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BioRank™

High-throughput in-silico screening of the epistatic landscape

- prediction of pMHC-TCR functional outcomes
- design of antigen-specific TCR sequences

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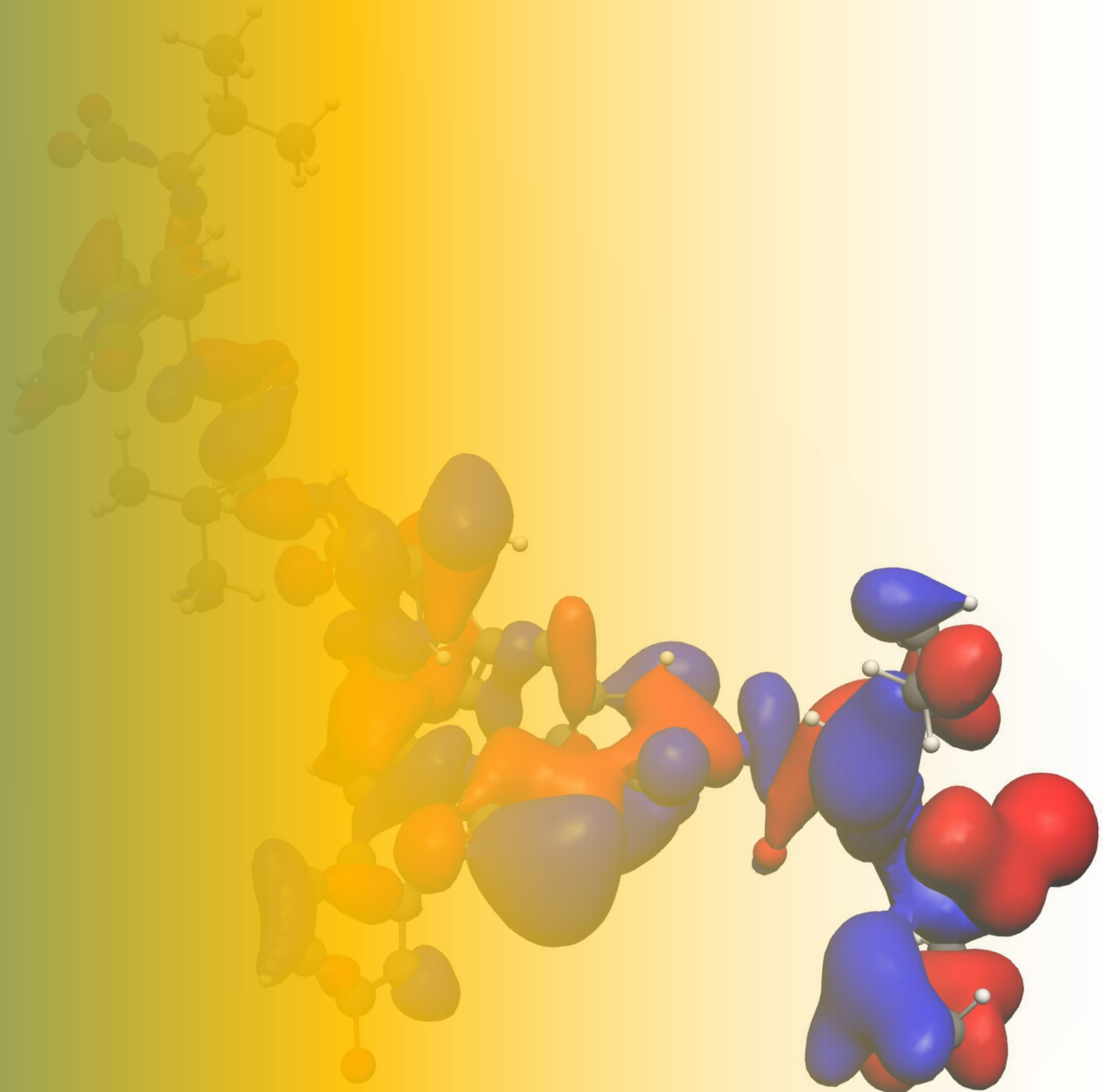

