Unlocking the potential of innovative medicines

PCI Biotech

PCI – Enhancing delivery in oncology

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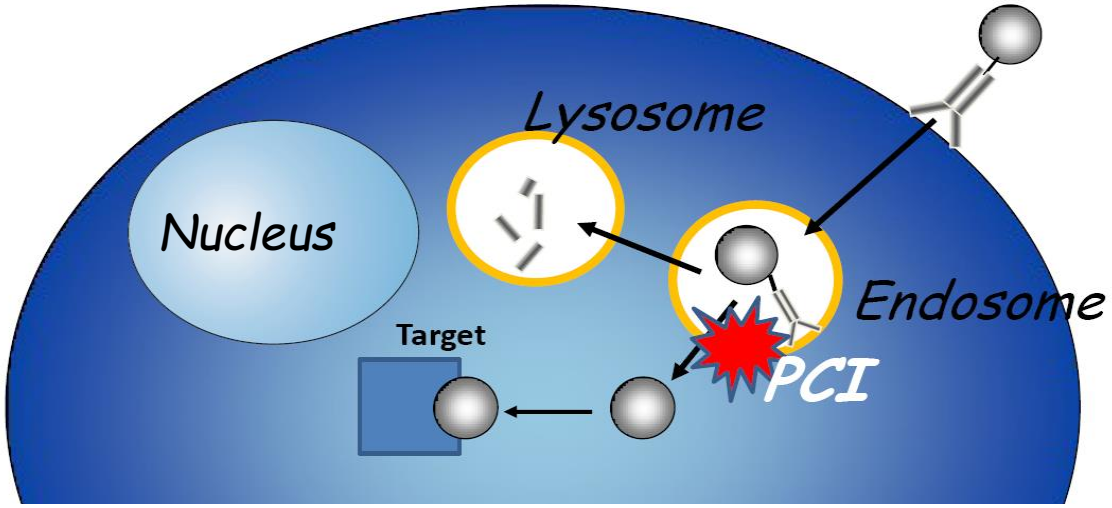
PCI Biotech at a glance

- A listed cancer-focused biotech company (PCIB, Oslo exchange)
- Market cap ~$10 mill.
- Lean organisation: 10 employees
- Photochemical internalisation (PCI) technology originates from the Norwegian Radium Hospital
  - Continued close collaboration
- Collaboration with ETH and University Hospital Zurich

- Clinical Program
  - Phase I/II with the photosensitiser Amphinex® for the orphan indication inoperable bile duct cancer
- Pre-clinical programs
  - Vaccine delivery technology to enhance T-cell responses
  - Efficient delivery of nucleic acid therapeutics

PCI technology – enabling drugs to reach intracellular therapeutic targets



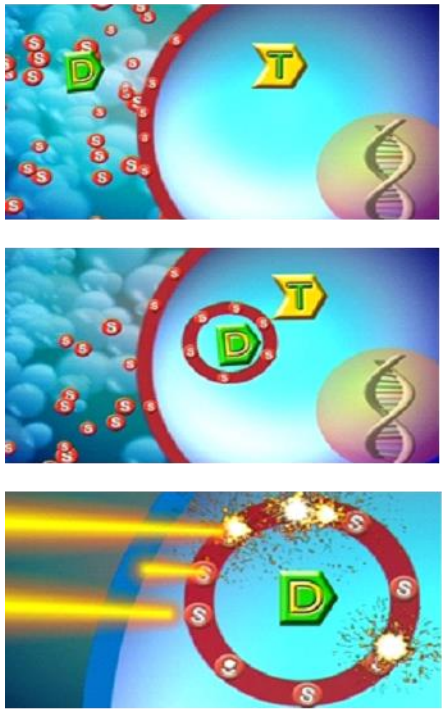
Therapeutic molecule

- mAb, protein toxins
- Peptides, mRNA
- DNA (gene encoding)
- Certain small molecules
- Oligonucleotides
- mAb, peptides, polymers, nanoparticles, liposomes

- Therapeutic proteins
- Cancer vaccines
- Gene therapy
- Chemotherapy
- Gene silencing
- Targeting, delivery

