

Design of Hybrid Gold Nanoparticles for Cancer Immunotherapy

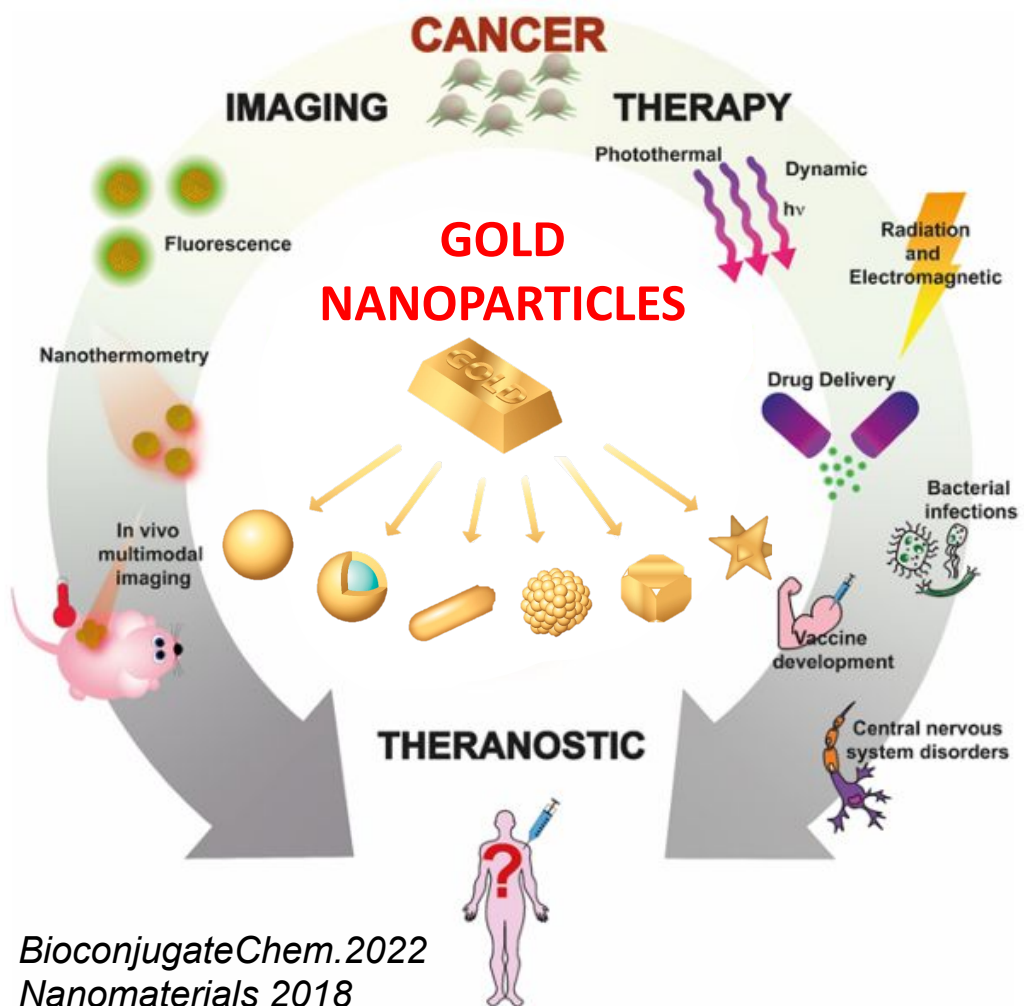
Gayong Shim

School of Systems Biomedical Science
Department of Bioinformatics and Life Science
Soongsil University