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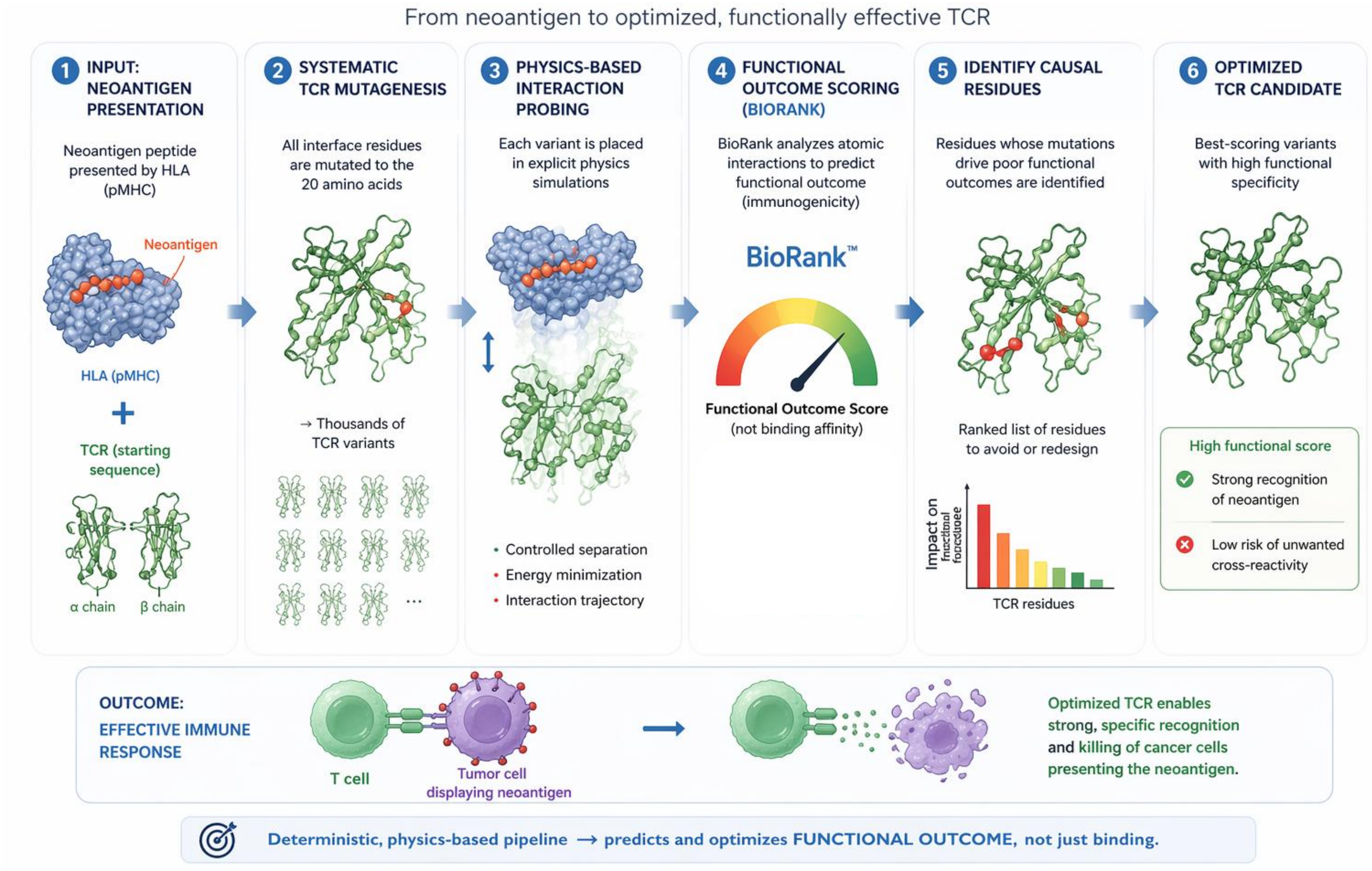
BioRank^{TM}: High-throughput mutagenesis engine for the production of neoantigen-specific TCR's



From neoantigen to optimized, functionally effective TCR

① INPUT: NEOANTIGEN PRESENTATION

Neoantigen peptide presented by HLA (pMHC)

② SYSTEMATIC TCR MUTAGENESIS

All interface residues are mutated to the 20 amino acids

→ Thousands of TCR variants

③ PHYSICS-BASED INTERACTION PROBING

Each variant is placed in explicit physics simulations

- Controlled separation
- Energy minimization
- Interaction trajectory

④ FUNCTIONAL OUTCOME SCORING (BIORANK)

BioRank analyzes atomic interactions to predict functional outcome (immunogenicity)

Functional Outcome Score
(not binding affinity)

⑤ IDENTIFY CAUSAL RESIDUES

Residues whose mutations drive poor functional outcomes are identified

Ranked list of residues to avoid or redesign

⑥ OPTIMIZED TCR CANDIDATE

Best-scoring variants with high functional specificity

High functional score

- ✓ Strong recognition of neoantigen
- ✗ Low risk of unwanted cross-reactivity

OUTCOME:
EFFECTIVE IMMUNE RESPONSE

Optimized TCR enables strong, specific recognition and killing of cancer cells presenting the neoantigen.