Photochemical internalization (PCI) technology – general principle

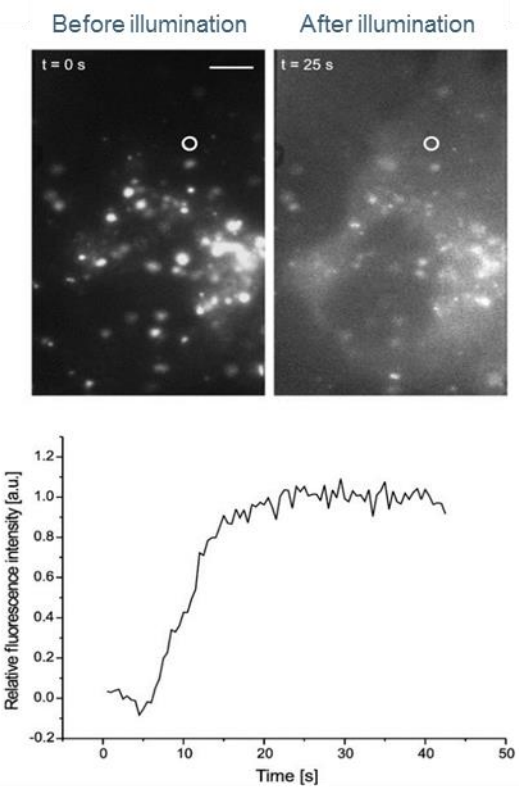
PCI mechanism of action – triggered endosomal escape through light activation



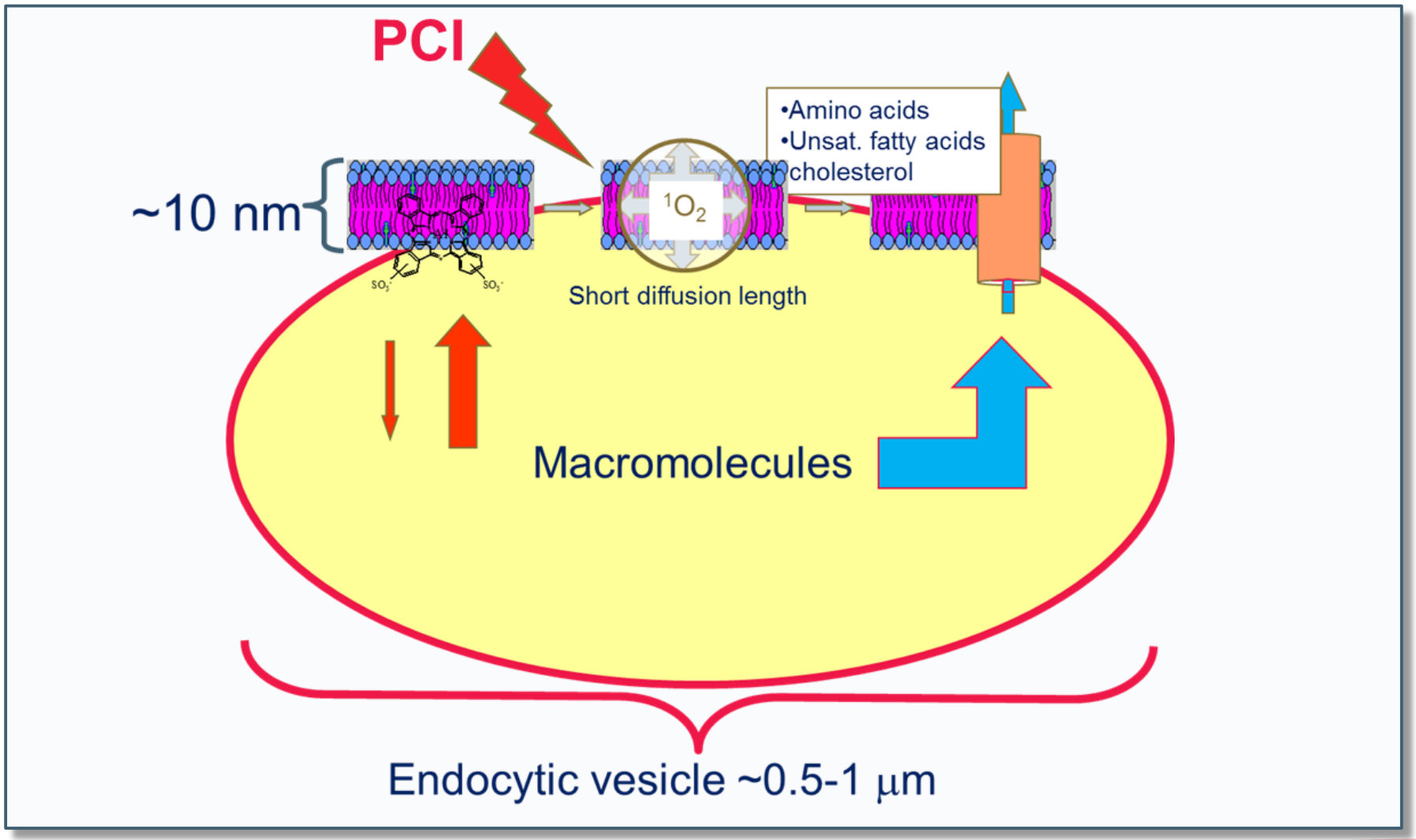
The active molecule
- Peptide: e.g. antigen
- Oligonucleotide, e.g. siRNA
- Anticancer agent, e.g. gemcitabine
- Protein, e.g. antibody-drug conjugate

