

A lighthouse with a glowing light sits atop a dark, forested cliff overlooking a calm sea at dusk. The sky is a soft, hazy grey. The lighthouse is white with a dark top section where the light is visible. The cliff is covered in dense trees. The water is still, reflecting the light from the lighthouse and the sky. In the distance, more land and rocks are visible under the twilight sky.

PCI BIOTECH

Unlocking the potential of innovative medicines

Kan man levere medisiner med lys?

15.mai, 2019

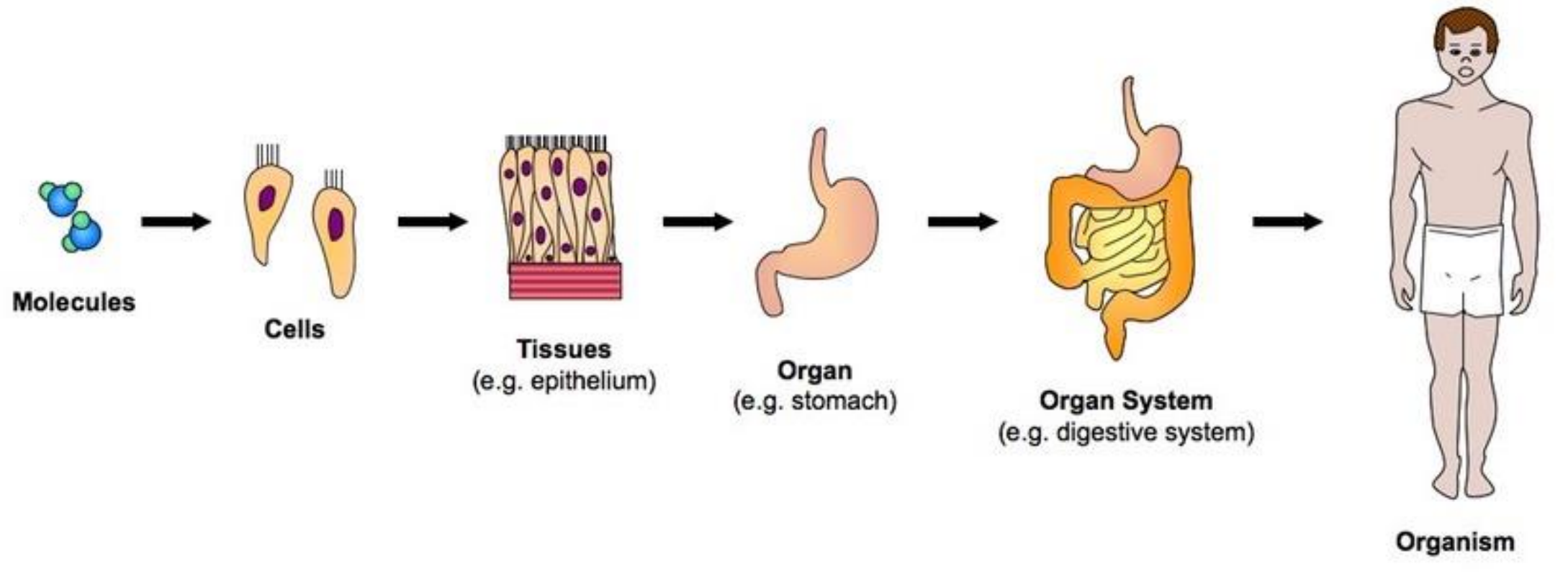
Per Walday



legemiddel

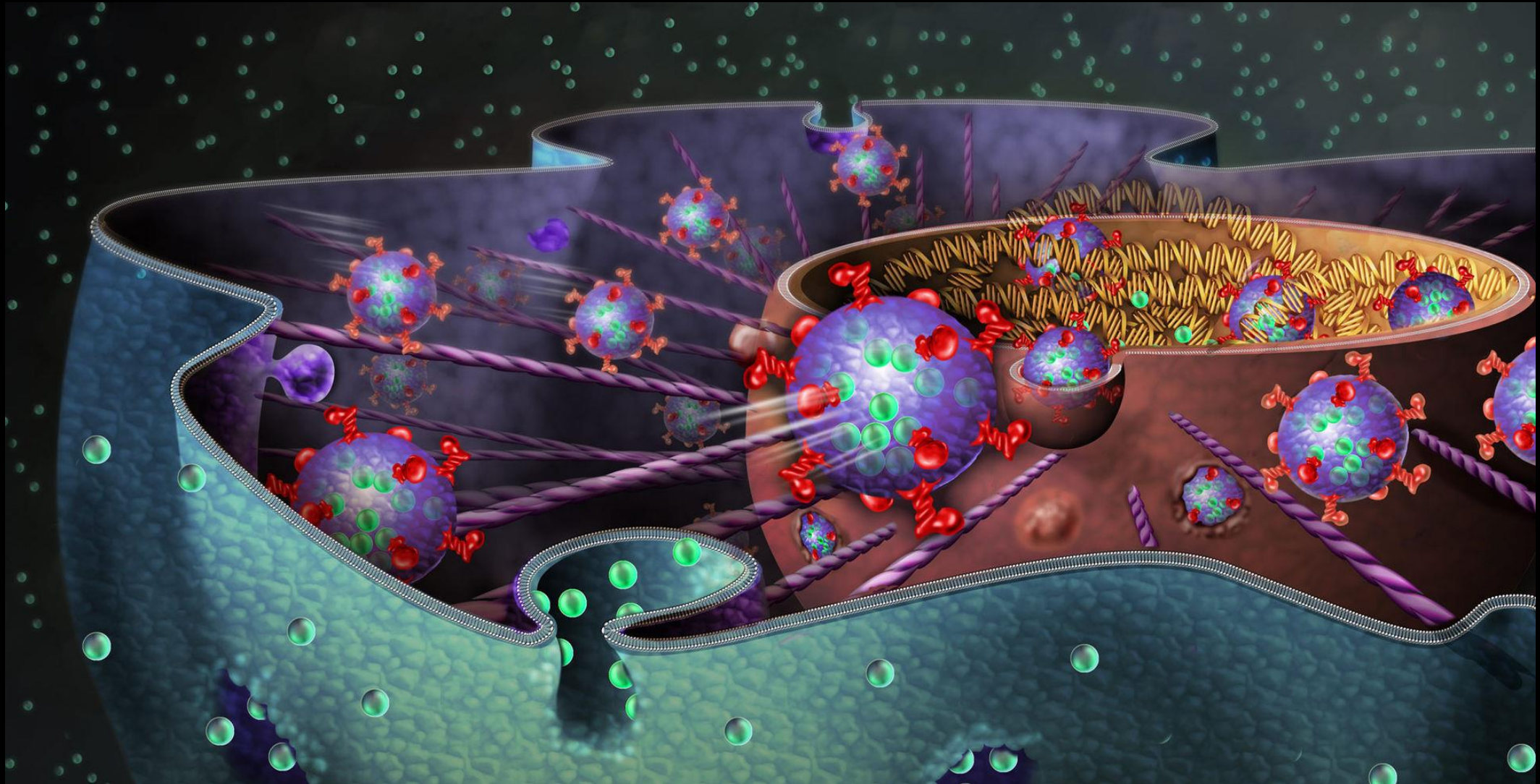
molekyler designet for å interagere med målmolekyler i kroppen