Deterministic, physics-based pipeline → predicts and optimizes FUNCTIONAL OUTCOME, not just binding.

BioRank™ highlights

What is BioRank™?

High-throughput directed evolution in-silico framework for TCR engineering/optimization, addressing the epistasis problem from first-principles. The approach operates directly at the pMHC–TCR structural level and is designed to optimize TCR sequence for neoantigen recognition (currently HLA Class I, with straightforward extension to Class II and antibody–ligand systems). The method does not rely on training datasets, enabling systematic exploration of sequence space with explicit control over binding and activation-relevant features.

Can BioRank™ help design antigen-specific TCR sequences? Yes – it can high-throughput screen any number of pMHC-TCR structures, assigning functional outcome metric to each and use this to determine the residue mutations for optimal functional outcome.

What input does BioRank™ require?

pMHC-TCR or TCR-mimic structure.

Can BioRank™ resolve Class II pMHC-TCR outcomes? Yes

Can BioRank™ resolve TCR-mimic outcomes? Yes

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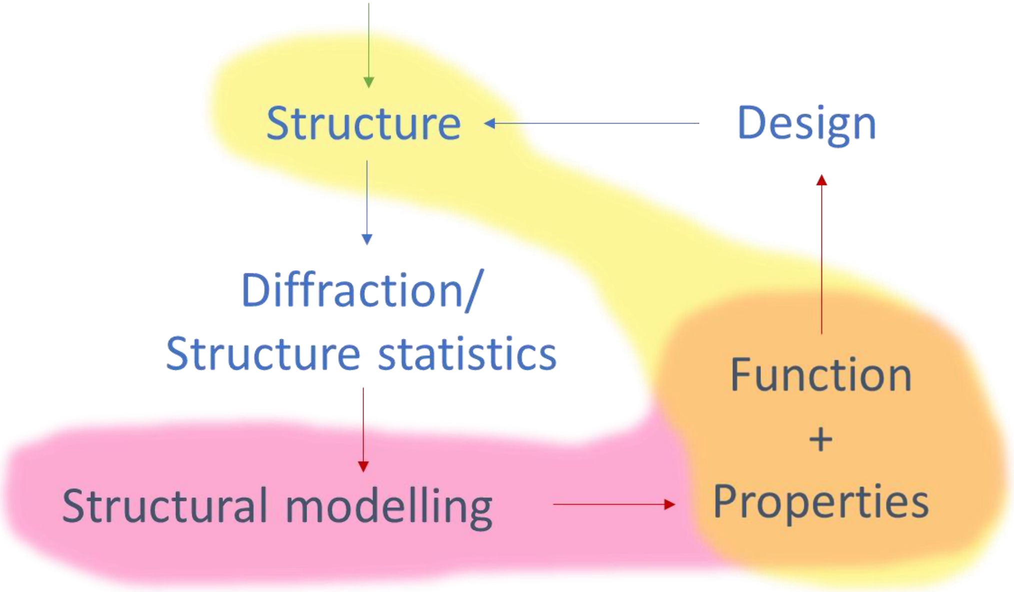
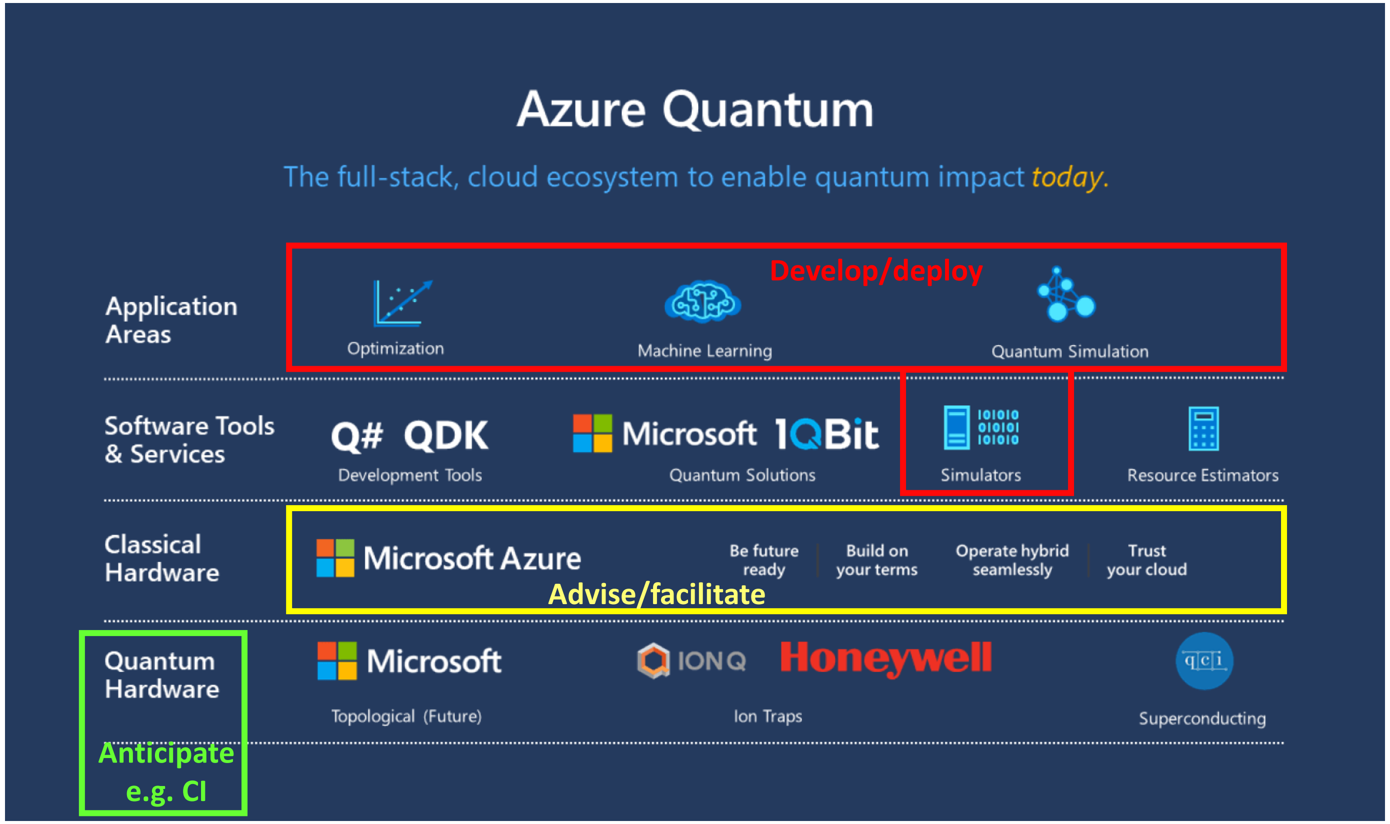
MML is a contract research organization (CRO) developing Life Sciences in-silico solutions. We work on segments such as amorphous solid dispersion stability, elementary reactions and pMHC-TCR interactions, applying both molecular modelling and AI and emphasizing on HPC (e.g. see details of the MML R6 cluster).