The PCI component
- Fimaporfin ($TPCS_{2a}$)

The target
- Target for the active molecule
- E.g. DNA, mRNA, enzyme, microtubuli



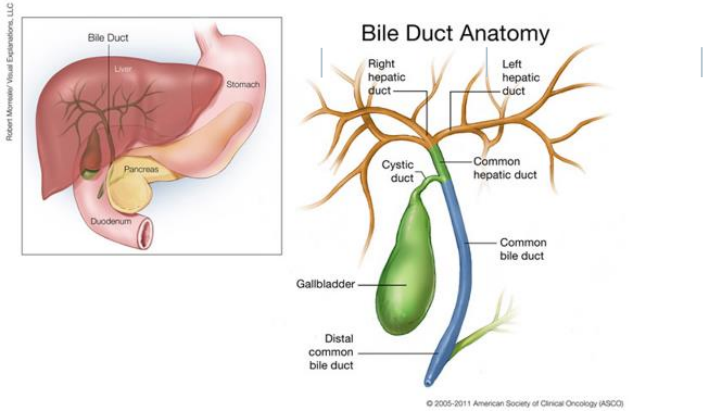
PCI technology – mode of action



PCI – a versatile technology with a pipeline of partnering opportunities

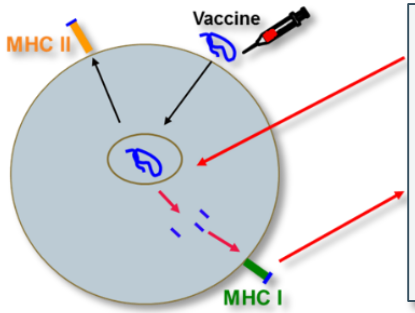
Local cancer treatment

- Bile duct cancer



Cancer vaccination

- Intradermal and intratumour vaccination

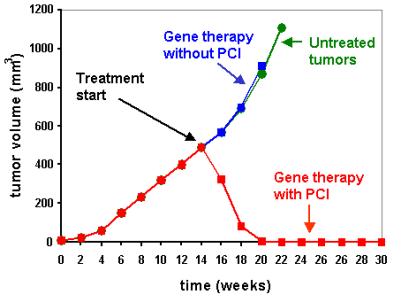


PCI – induce presentation on MHC class I

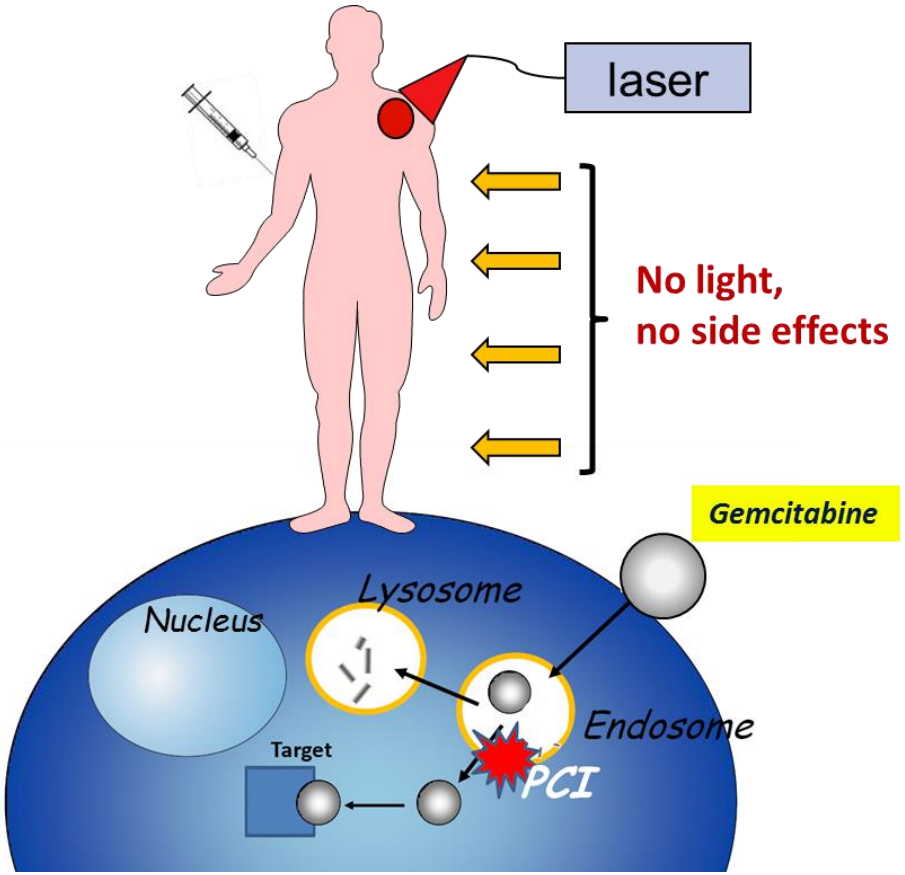
- Make it possible to achieve cytotoxic T-cell response with protein/ peptide vaccines
- Can solve a key challenge for many vaccine approaches