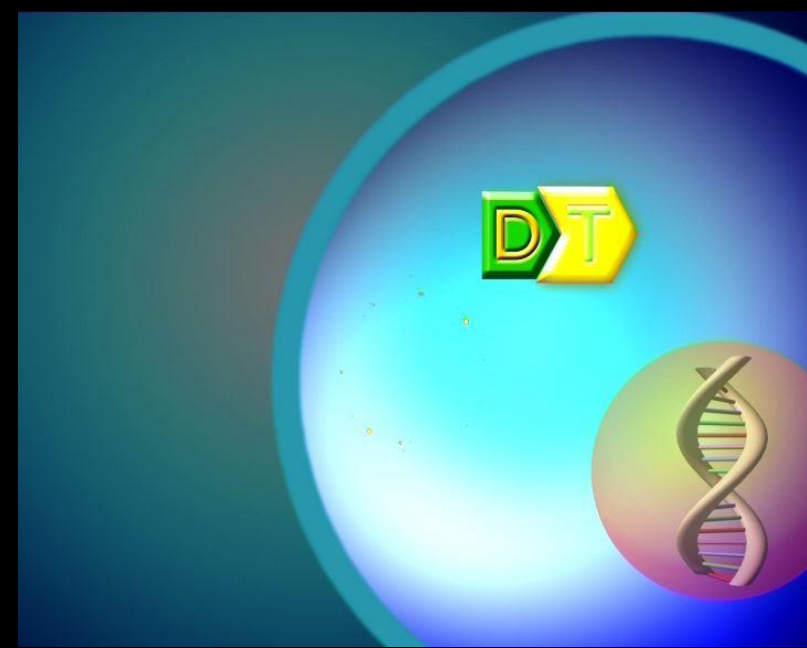
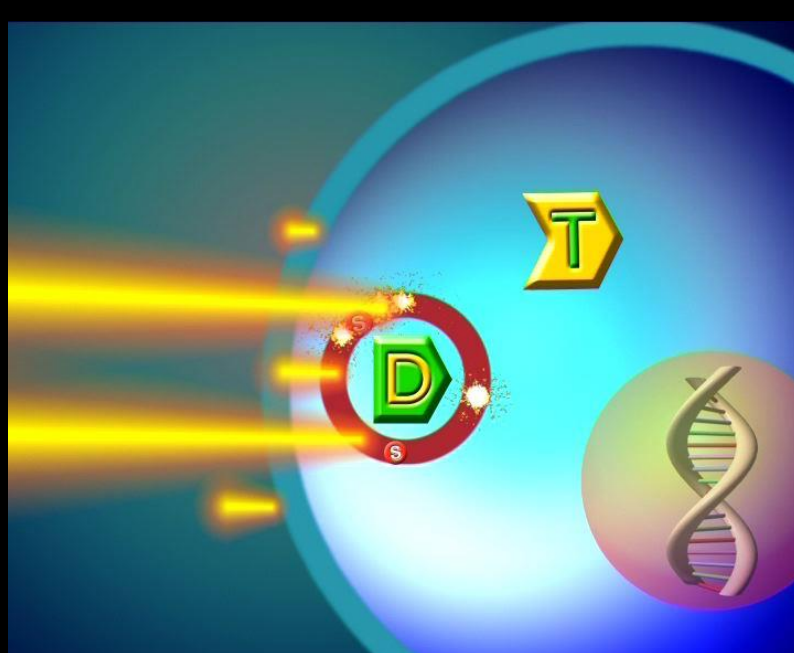
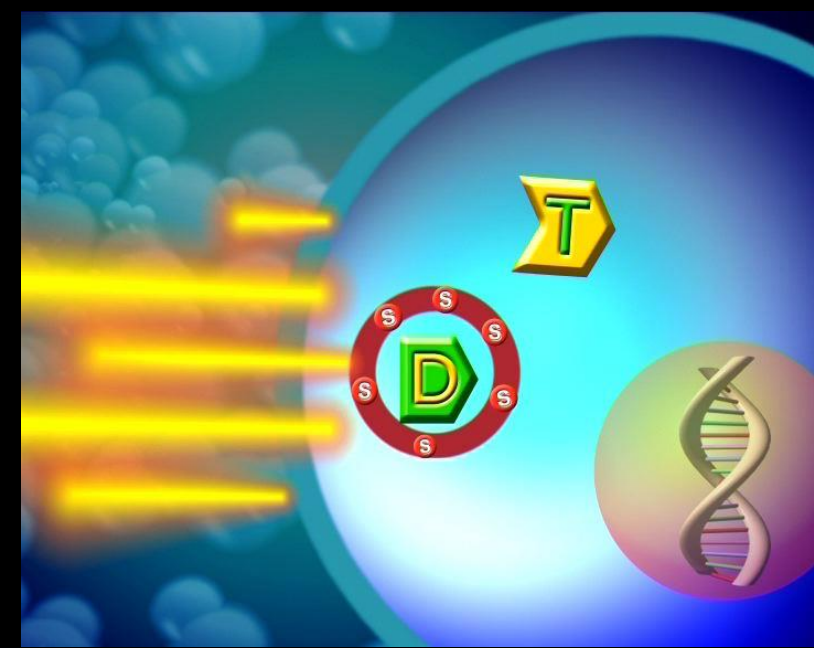
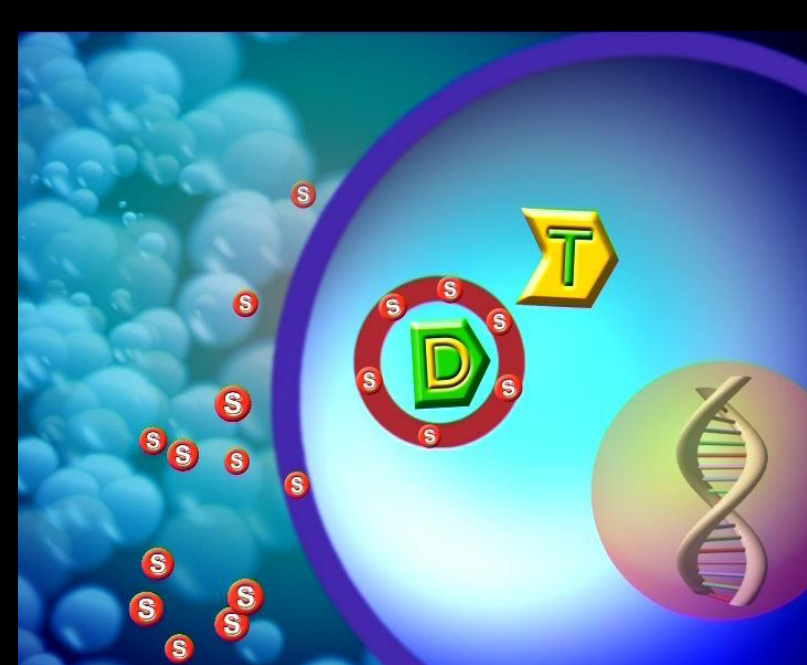
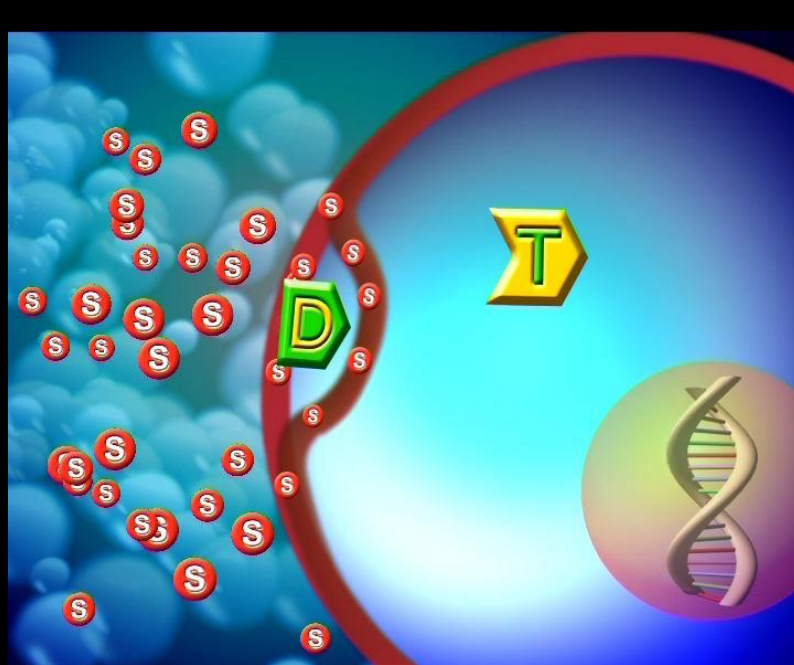
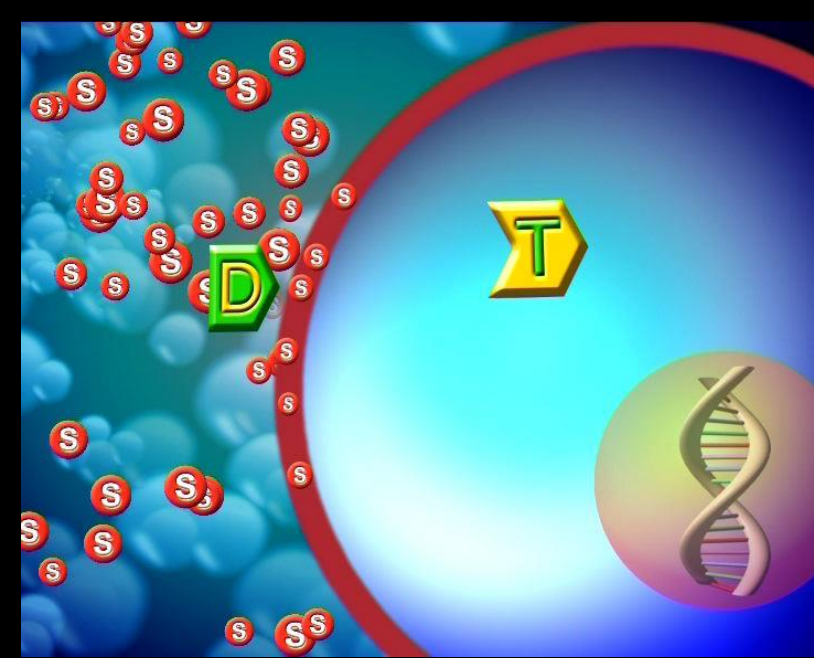