- Innovation-driven Computational Materials Science (CMS) / Chemistry (CC) R&D
- Focus on Pharmaceutics + Chemicals industries
- Provide solutions of industrial relevance


Structure
Design
Diffraction/ Structure statistics
Function + Properties
Structural modelling


Azure Quantum

The full-stack, cloud ecosystem to enable quantum impact *today*.

Application Areas: Optimization; Machine Learning; Quantum Simulation
Develop/deploy

Software Tools & Services: Q# QDK Development Tools; Microsoft 1QBit Quantum Solutions; Simulators; Resource Estimators

Classical Hardware: Microsoft Azure; Be future ready; Build on your terms; Operate hybrid seamlessly; Trust your cloud
Advise/facilitate

Quantum Hardware: Microsoft Topological (Future); IONQ Honeywell Ion Traps; qci Superconducting
Anticipate e.g. CI

Multi scale modelling

- Atomic
- Mesoscale
  - Coarse graining
- Continuum/process modelling
  - CFD, FEM, bespoke (EAF, Atomization + Break up)

System classes

- Organic
  - Small organics (drugs)
  - Biomolecular (Proteins)
  - Polymers/excipients
- Inorganic

Azure CMS/CC solutions

1. Solid solution stability (solubility) e.g. amorphous solid solutions
2. Macromolecule parametrization
3. Chemical reactivity pathways/AI training sets, e.g., API degradation
4. ReaxFF generation
5. Adsorption