Nucleic acids delivery

- **siRNA**
- **mRNA**
- **Gene therapy**



Clinical applications - enhancement of systematically administered chemotherapeutics



Phase Ib/II in advanced bile duct cancer – PCI-induced enhancement of gemcitabine

- Single treatment of locally advanced inoperable bile duct cancer
- Multi-site adaptive phase Ib/II in up to 45 patients
- Primary endpoint phase II: PFS

Phase I completed – providing excellent safety results and promising early tumour response

- Single treatment: i.v. fimaprofin and bleomycin + surface illumination of metastatic/recurrent tumour
- Single site study (University College London Hospital) in 22 patients
- Including head & neck, breast (skin mets), sarcoma and skin adnexal cancer

Clinical Phase I/II study PCIA202/12 – design

Phase I

▪ **Objective**: to find a tolerable dose, and establish the safety profile of Amphinex-induced PCI of gemcitabine followed by systemic gemcitabine and cisplatin*

- 3+3 dose escalation design (light and/or Amphinex)
- Cohort review committee evaluates each cohort
- window lasts until end of first 21 day cycle with gem/cis
- PCI + up to 8 cycles of gem/cis
- Endpoints: DLTs, safety (AEs, labs, physical findings), PK

Cohort	Amphinex dose	Light dose
Cohort 1	0.06 mg/kg	15 J/cm
Cohort 2	0.06 mg/kg	30 J/cm
Cohort 3	0.12 mg/kg	30 J/cm
Cohort 4	0.25 mg/kg	30 J/cm