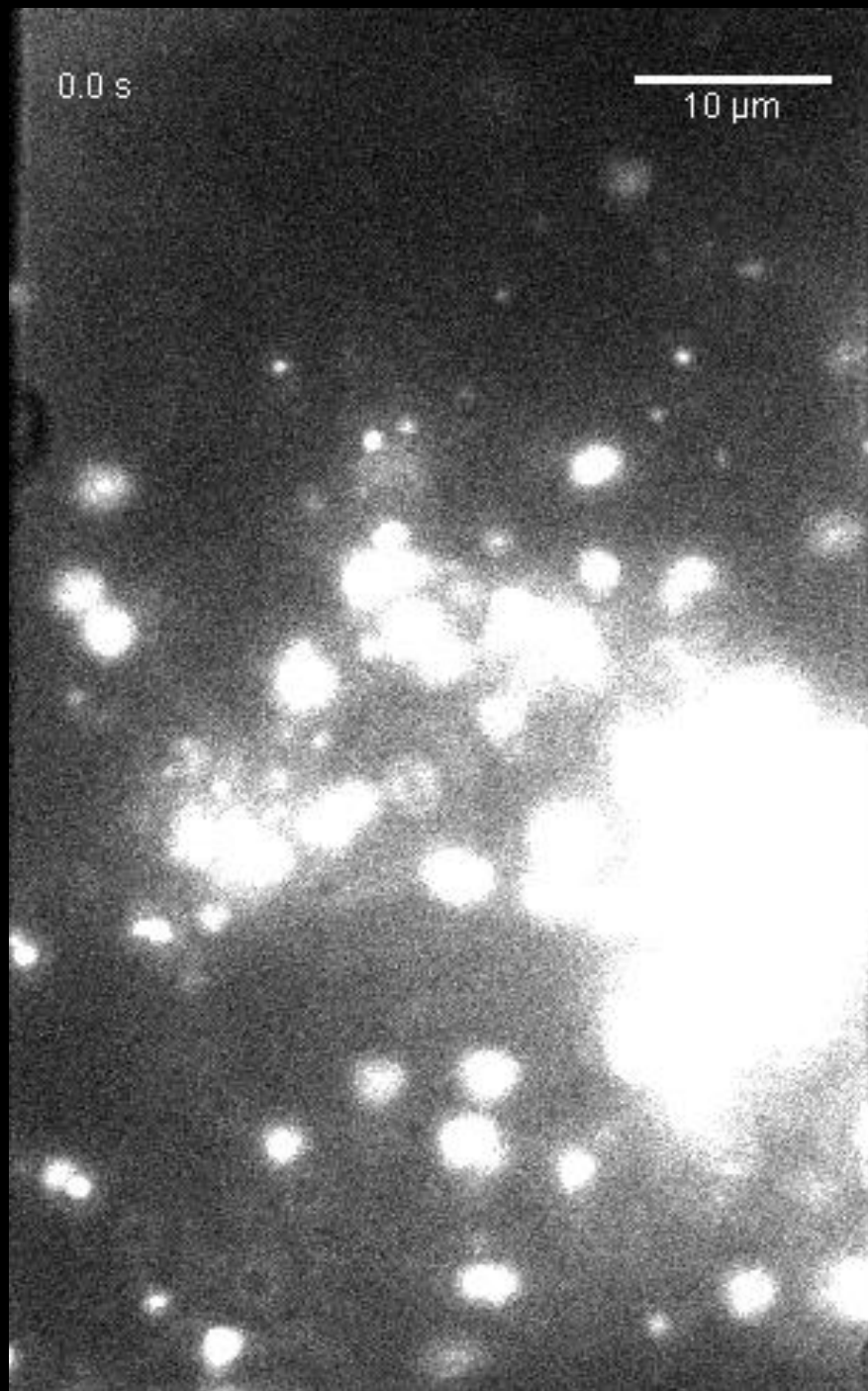


endocytose

av gresk endon, 'inne i', kytos, 'celle', og -osis, 'tilstand'

