ELECTROMed: a programmable peptide-protein screening platform.

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Why Electromed

EDITORIAL

nature biotechnology

The problem with neoantigen prediction

Personalized immunotherapy is all the rage, but neoantigen discovery and validation remains a daunting problem.

last December, the newly minted Parker Institute for Cancer Immunotherapy and its venerable East Coast counterpart, the Cancer Research Institute, announced the formation of the Tumor Neoantigen Selection Alliance. This initiative, involving researchers from 30 universities, non-profit institutions and companies, aims to identify software that can best predict mutation-associated cancer antigens, also known as neoantigens, from patient tumor DNA. The hope is that solving the shortcomings of current *in silico* methods for identifying neoantigens will galvanize a new wave of personalized cancer immunotherapies. But, for now, computational prediction of neoantigens capable of eliciting efficacious antitumor responses in patients remains a hit-or-miss affair.

for a particular allele to build a model with sufficient accuracy. But as many MHC alleles lack such data, 'pan-specific' methods—capable of predicting binders based on whether MHC alleles with similar contact environments have similar binding specificities—have increasingly come to the fore.

Today, a raft of software tools for predicting MHC binders are now available (http://cancerimmunity.org/resources/webtools/). But each of these packages has its own idiosyncrasies, strengths and weaknesses. What's more, it has proven difficult to benchmark which tools and combinations of tools work best for particular contexts.

The Tumor Neoantigen Selection Alliance seeks to address these

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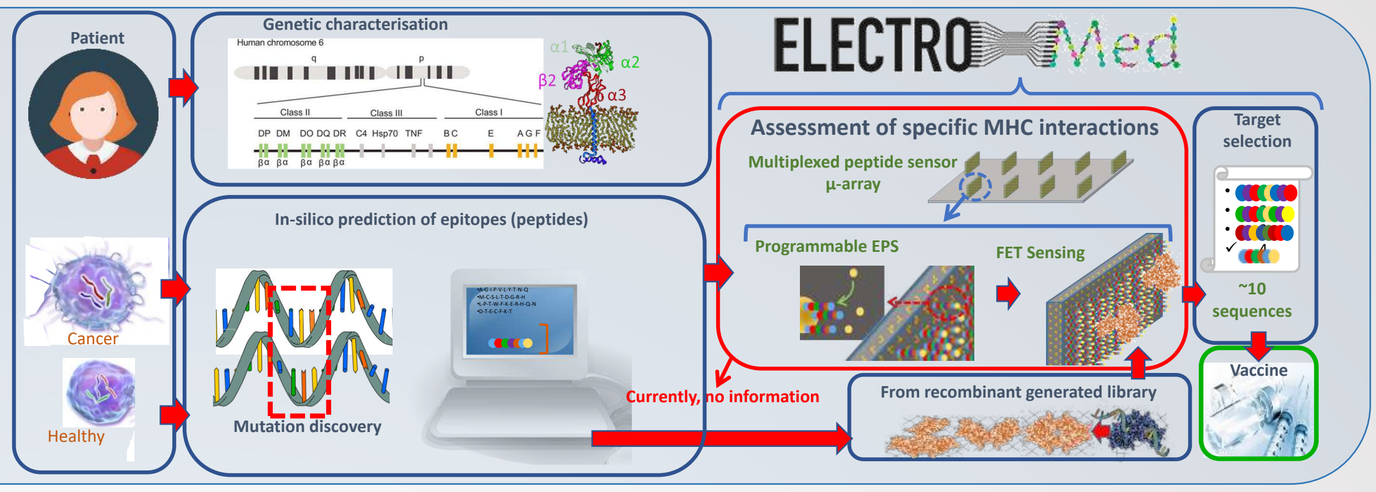


