



Unlocking the potential of innovative medicines

Photochemical internalization – an innovative technology giving strong enhancement of cytotoxic T-cell responses to peptide-and protein based vaccines.

Anders Høgset – CSO PCI Biotech AS

Washington Jan 2015



Disclaimer

This document (the "Presentation") has been produced by PCI Biotech Holding ASA (the "Company"). The Presentation is for information purposes only. The information contained in this Presentation does not constitute or form part of, and should not be construed as, an offer or invitation to subscribe for or purchase the securities of the Company in any jurisdiction. Neither this Presentation nor any part of it shall form the basis of, or be relied upon in connection with any offer, or act as an inducement to enter into any contract or commitment whatsoever.

This Presentation contains certain forward-looking statements relating to the business, financial performance and results of the Company and/or the industry in which it operates. Forward-looking statements concern future circumstances and results and other statements that are not historical facts, sometimes identified by the words "believes", "expects", "predicts", "intends", "projects", "plans", "estimates", "aims", "foresees", "anticipates", "targets", and similar expressions. The forward-looking statements contained in this Presentation, including assumptions, opinions and views of the Company or cited from third party sources are solely opinions and forecasts which are subject to risks, uncertainties and other factors that may cause actual events to differ materially from any anticipated development. None of the Company or any of its subsidiary undertakings or any such person's officers or employees provides any assurance that the assumptions underlying such forward-looking statements are free from errors nor does any of them accept any responsibility for the future accuracy of the opinions expressed in this Presentation or the actual occurrence of the forecasted developments. The Company assumes no obligation, except as required by law, to update any forward-looking statements or to conform these forward-looking statements to our actual results.

No representation or warranty (express or implied) is made as to the accuracy or completeness of any information contained herein, and it should not be relied upon as such. None of the Company or its subsidiary undertakings or any such person's officers, employees or advisors shall have any liability whatsoever arising directly or indirectly from the use of this Presentation. By attending the presentation you acknowledge that you will be solely responsible for your own assessment of the Company, the market and the market position of the Company and that you will conduct your own analysis and be solely responsible for forming your own view of the potential future performance of the Company's business. The content of this Presentation are not to be construed as legal, business, investment or tax advice. Each recipient should consult with its own professional advisors for any such matters and advice.

The Presentation has not been reviewed or registered with, or approved by, any public authority, stock exchange or regulated market place. The distribution of this Presentation, as well as any purchase, sale or transfer of securities issued by the Company, may be restricted by law in certain jurisdictions, and persons into whose possession this Presentation comes should inform themselves about, and observe, any such restriction. Any failure to comply with such restrictions may constitute a violation of the laws of any such jurisdiction. None of the Company or its subsidiary undertakings or any such person's officers, employees or advisors shall have any responsibility for any such violations.

This Presentation and the information contained herein do not constitute an offer of securities for sale in the United States and are not for publication or distribution to U.S. persons (within the meaning of Regulation S under the U.S. Securities Act of 1933, as amended (the "Securities Act")). The securities of the Company have not been and will not be registered under the Securities Act and may not be offered or sold in the United States or to U.S. persons except pursuant to an exemption from the registration requirements of the Securities Act.

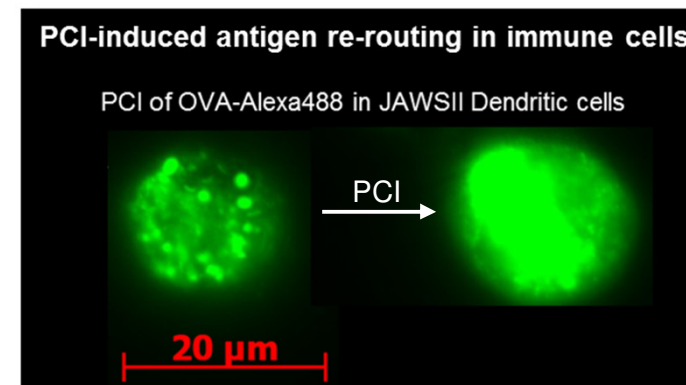
Neither the delivery of this Presentation nor any further discussions of the Company with any of the recipients shall, under any circumstances, create any implication that there has been no change in the affairs of the Company since the date of this Presentation.

This Presentation is subject to Norwegian law, and any dispute arising in respect of this Presentation is subject to the exclusive jurisdiction of the Norwegian courts.