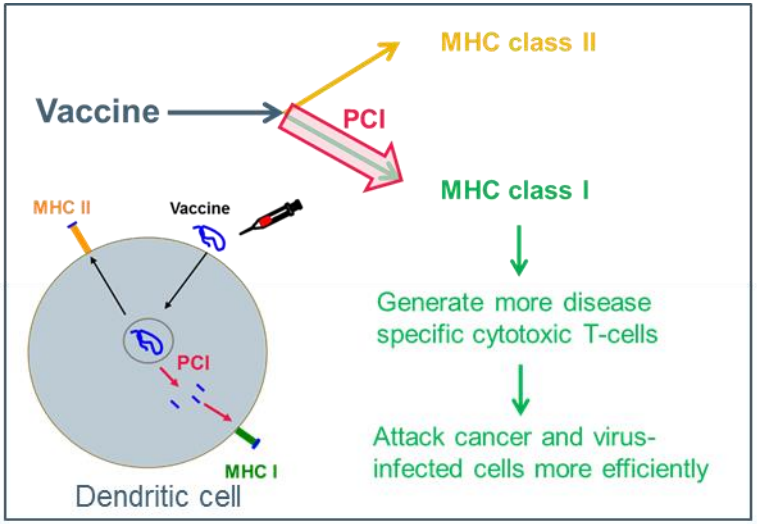
Phase II

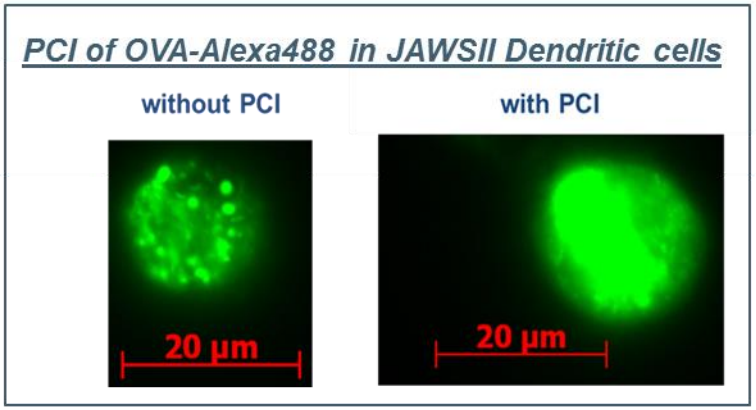
▪ **Objective**: to make a preliminary assessment of the efficacy of Amphinex-induced PCI of gemcitabine followed by systemic gemcitabine and cisplatin

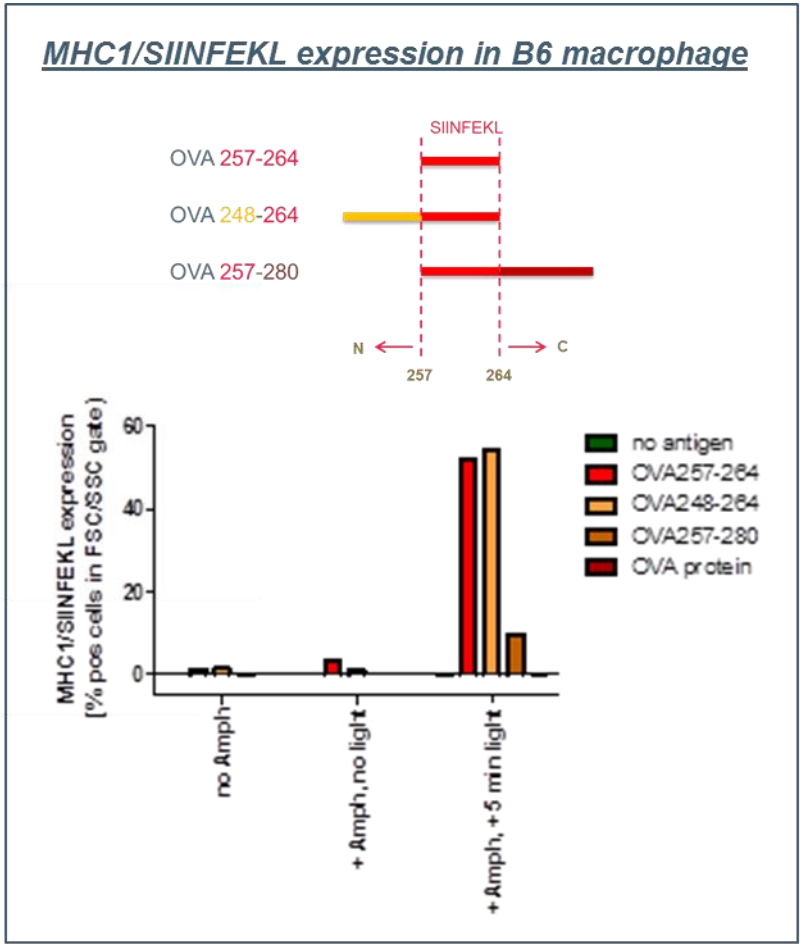
- 5:2 randomization, PCI+stenting +gem/cis vs. stenting+gem/cis. Up to 8 cycles of gem/cis, 35 patients
- Endpoints: PFS, ORR, DCR, OS

PCI for vaccination – enhancing cytotoxic T-cell response by light-induced cross presentation

Well characterized mode of action







Intradermal setting with HPV peptide + PCI + poly(IC)

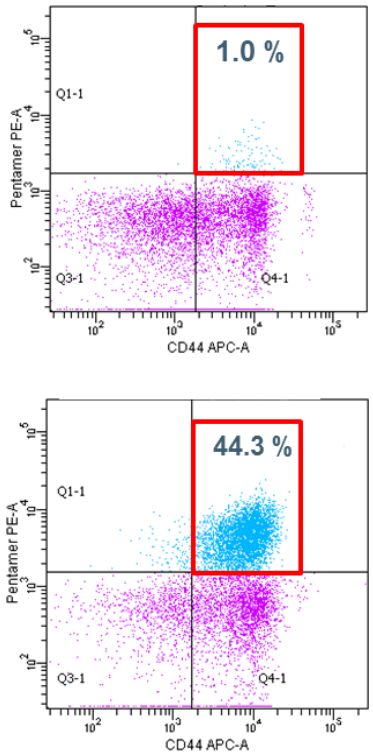
HPV peptide – intradermal vaccination with Poly(IC)