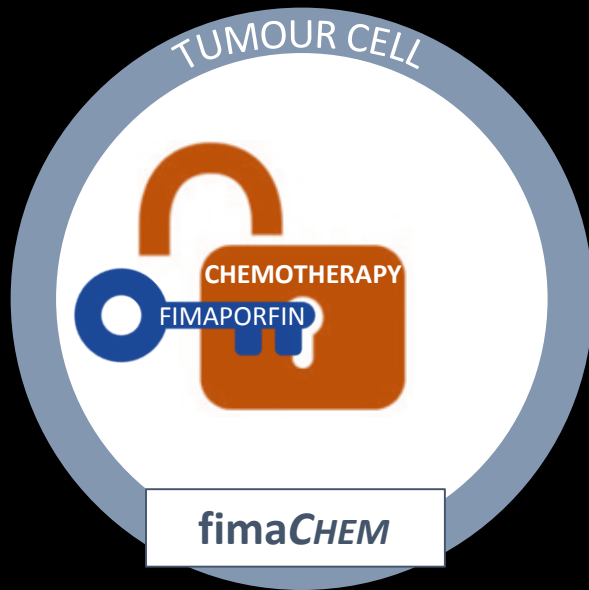




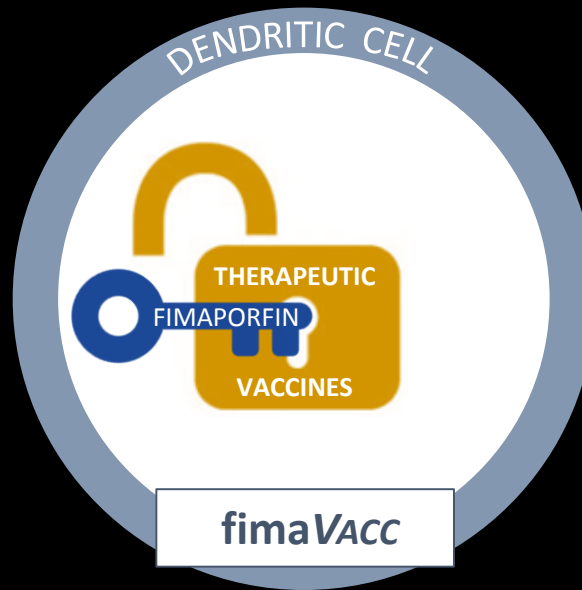


**PCI-behandling av en
celle som har tatt opp
fluorescerende dextran
(endocytose-markør)**

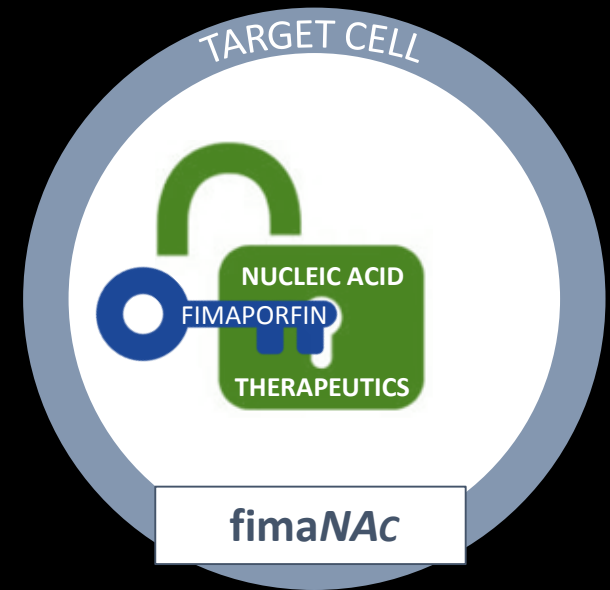
PCI – nøkkelen til effektiv levering



Utvider eksisterende
legemidlers
mulighet å dekke
medisinske behov



Øker den cellulære
effekten av vaksiner,
viktig for terapeutisk
effekt



Effektiv lokal
leveringsløsning for
nukleinsyrebaserte
legemidler





Det fremste tidsskriftet i verden
for originalartikler på klinisk
utprøving innen kreft

THE LANCET Oncology

Articles



Disulfonated tetraphenyl chlorin (TPCS_{2a})-induced photochemical internalisation of bleomycin in patients with solid malignancies: a phase 1, dose-escalation, first-in-man trial

Ahmed A Sultan*, Waseem Jerjes*, Kristian Berg, Anders Høgset, Charles A Mosse, Rifat Hamoudi, Zaid Hamdoon, Celia Simeon, Dawn Carnell, Martin Forster, Colin Hopper

Summary

Background Photochemical internalisation, a novel minimally invasive treatment, has shown promising preclinical results in enhancing and site-directing the effect of anticancer drugs by illumination, which initiates localised chemotherapy release. We assessed the safety and tolerability of a newly developed photosensitiser, disulfonated tetraphenyl chlorin (TPCS_{2a}), in mediating photochemical internalisation of bleomycin in patients with advanced and recurrent solid malignancies.

Methods In this phase 1, dose-escalation, first-in-man trial, we recruited patients (aged ≥18 to <85 years) with local recurrent, advanced, or metastatic cutaneous or subcutaneous malignancies who were clinically assessed as eligible for bleomycin chemotherapy from a single centre in the UK. Patients were given TPCS_{2a} on day 0 by slow intravenous injection, followed by a fixed dose of 15 000 IU/m² bleomycin by intravenous infusion on day 4. After 3 h, the surface of the target tumour was illuminated with 652 nm laser light (fixed at 60 J/cm²). The TPCS_{2a} starting dose was 0.25 mg/kg and was then escalated in successive dose cohorts of three patients (0.5, 1.0, and 1.5 mg/kg). The primary endpoints were safety and tolerability of TPCS_{2a}; other co-primary endpoints were dose-limiting toxicity and maximum tolerated dose. The primary analysis was per protocol. This study is registered with ClinicalTrials.gov, number NCT00993512, and has been completed.