PCI Biotech at a glance

- A listed cancer-focused Norwegian biotech company
- Photochemical internalisation (“PCI”), - light-induced enhancement of the effect of drugs
- Phase II clinical studies with cytotoxic drugs in two indications; head & neck and bile duct cancer
- PCI is also a very good technology for delivery of oligonucleotides and other nucleic acids
- Pre-clinical program on therapeutic vaccination, with promising results showing substantial enhancement of the important cytotoxic T-cell response

PCI induces endosomal escape by illumination



PCI technology – enabling drugs to reach intracellular therapeutic targets

STEP 1:

- TPCS_{2a} (S) and the active molecule (D) are injected into the body and reaches the target cells

STEP 2:

- TPCS_{2a} (S) and the active molecule (D) are taken up by the cell, but D is unable to reach the target (T), as it is encapsulated in an endosome
- S is washed away from the cell membrane, but trapped in endosomes

STEP 3:

- Light activates TPCS_{2a} (S) in the membrane of the endosome
- The membrane integrity is affected and the active molecule released

STEP 4:

- The active molecule (D) can now bind to its target (T) and initiate the therapeutic response



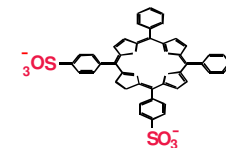
The active molecule

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



The PCI component

- Light sensitive component
- Amphinex® - TPCS_{2a}

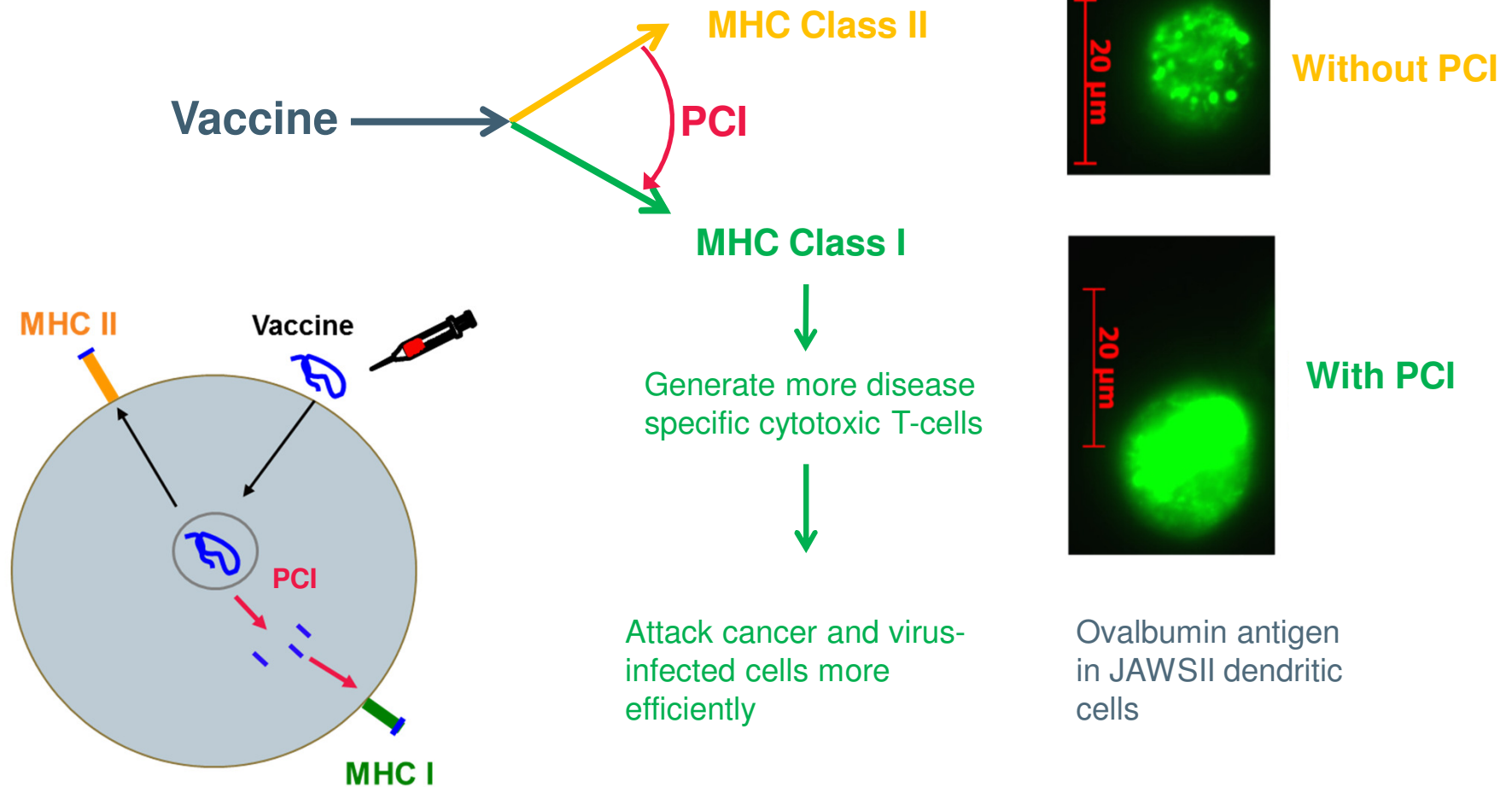


The target

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

PCI mechanism of action – triggered endosomal escape through illumination

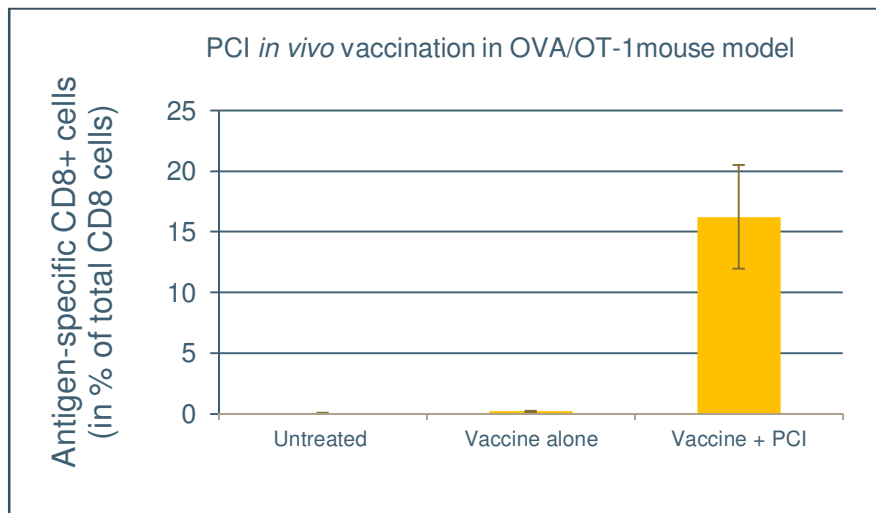
PCI for vaccination – enhancing cytotoxic T-cell response by light-induced cross presentation



PCI enhances *in vivo* vaccination in mouse OVA/OT-1 model (collaboration University Hospital Zurich)

