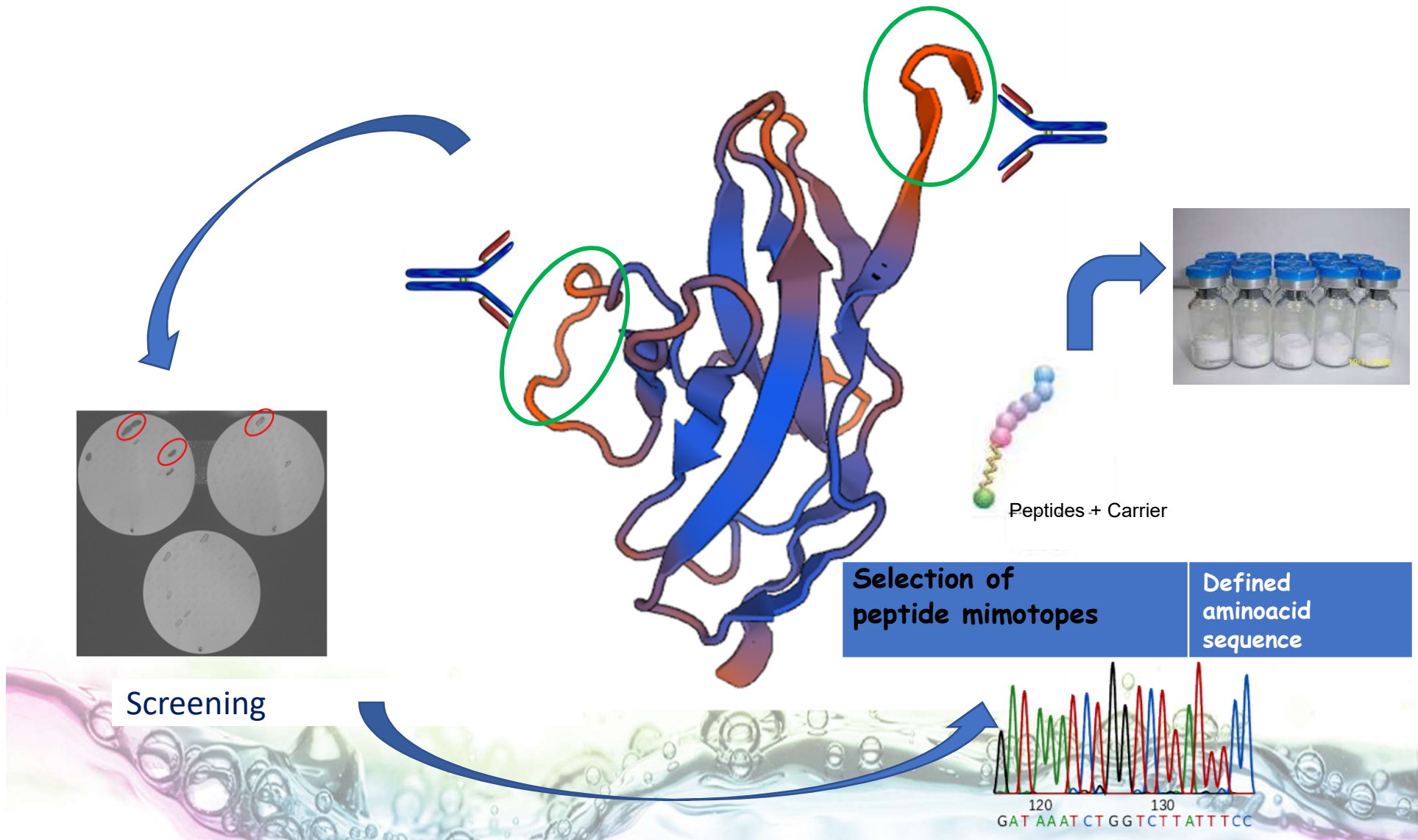
IL-2 production



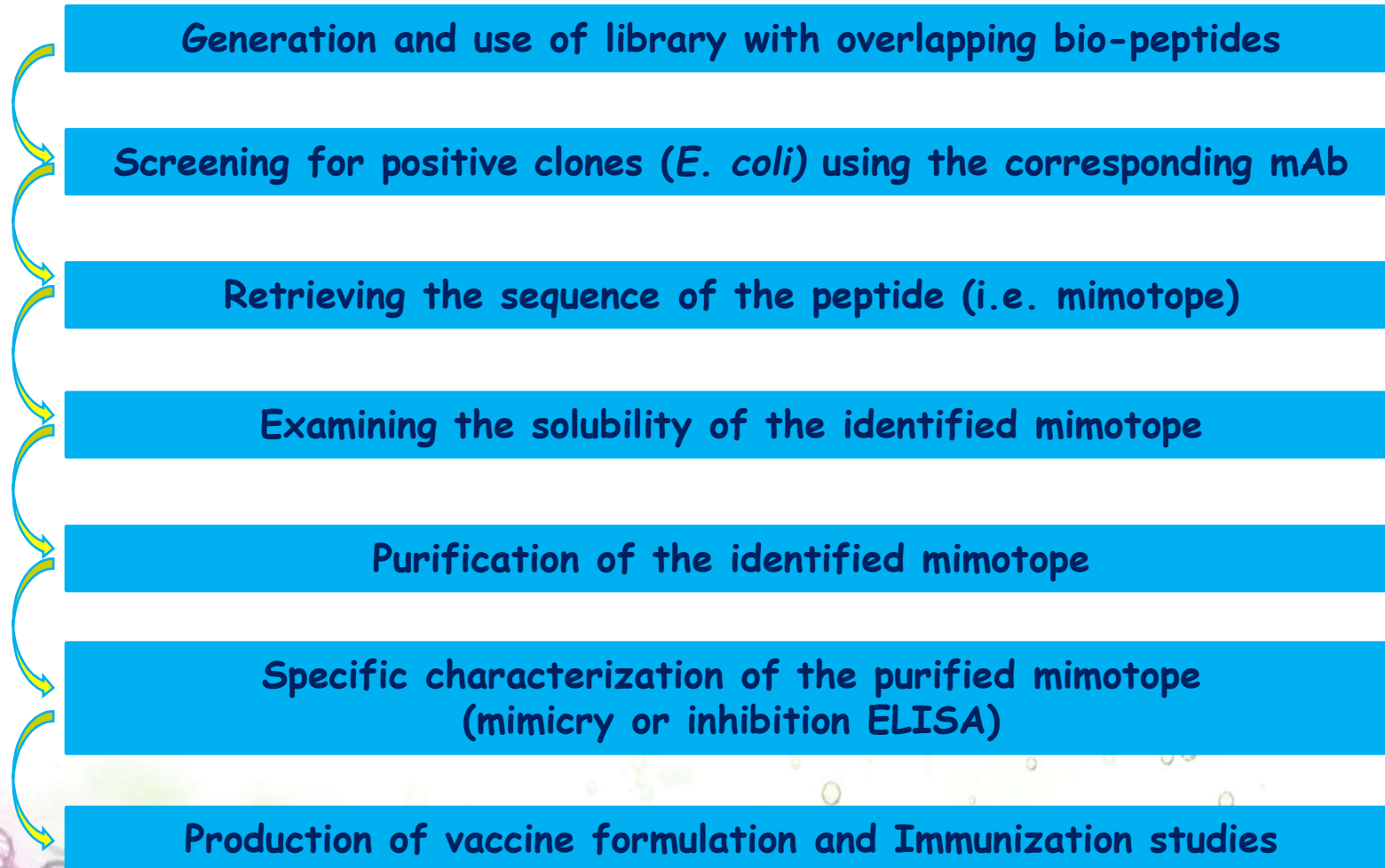
IL-5 production



Identification of Mimotope – Vaccine candidates



Mimotope Plattform for generation of vaccine candidates of interest



R&D Team at the Medical University of Vienna



Thank you for your attention !



Joshua Tobias, PhD



Erika Garner-Spitzer, PhD



Joanna Jasinska Dipl Ing



Karin Baier



Kathi Ambroz