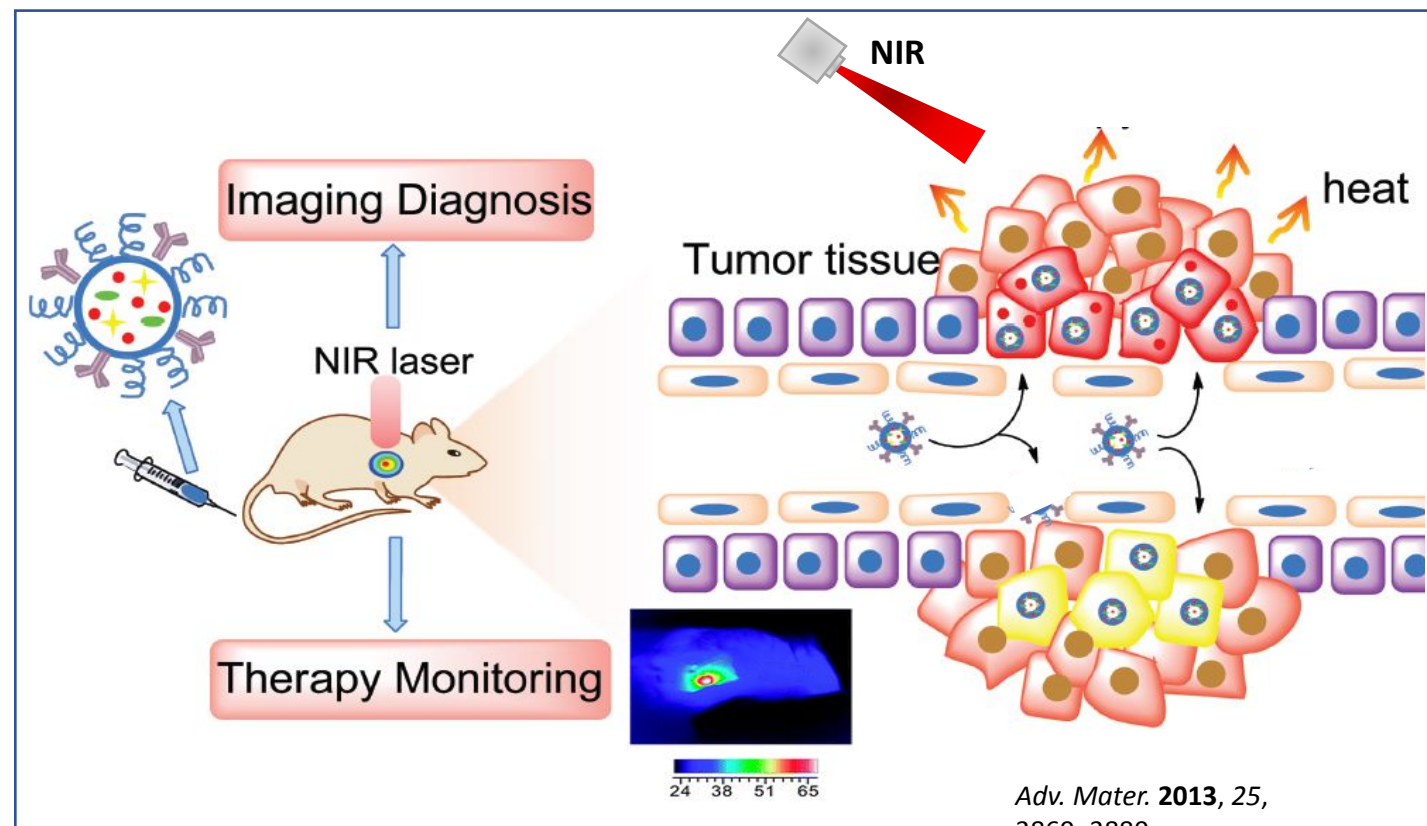
CONTROLLED RELEASE SOCIETY
CRS 2023 ANNUAL MEETING & EXPOSITION
JULY 24-28, 2023 **Paris Hotel** » **Las Vegas, NV, USA**