Findings Between Oct 3, 2009, and Jan 14, 2014, we recruited 22 patients into the trial. 12 patients completed the 3-month follow-up period. Adverse events related to photochemical internalisation were either local, resulting from the local inflammatory process, or systemic, mostly as a result of the skin-photosensitising effect of TPCS_{2a}. The most common grade 3 or worse adverse events were unexpected higher transient pain response (grade 3) localised to the treatment site recorded in nine patients, and respiratory failure (grade 4) noted in two patients. One dose-limiting toxicity was reported in the 1.0 mg/kg cohort (skin photosensitivity [grade 2]). Dose-limiting toxicities were reported in two of three patients at a TPCS_{2a} dose of 1.5 mg/kg (skin photosensitivity [grade 3] and wound infection [grade 3]); thus, the maximum tolerated dose of TPCS_{2a} was 1.0 mg/kg. Administration of TPCS_{2a} was found to be safe and tolerable by all patients. No deaths related to photochemical internalisation treatment occurred.

Interpretation TPCS_{2a}-mediated photochemical internalisation of bleomycin is safe and tolerable. We identified TPCS_{2a} 0.25 mg/kg as the recommended treatment dose for future trials.

Funding PCI Biotech.

Introduction

Photochemical internalisation is a novel technology that facilitates the delivery of therapeutic molecules into the cytosol of cells. It was developed to enhance targeted intracellular delivery of therapeutics that are not able to penetrate cellular membranes, including nucleic acids, and various nanoparticles. The mechanism of action involves the formation of reactive oxygen species and nucleic acids, and various nanoparticles. The mechanism of action involves the formation of reactive oxygen species and nucleic acids, and various nanoparticles. The mechanism of action involves the formation of reactive oxygen species and nucleic acids, and various nanoparticles.

oxygen species are induced and lysosomes, the cytosol, and the nucleus are targeted.

Lancet Oncol 2016

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[http://dx.doi.org/10.1016/S1473-2045\(16\)30274-1](http://dx.doi.org/10.1016/S1473-2045(16)30274-1)

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[http://dx.doi.org/10.1016/S1473-2045\(16\)30274-1](http://dx.doi.org/10.1016/S1473-2045(16)30274-1)

*Contributed equally

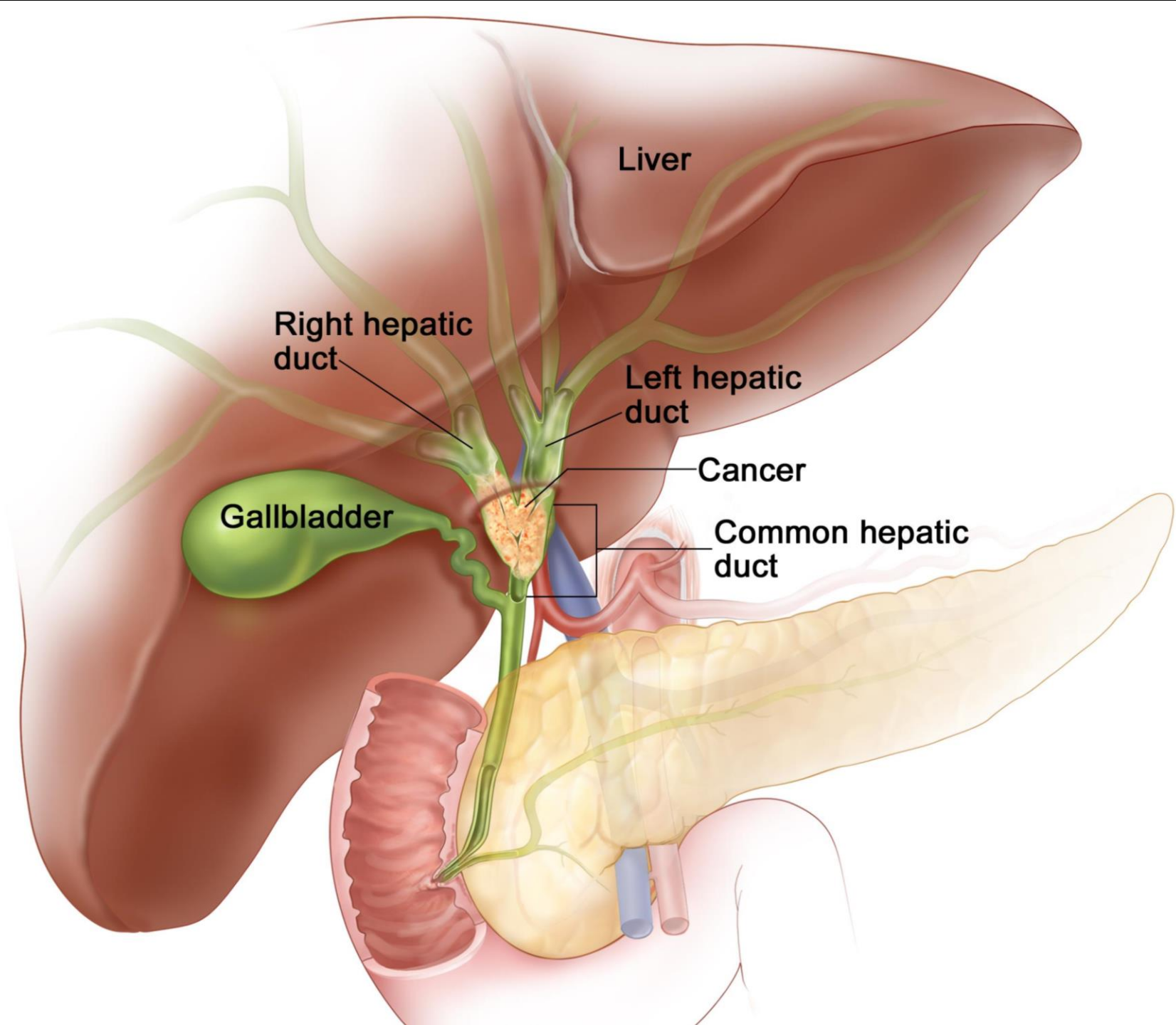
Academic Unit of Oral and Maxillofacial Surgery, UCL

Eastman Dental Institute, London, UK (A A Sultan PhD, Z Hamdoon PhD, C Hopper MD);

Division of Surgery and Interventional Science, University College London, London, UK (W Jerjes PhD, C A Mosse PhD, R Hamoudi PhD);