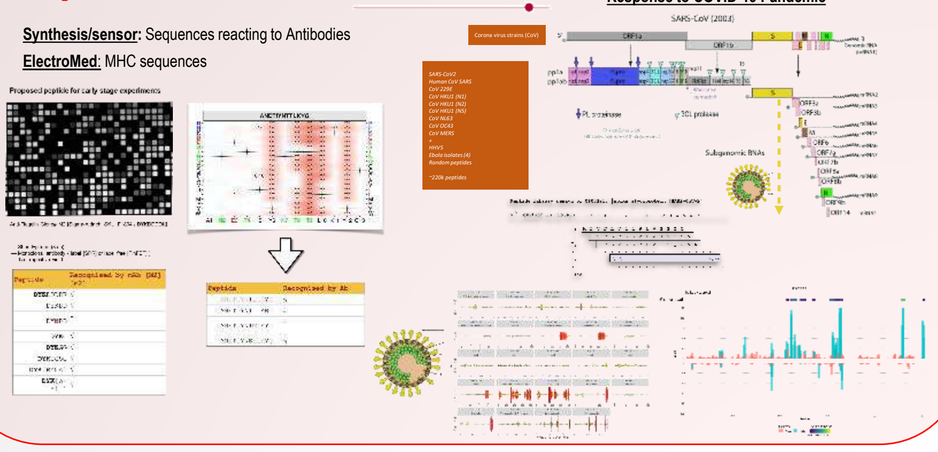
Sequence selections

UNIVERSITY OF COPENHAGEN

Synthesis/sensor: Sequences reacting to Antibodies

ElectroMed: MHC sequences

Response to COVID-19 Pandemic

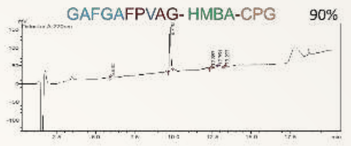


Peptide synthesis

upf. Universitat Pompeu Fabra Barcelona

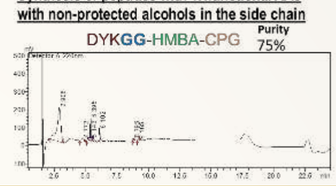
Synthesis of peptides with bifunctional or Trifunctional AAs with commercially available protecting groups

Decapeptide (10)	Sequence-Linker-Resin	Purity
	GAFGAFPVAG- HMBA-CPG	90%



Synthesis of peptides with Trifunctional AAs with non-protected alcohols in the side chain

		Purity
DYK	GG-HMBA-CPG	75%



June 2021- October 2021

- Protected trifunctional AAs (E and D): ≥90% purity
- Bifunctional AAs (L and I): room for improvement
- ACN can be used as a solvent
- No clear difference between TFA and HCl deprotection
- Purity highly dependent on AA sequence

October 2021- April 2022

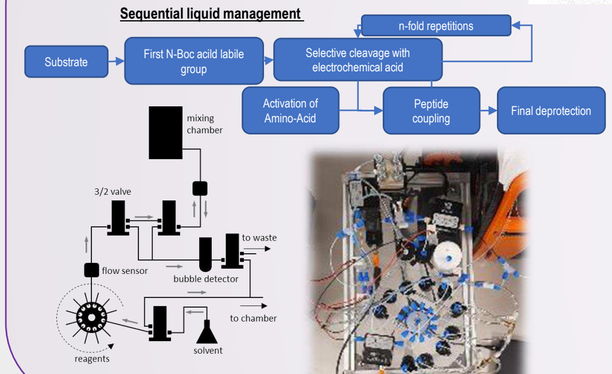
- Longer sequences (octa/decapeptide) ≥90% purity
- Unprotected hydroxy AAs (S, T, Y) still a challenge although T ≥81% purity
- Bifunctional AAs optimized (L, I and V): ≥93% purity
- The scope of the CPG platform was extended to:
  a) W and Q: ≥96% purity
  b) N: ≥80% purity
- R and H are clearly incompatible with CPG model and Boc chemistry.
- Un protected DYK peptides were synthesized with moderate results: 57-75% purity