THE FUTURE OF DELIVERY SCIENCE

Gold nanoparticles for phototherapy

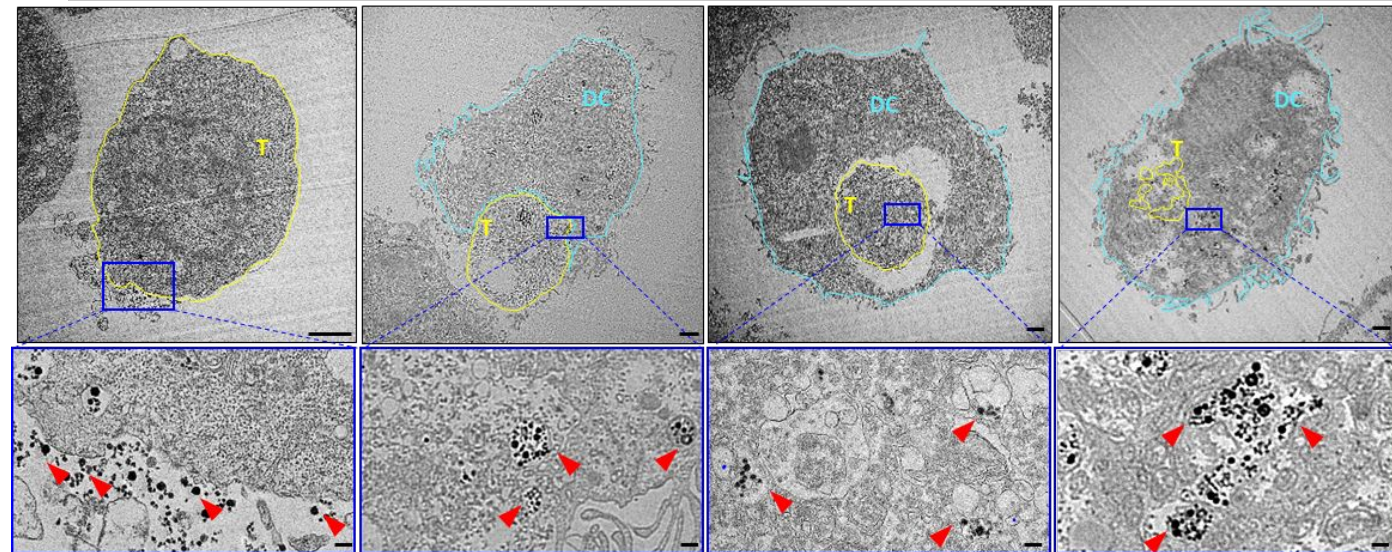
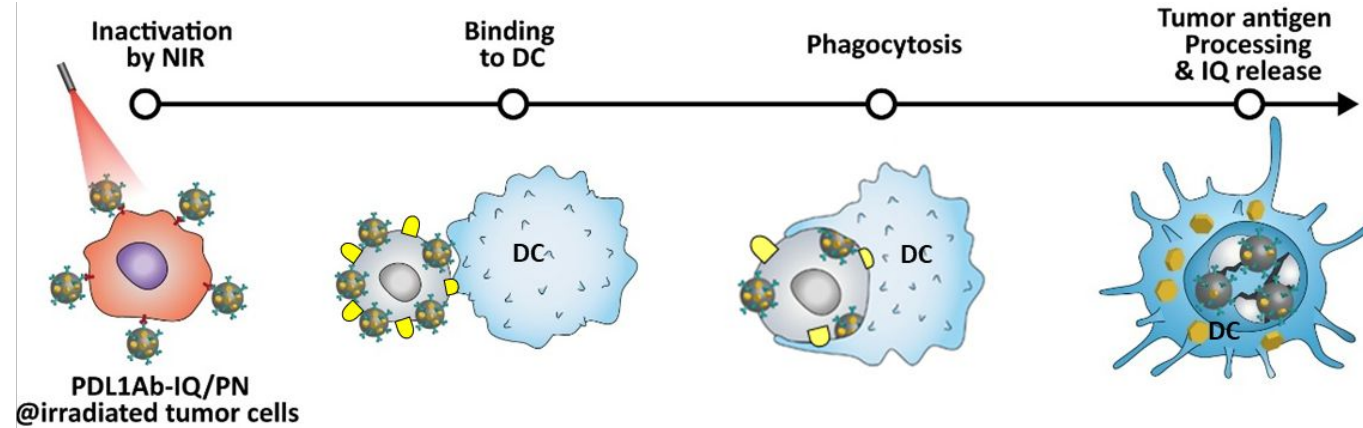
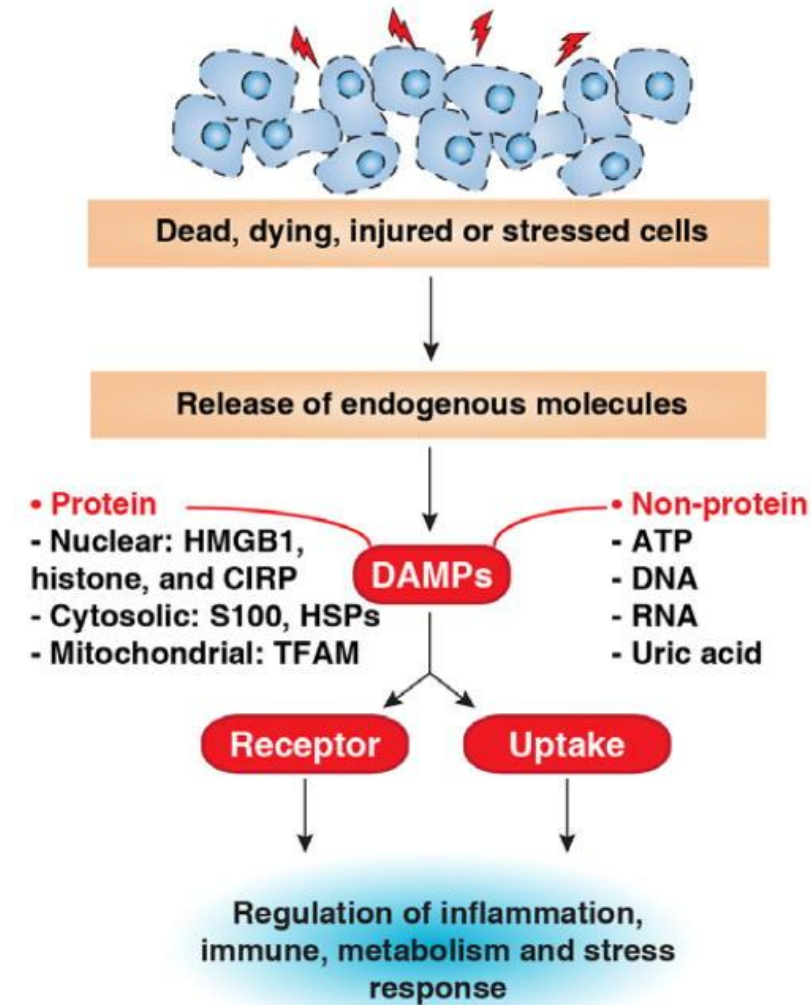


BioconjugateChem.2022
Nanomaterials 2018



Adv. Mater. 2013, 25,
3869–3880

Phototherapy-mediated immunogenic cell death

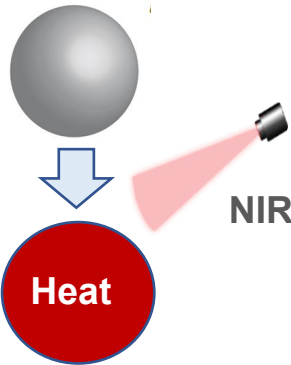
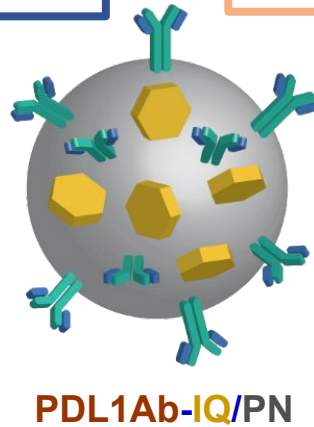
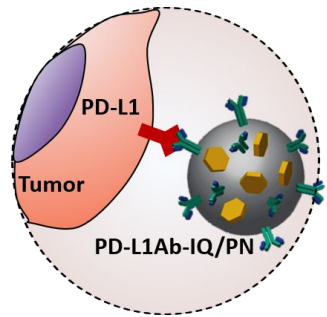