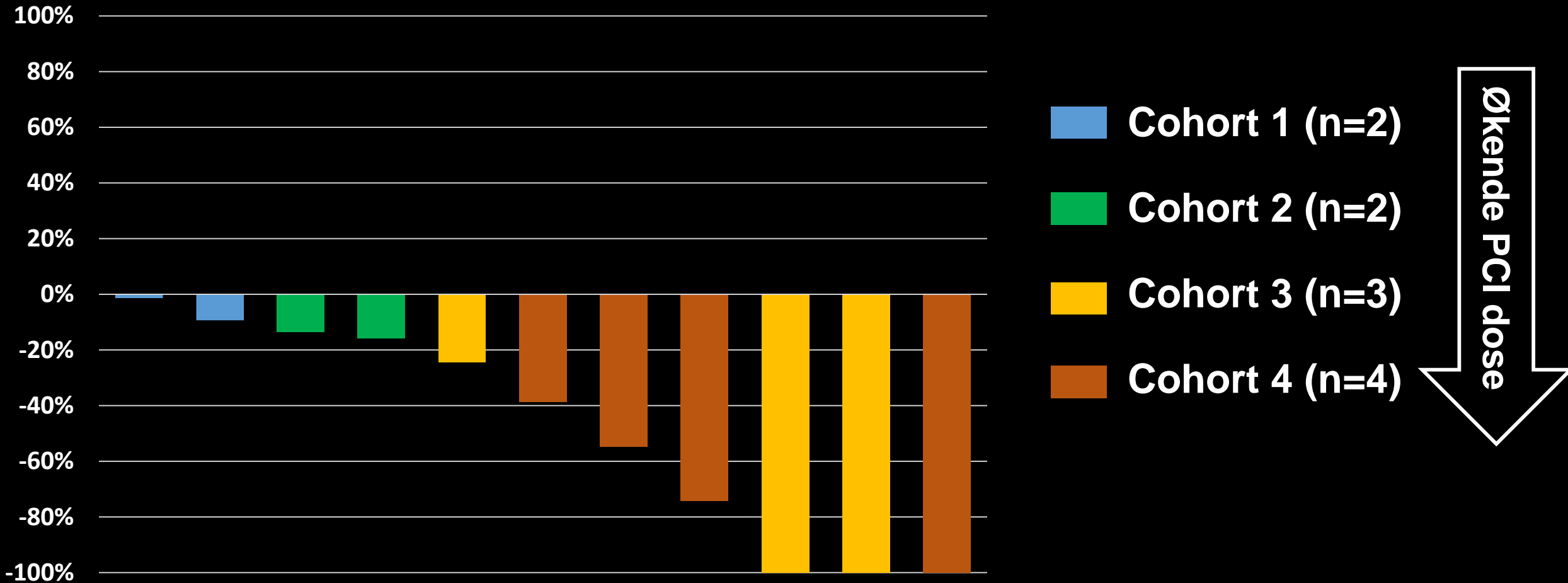
Department of Radiation Biology, Oslo University Hospital, Oslo, Norway (Prof K Berg PhD); PCI Biotech AS, Oslo, Norway (A Høgset PhD); Cancer Clinical Trials Unit (C Simeon BSc) and Head and Neck Unit (D Carnell MD, M Forster PhD, C Hopper), University College London Hospitals, London, UK; and UCL Cancer Institute, London, UK (M Forster, C Hopper)