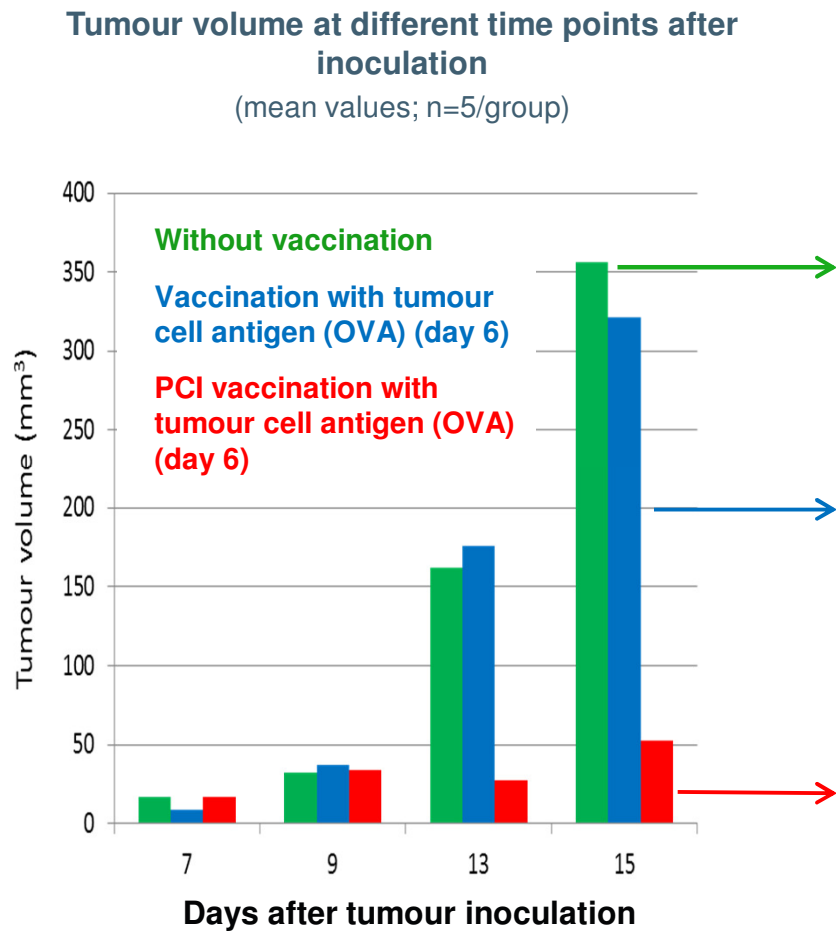


→ Vaccinated mice were anaesthetized and placed with the abdominal side down directly on the glass plate on a LumiSource light table for PCI treatment

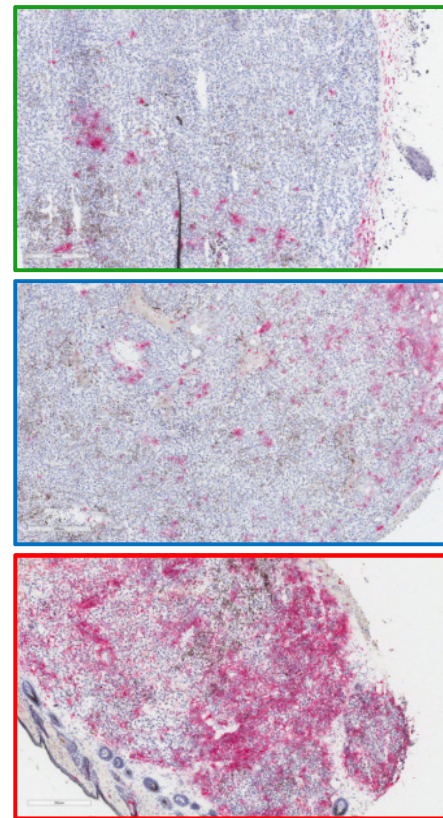


→ With PCI vaccination enhancement of up to > 100 can be achieved

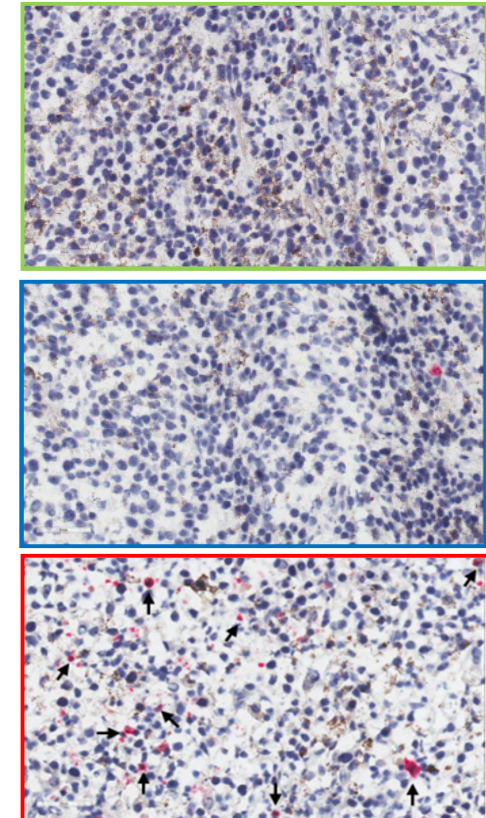
PCI induced immune response translates into therapeutic effect in animal tumour model (B16-OVA melanoma/OT-1)