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In situ cancer vaccination for adaptive immunity

Immune checkpoint inhibitor

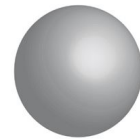
Therapeutic nanoparticles



PD-L1
antibody

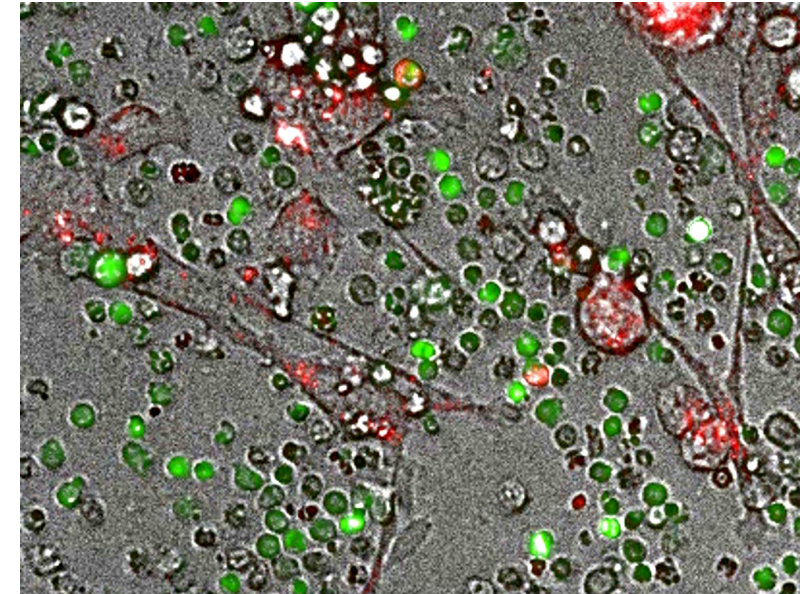
Inhibition of
Immune checkpoint
in tumor
microenvironment

Induction of
“Eat me” signals
on tumor cells
by heating



Therapeutic
nanoparticle

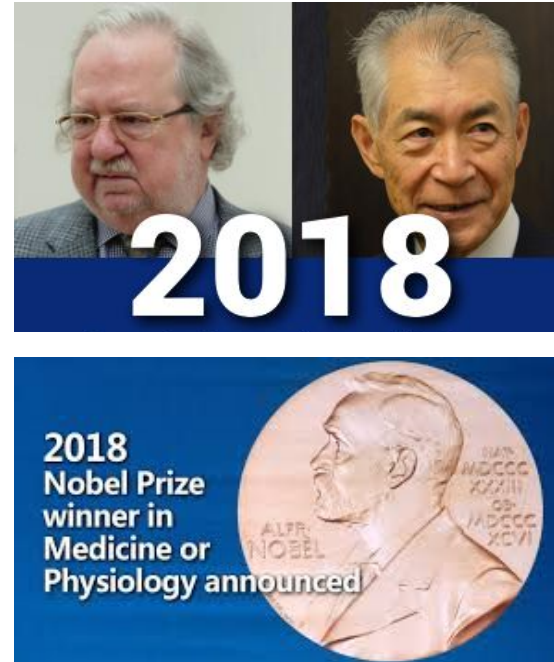
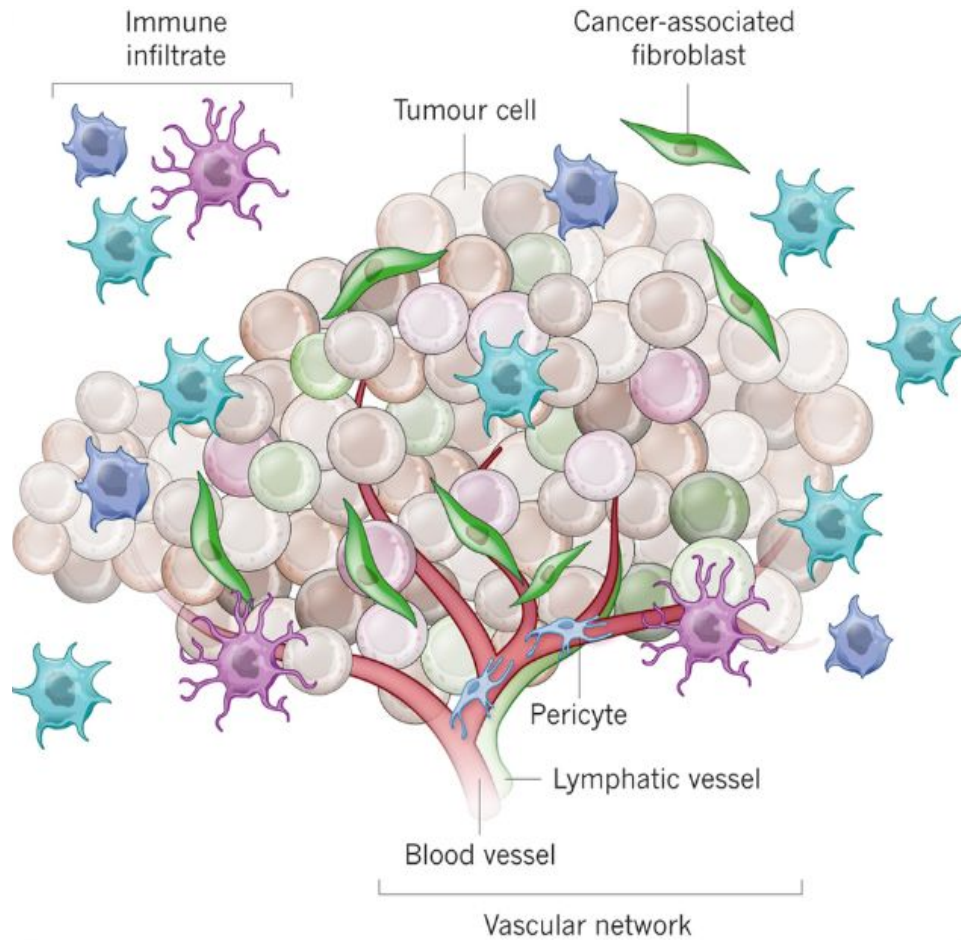
T cells from the mouse
treated with PDL1Ab-IQ/PN+NIR