90% AA (over 10 AA sequence): Glicine (G), Alanine (A), Proline (P), Fenilalanina (F), Isoleucine (I), Leucine (L), Valine (V) – Aspartic acid (D), Glutamic acid (E) – Triptofano (W), Glutamine (Q)
80% AA: Lysine (K). Asparagine (N), Treonine (K)
70% AA: Serine (S), Tyrosine (Y)
Pending: Cisteine (C), Metionine (M)

Microfluidic management

ELVESYS MICROFLUIDICS INNOVATION CENTER

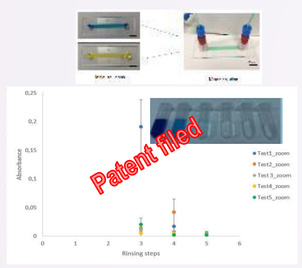
Sequential liquid management



Active mixing in airtight reactor

Suited for **work under controlled atmosphere** (N_2, Ar …)

- Development of an adapted pressure controller
- Novel airtight mixing chamber/millifluidic reactor (patent filed)



Control of local acidity

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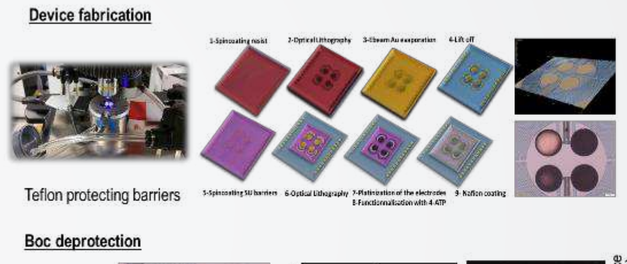
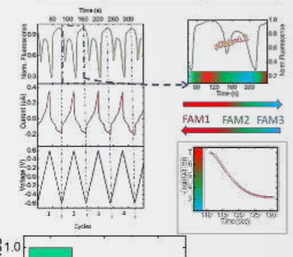
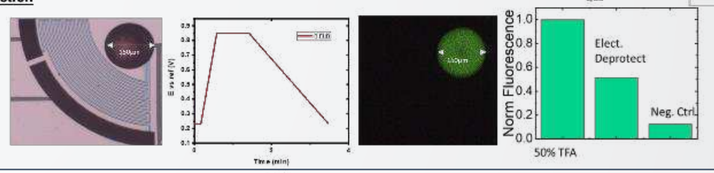
Device fabrication