Tumour infiltration of CD8⁺ T-cells



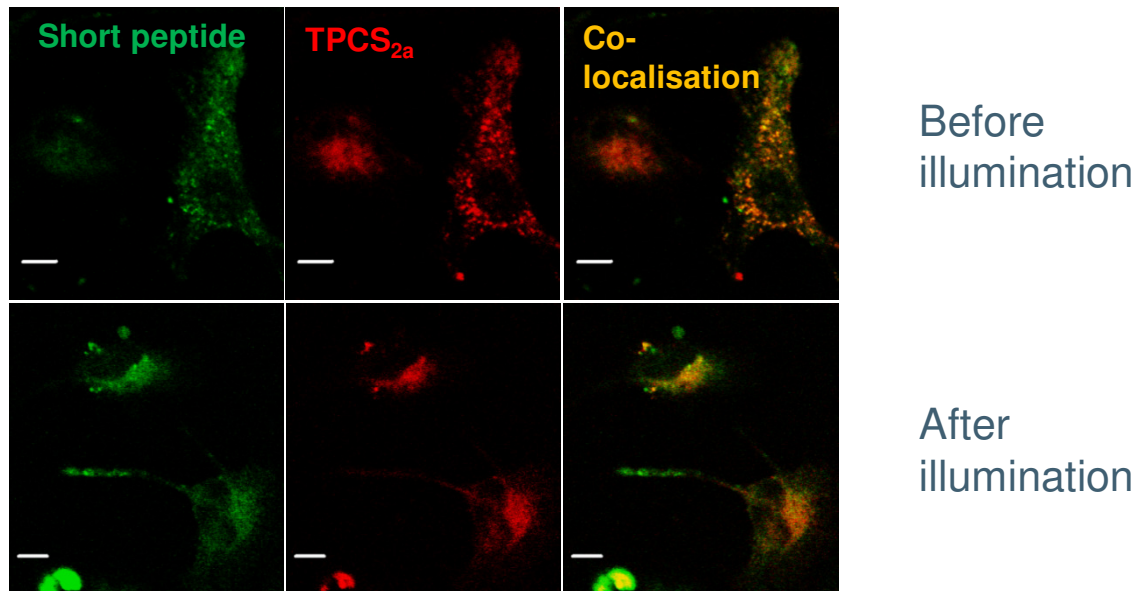
Apoptosis induction / Caspase-3



Short peptide antigens are taken up in endosomes – cytosolic release induced by PCI



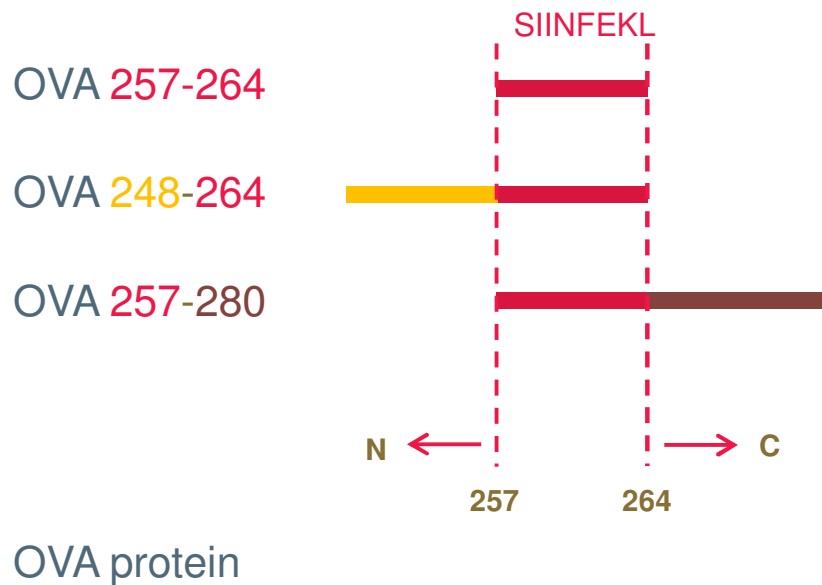
Also short peptides are taken up by endocytosis, co-localises with TPCS_{2a} in endosomes and are re-localised upon illumination



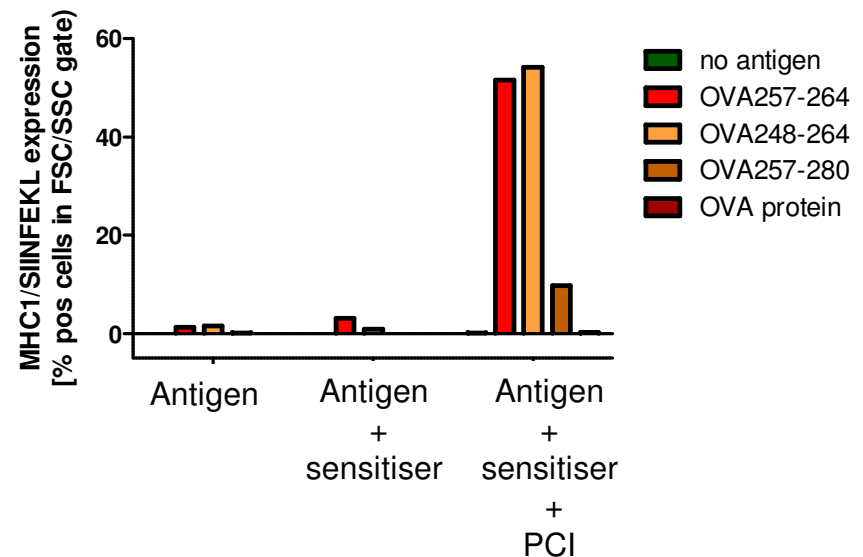
PCI with N- and C-terminal extended SIINFEKL (OVA) peptides increases MHC I presentation in macrophages