Red: CT26 tumor cell
Green: T cell

ACS Nano 2019

Tumor immune microenvironment : An alternative cancer therapy?

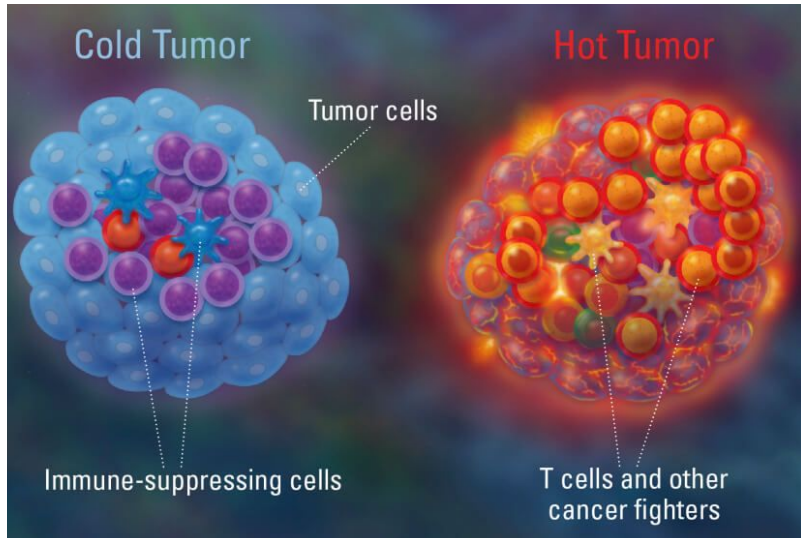


New immunotherapy drug behind Jimmy Carter's cancer cure

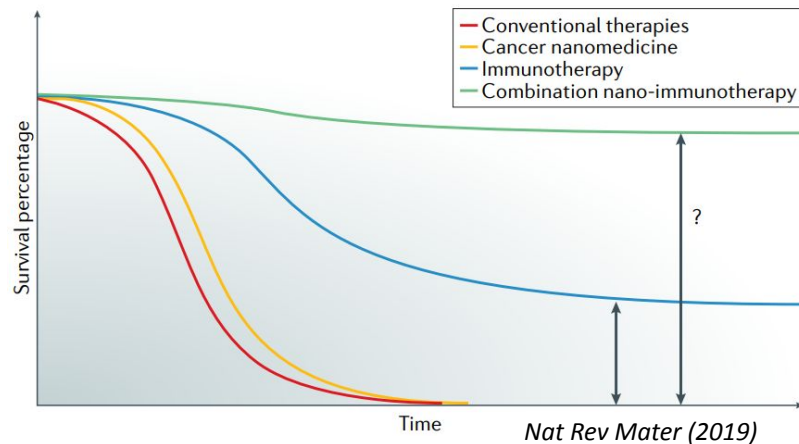
Former president given pembrolizumab, one of the most promising new drugs in the treatment of cancer