(3 i.d. vaccinations)

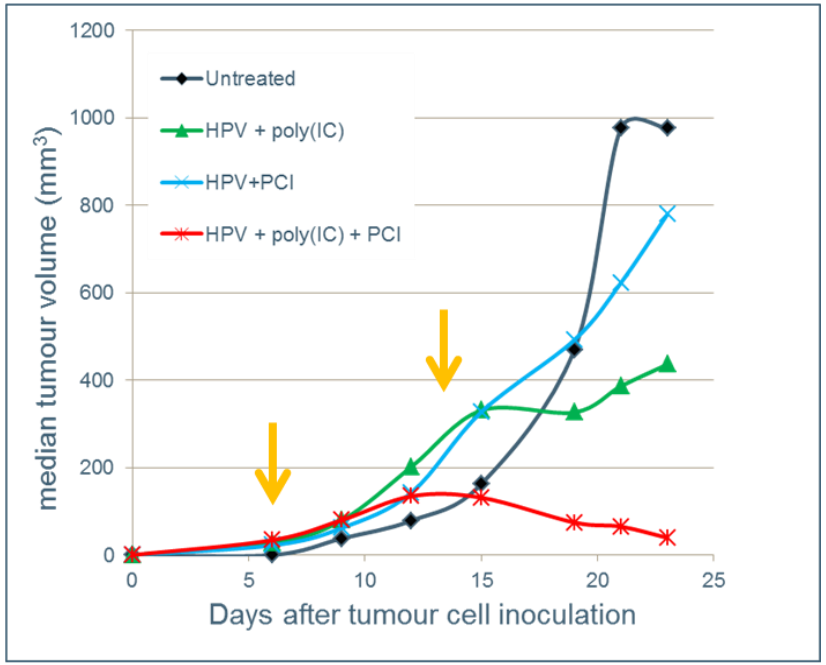
Without PCI:

Antigen specific CD8 T-cells in blood

With PCI:



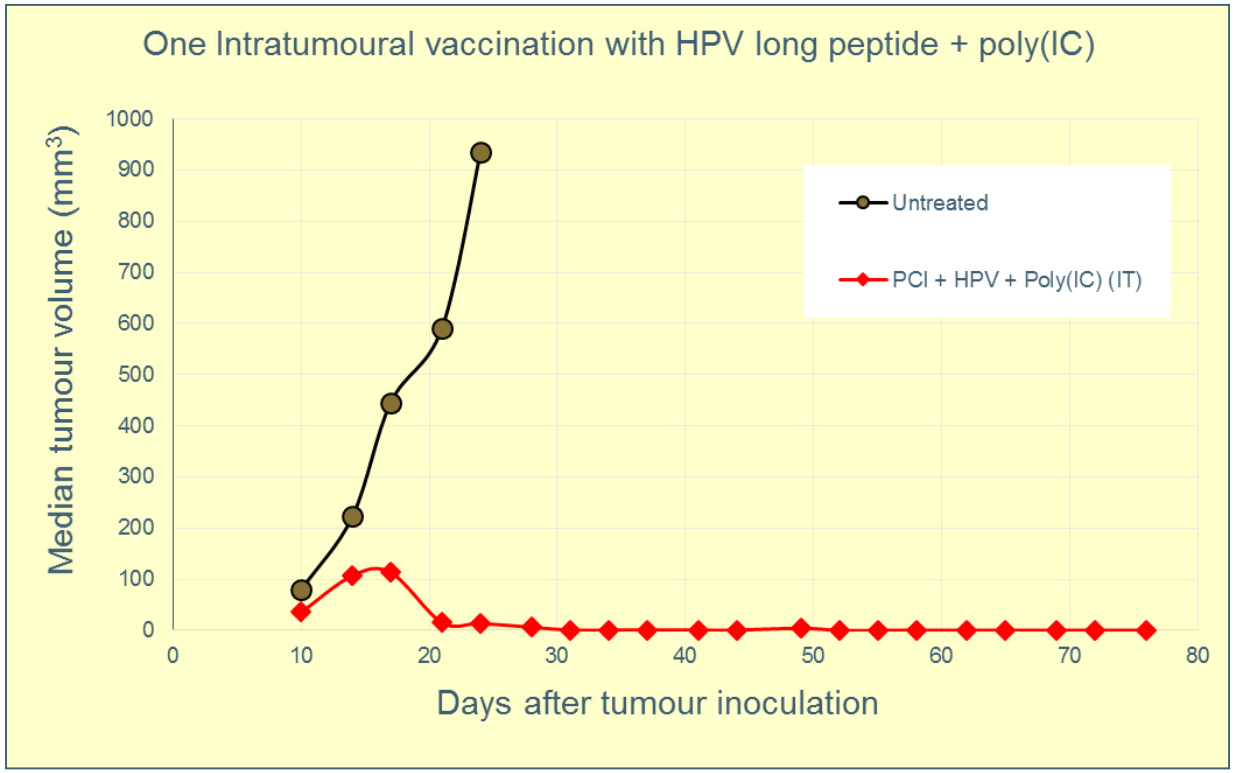
TC-1 mouse tumour model



- Intradermal vaccination at days 6 and 13 after tumour cell inoculation
- 5 animals per group

antigen specific CD8 T-cells in blood and tumour regression

Intratumoural setting with HPV peptide + PCI + poly(IC)



Intratumoural vaccination

- Tumour accessibility
- Tumour «vaccine factory», neoantigens
- More efficient
  - -Immune cells present in tumours
  - -Immunogenic cell death
  - -Tumour cell lysing

Cancer therapeutic vaccines – competitive advantages and user-friendly PCI solutions

Clinical safety and preclinical efficacy evidence, combined with a comprehensive patent estate on PCI-mediated CTL-induction (products, uses and devices)

Safety – $TPCS_{2a}$ tested in Phase I study (i.v. inj)

Stability – $TPCS_{2a}$ is stable at room temperature, also in solution

Innovation – Unique mode of action

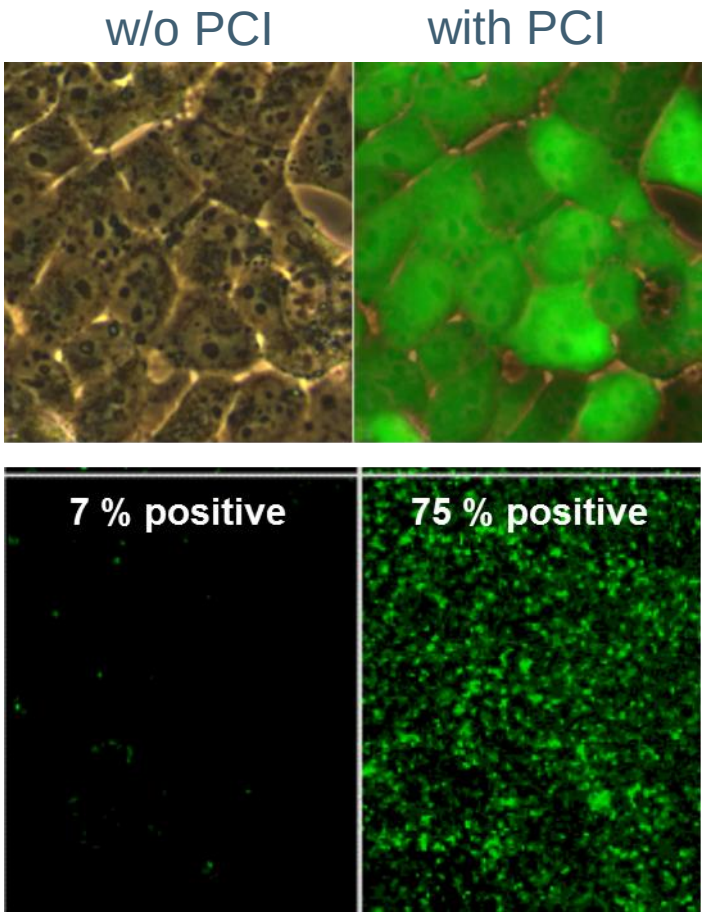
Light activation – User friendly blue LED light