Quantification of acidity down to 0.1M in aqueous and organic media



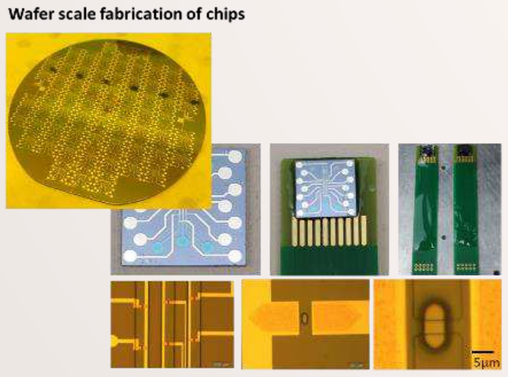
Boc deprotection



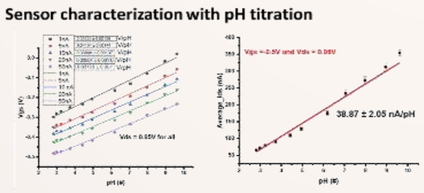
Sensor Fabrication

UNIVERSITY OF TWENTE. | MESA+ INSTITUTE | BIOS

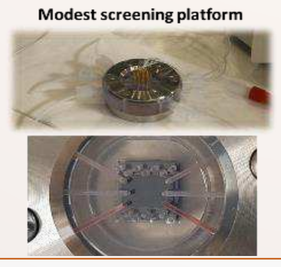
Wafer scale fabrication of chips



Sensor characterization with pH titration



Modest screening platform



Sensor interface

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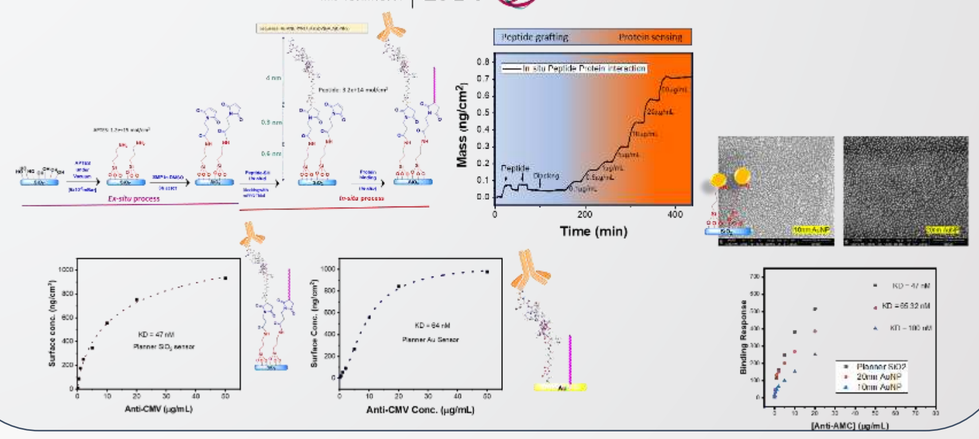
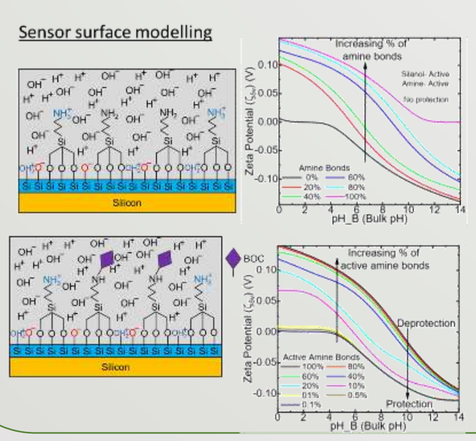
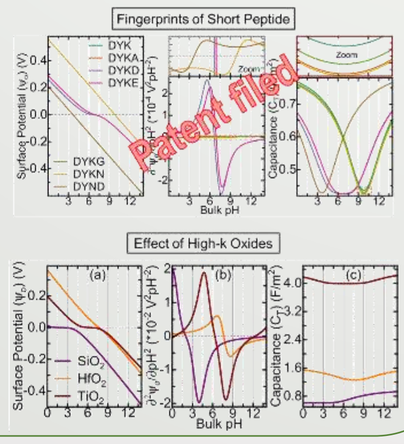


Sensor modelling

University of Glasgow | DEVICE MODELLING GROUP

Sensor surface modelling





Integration

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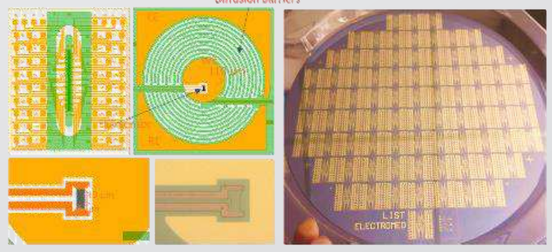
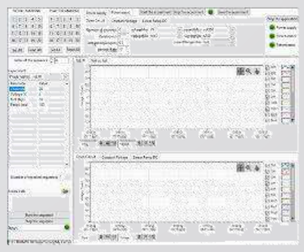
Chip fabrication



Software control customization



Microfluidic platform

Features:

- Demonstration with 20 programmable sensors
- Sequential liquid microfluidic management with laminar flow
- Optical and electrical probes

ELECTROMed Potential Technology

• Proof of concept with 20 sensors programmable sensors	• Density of 10^3 sensors/cm^2
• In situ analysis of the yield of chemical reactions using our sensors	• On-line sequencing?
• 15/20 amino acids available for la synthesis	• Possibility to develop protecting groups for the 20 standard amino-acids
• Screening of DYK flag antibody and mutations	• Detection of working with nanomolar concentrations of target proteins
• In-silico study of sequence screening for MHC molecules	• Screening of neo-antigen sequences

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