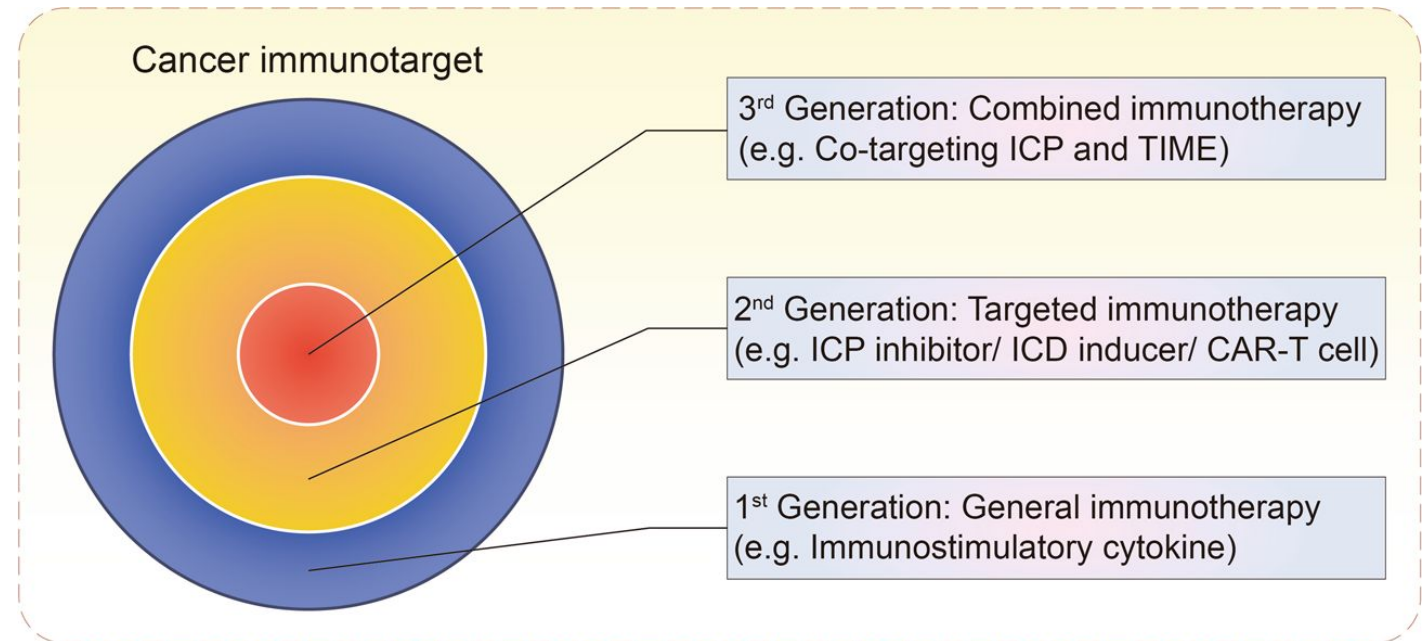
How to turn Cold tumors Hot?