Cost effectiveness – Simple synthesis of $TPCS_{2a}$

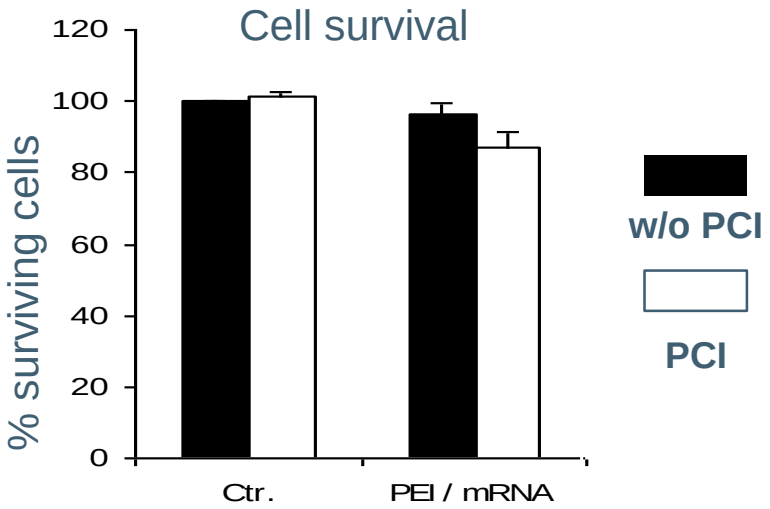
Broad applicability

- Peptide and protein antigens as well as particulate
- Intradermal and intratumoural vaccination
- In vivo and autologous possible

PCI strongly improves mRNA delivery by a PEI vehicle



- EGFP mRNA
- Polyethylenimine (PEI) vehicle
- N/P ratio 2/1

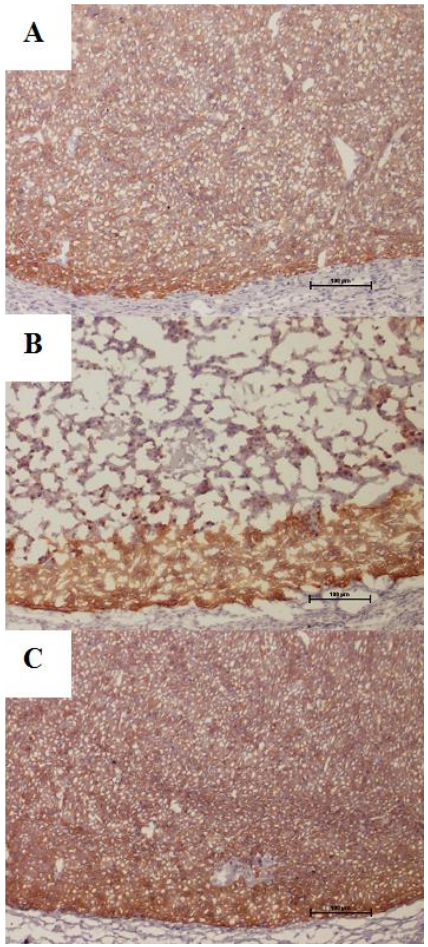


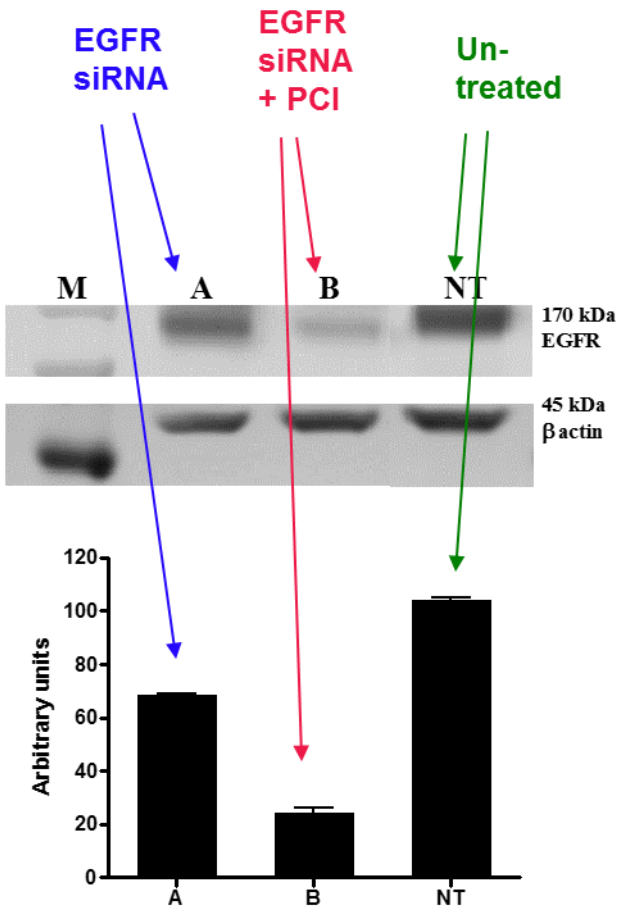
In vivo siRNA – EGFR siRNA Lipofectamine

EGFR siRNA

EGFR siRNA + PCI

Non-specific siRNA + PCI





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