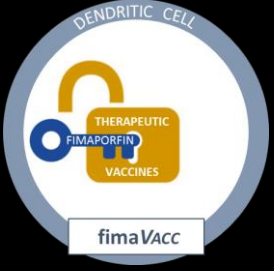
Correspondence





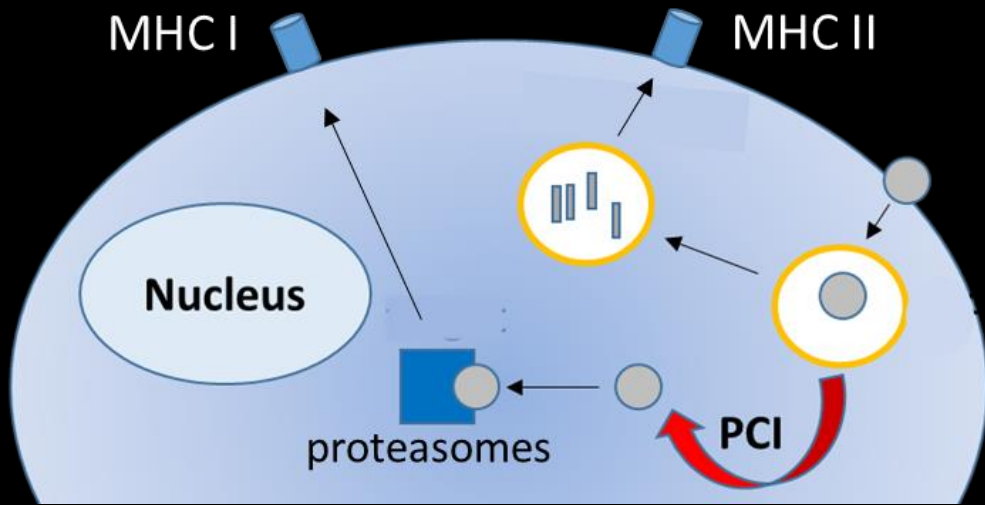
prosent forandring total tumorvev





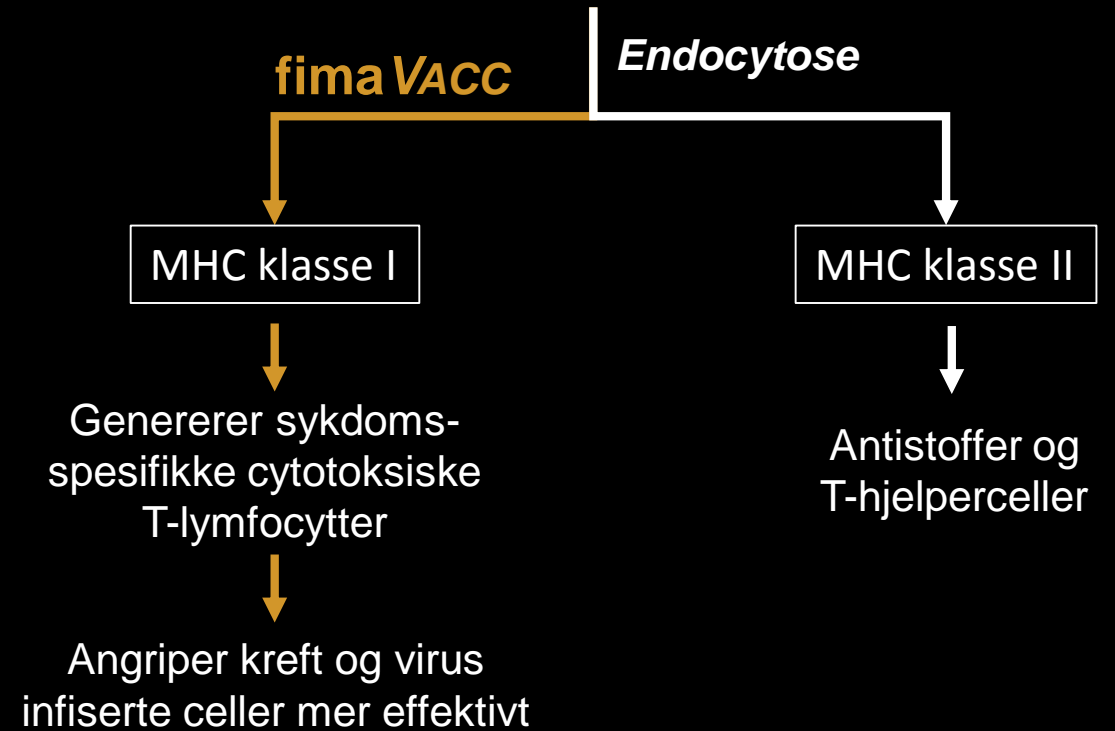
dendritisk celle

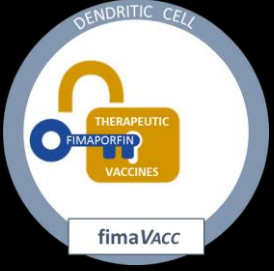
immunsystemets vaktpost



● vaksineantigen

Vaksine

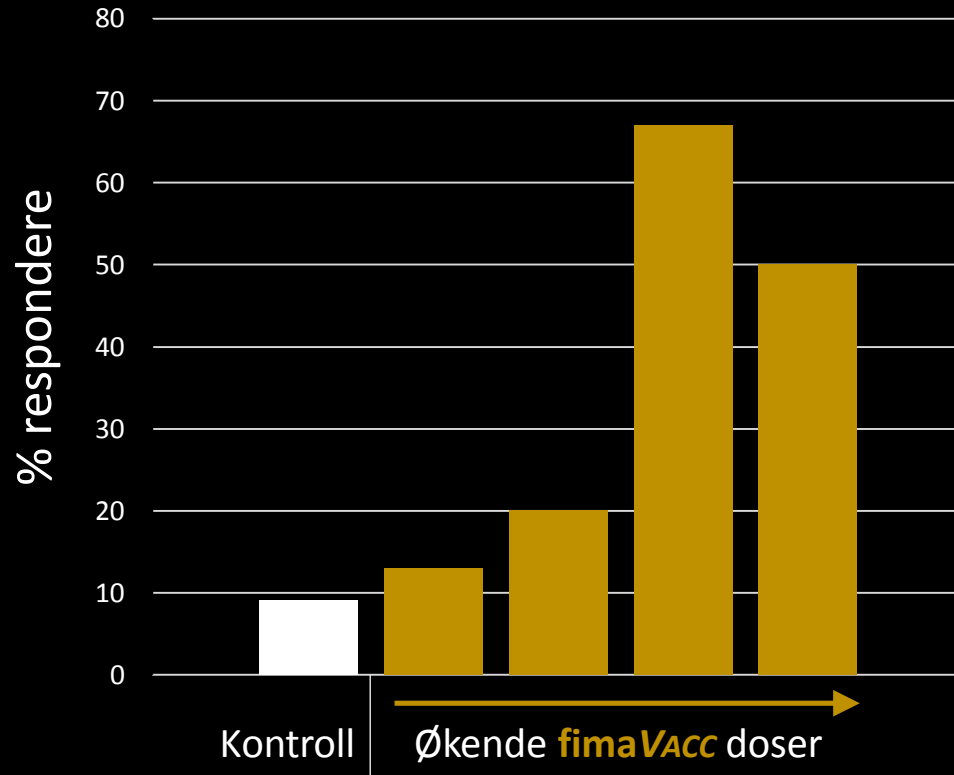




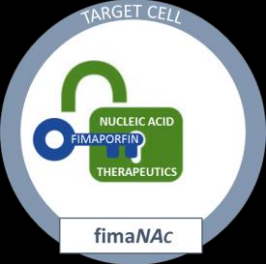
studie i friske frivillige

vaksinering med HPV peptid

% HPV respondere etter tre
vaksinasjoner

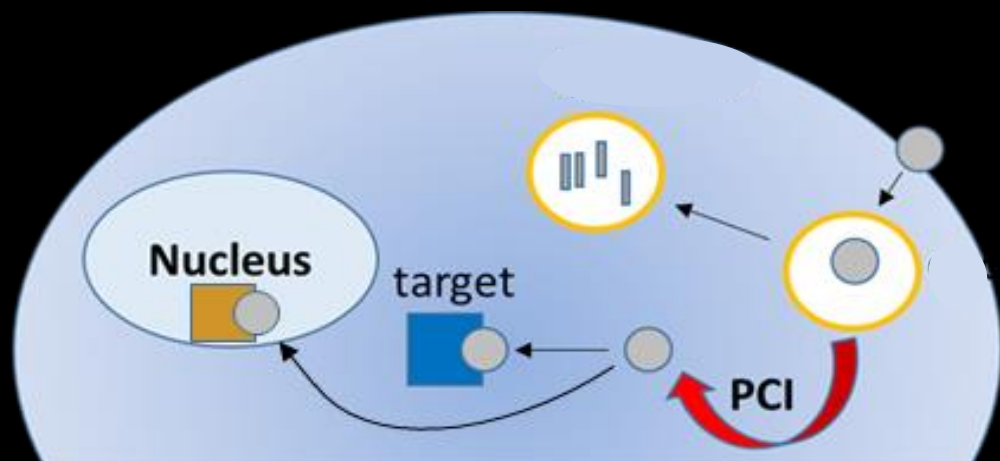


fimaVacc gir en kraftig økning av antall forsøkspersoner med T-celle respons sammenlignet med kontrollgruppen med en annen vaksine-teknologi (Hiltonol) som er under utvikling