Dana-Farber Cancer Institute

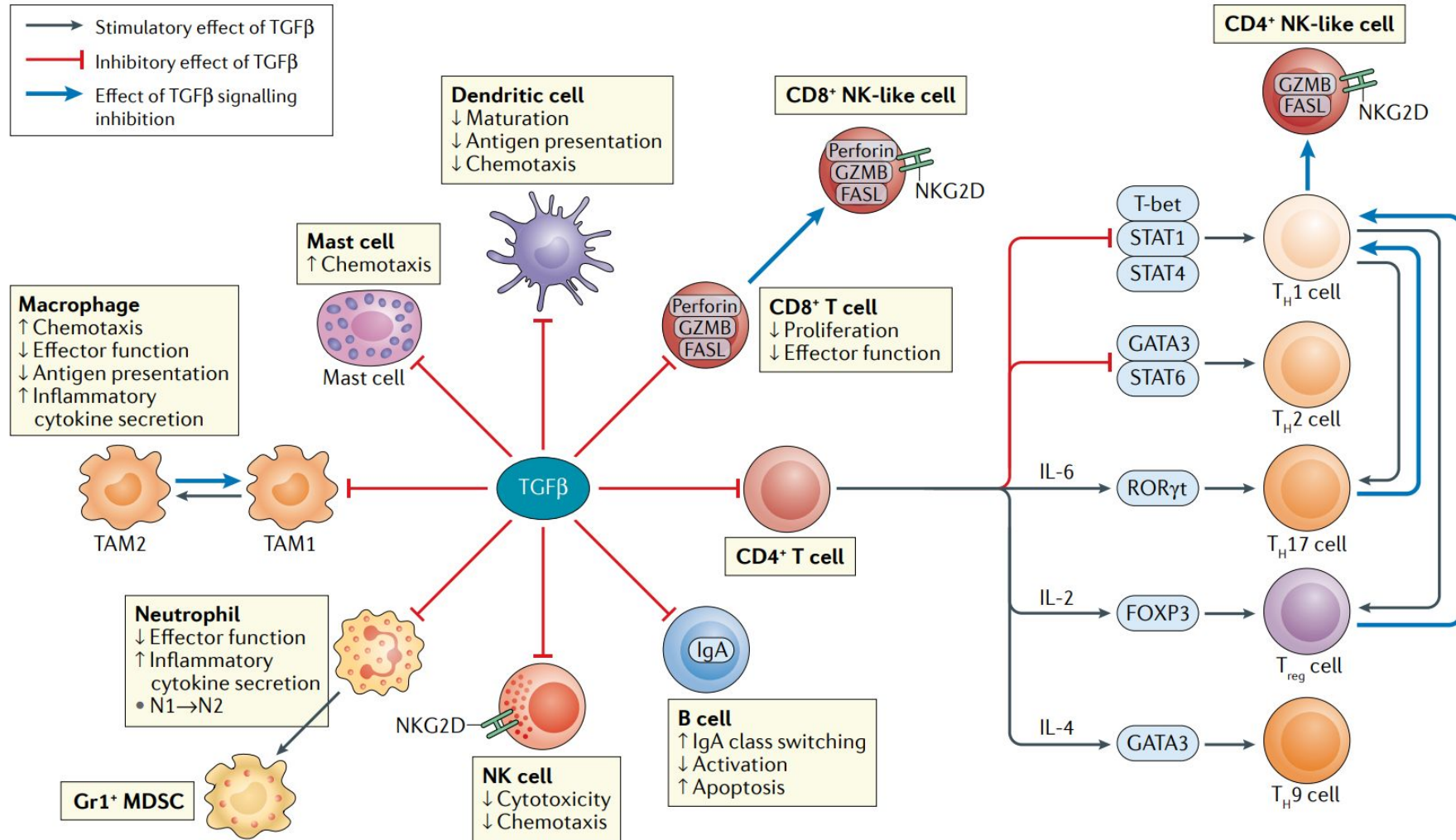


Nat Rev Mater (2019)



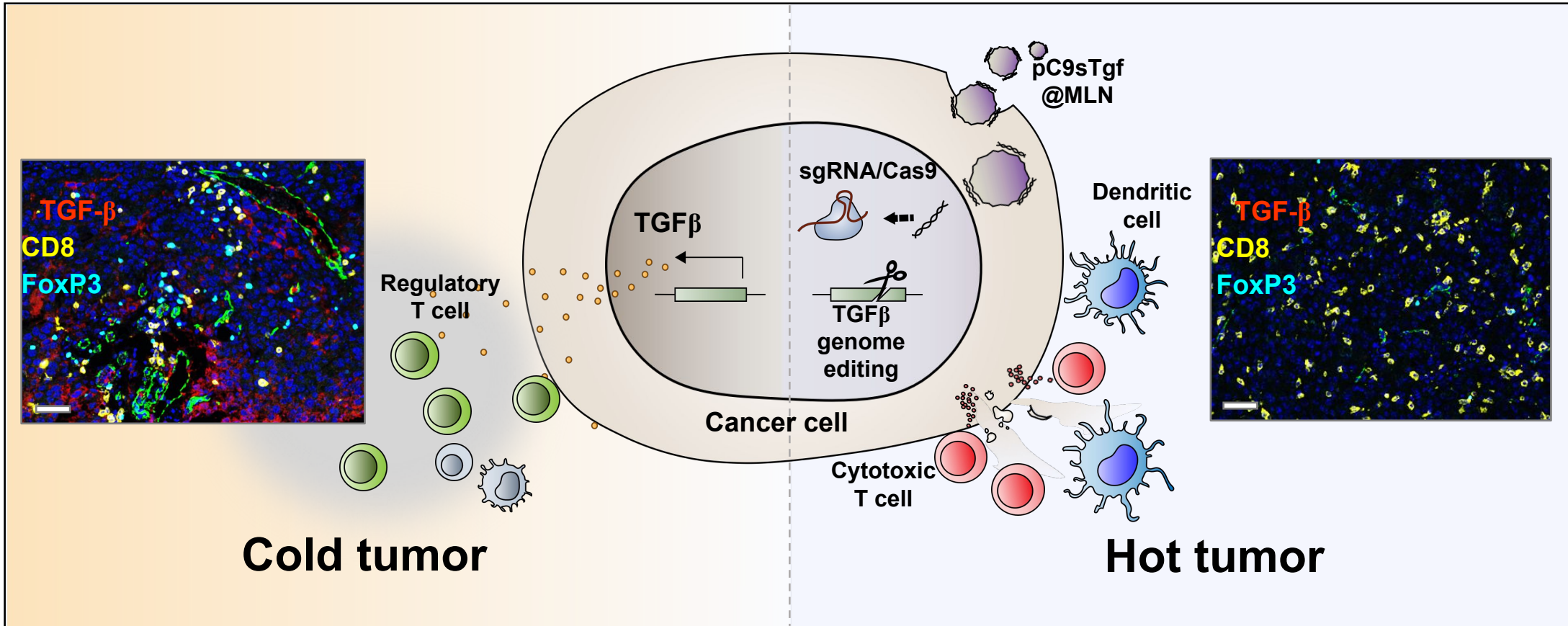
Signal Transduct Target Ther (2021)

What happens in a TGF- β -rich tumor microenvironment?