Cells stained with antibody specific for SIINFEKL/MHC I complex



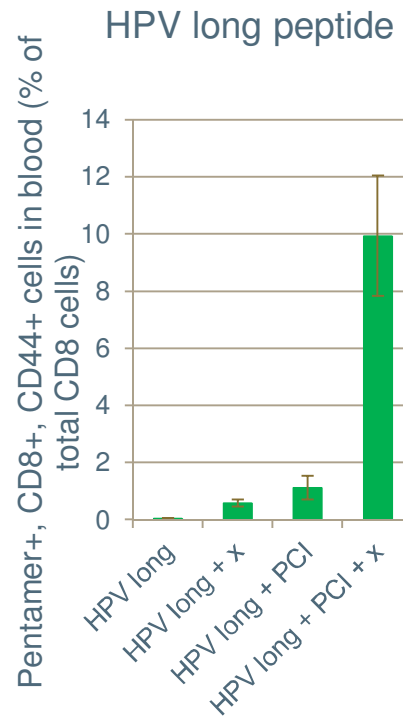
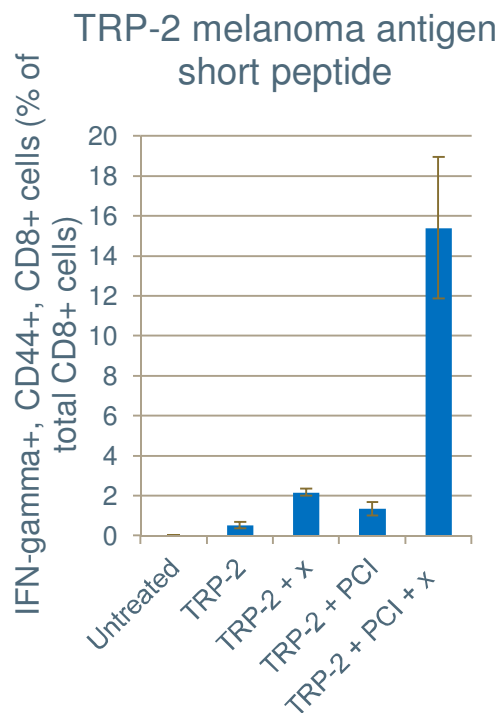
MHC1/SIINFEKL expression in B6 macrophage cell line, OVA peptides and proteins, concentrations of all antigens corresponds to 3 µg/ml of SIINFEKL



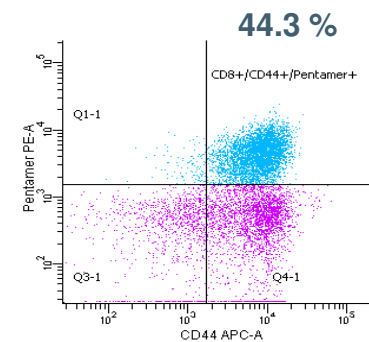
With peptide antigens PCI acts in synergy with other vaccination technologies.



- PCI provides increased antigen presentation
- An additional “danger signal” (X) may enhance effect further



HPV Vaccine with PCI



- Studies with PCI therapeutic vaccination in animal model for HPV induced cancer on-going – initial results very promising

Conclusions

- The PCI vaccination technology can enhance CD8-cell immune responses > 100 times.
- PCI acts by enhancing MHC class 1 antigen presentation by releasing antigens into the cytosol of antigen presenting cells
- The technology can be used with both protein, long peptide and short peptide antigens.
- PCI acts in synergy with other vaccination enhancing technologies
- The photosensitising compound used in PCI is already tested in clinical trials, has a good safety profile and is stable and easily produced.
- PCI is an innovative technology with an unique mechanism for enhancing the effect of many types of vaccines where a CD8 T-cell response is desired



Enquiries

PCI Biotech

CSO Anders Høgset

Cell phone: +47 905 02 732

Telephone: +47 67 11 54 04

E-mail: ah@pcibiotech.com

Thank you