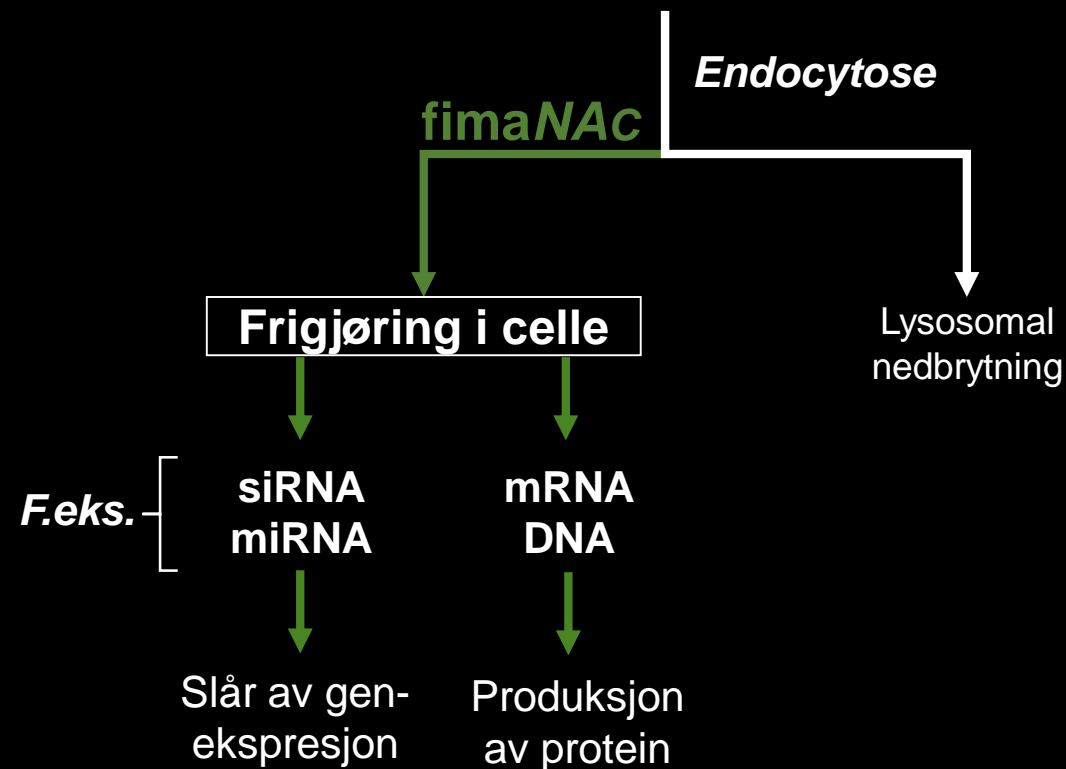
målcelle

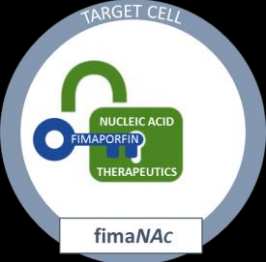
for modifisering av genuttrykk



● nukleinsyre terapi

Nukleinsyre-terapi

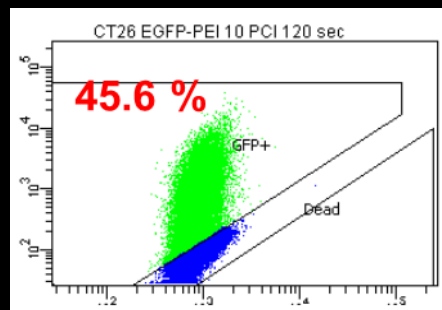
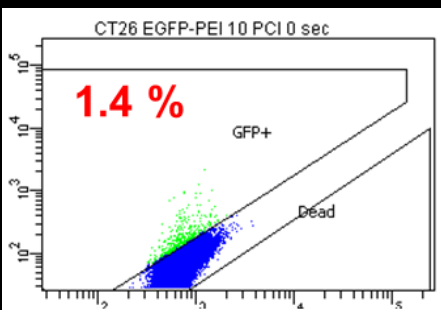




levering av mRNA

som koder for grønt fluorescerende protein

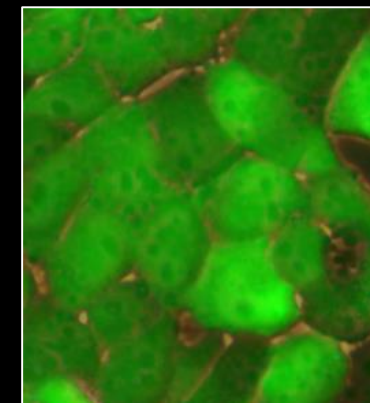
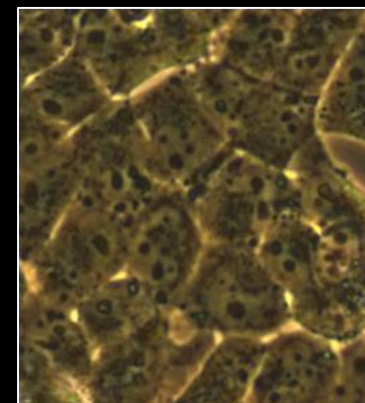
0 sek



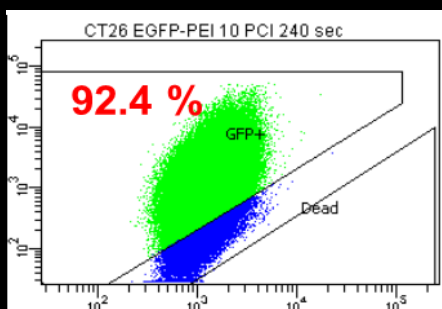
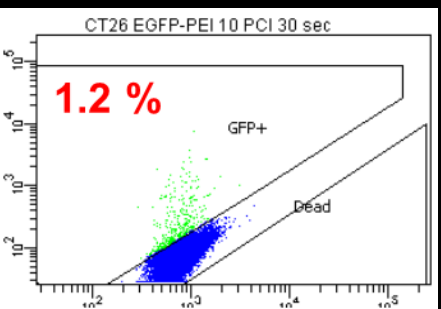
90 sek

kontroll

fimaNAC



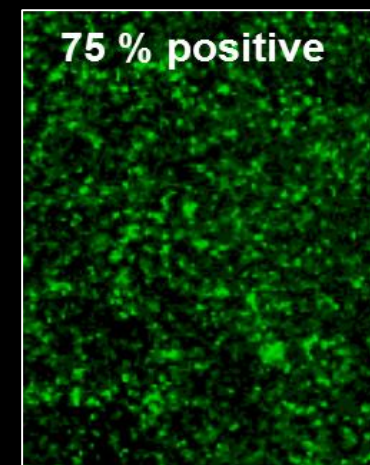
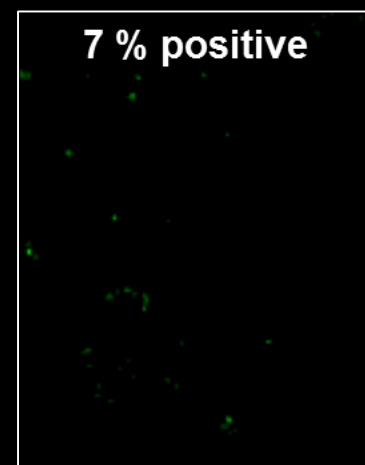
30 sek



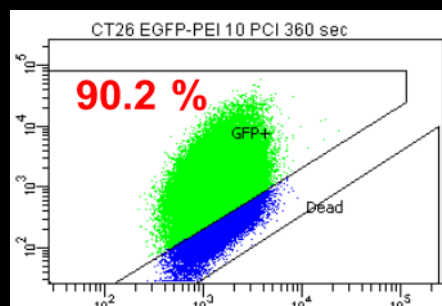
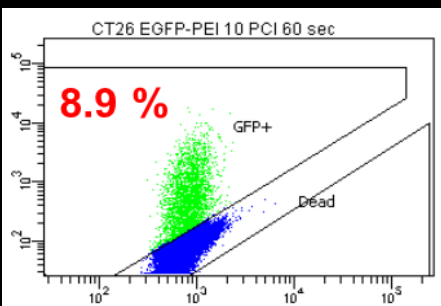
120 sek

7 % positive

75 % positive



60 sek



360 sek

Kan man levere medisiner med lys?

JA!

ved hjelp av PCI teknologien

**Takk for
oppmerksomheten**

PCI BIOTECH

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