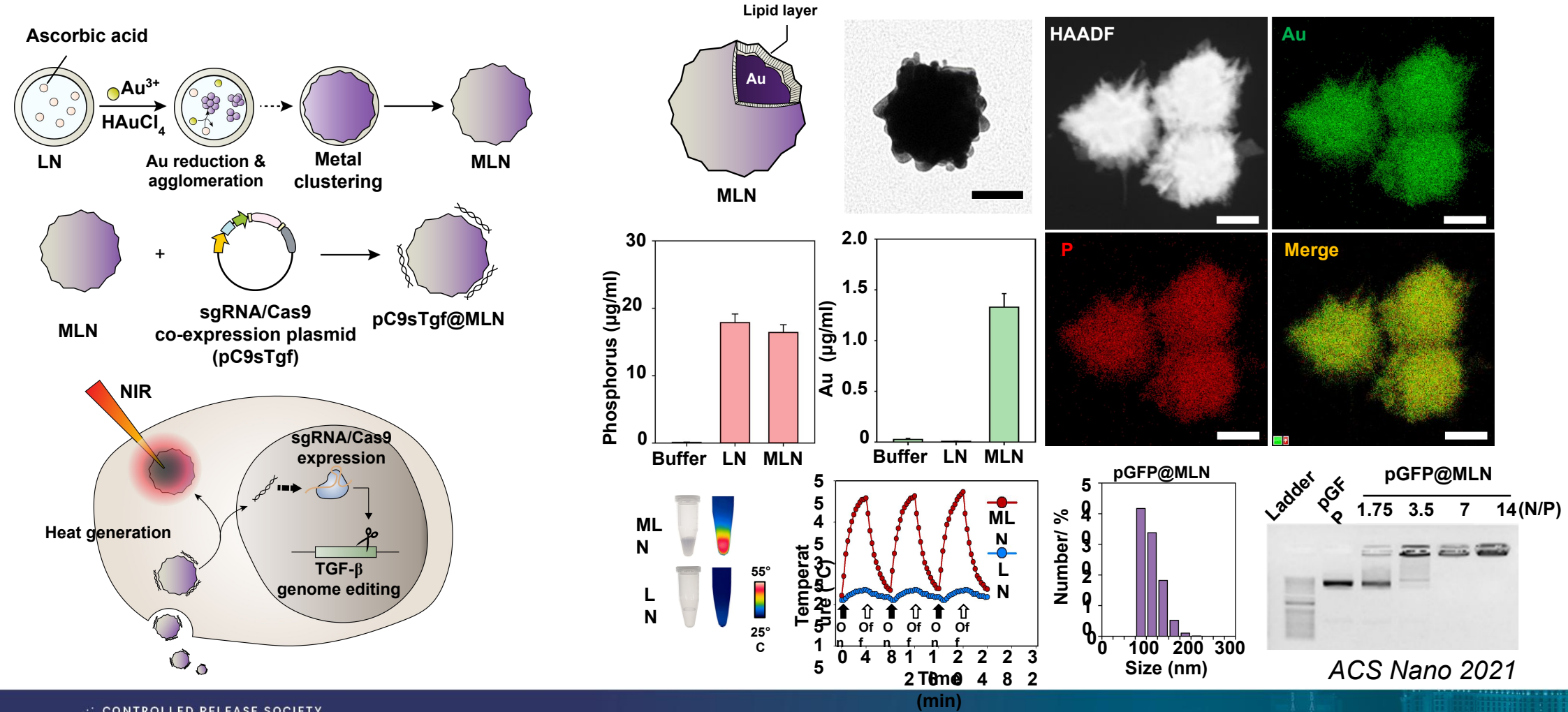
Nat Rev Clin Oncol (2021)

Hypothesis: Turn-off TGF- β to turn cold tumors Hot



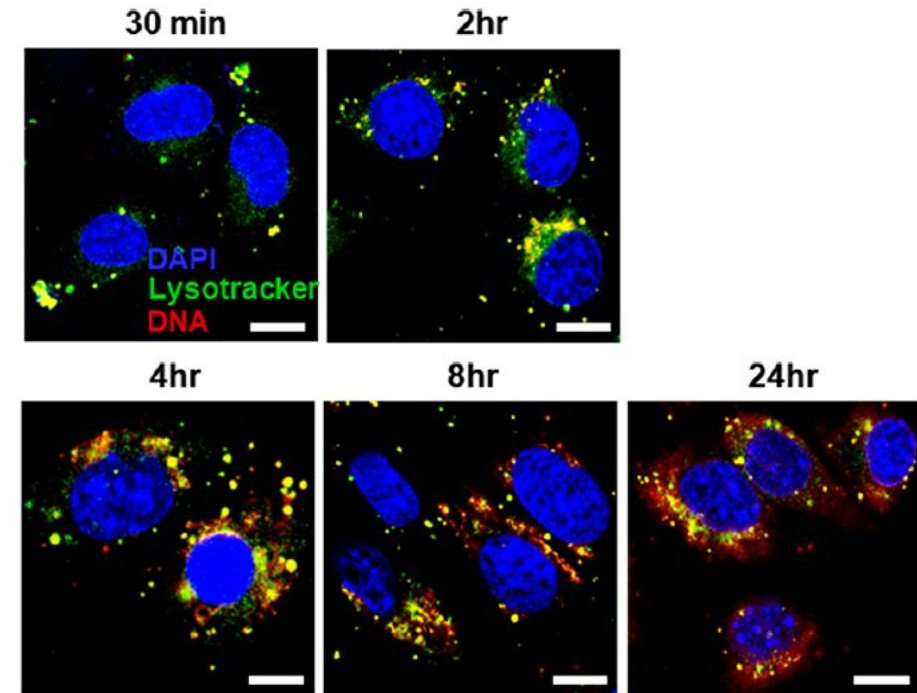
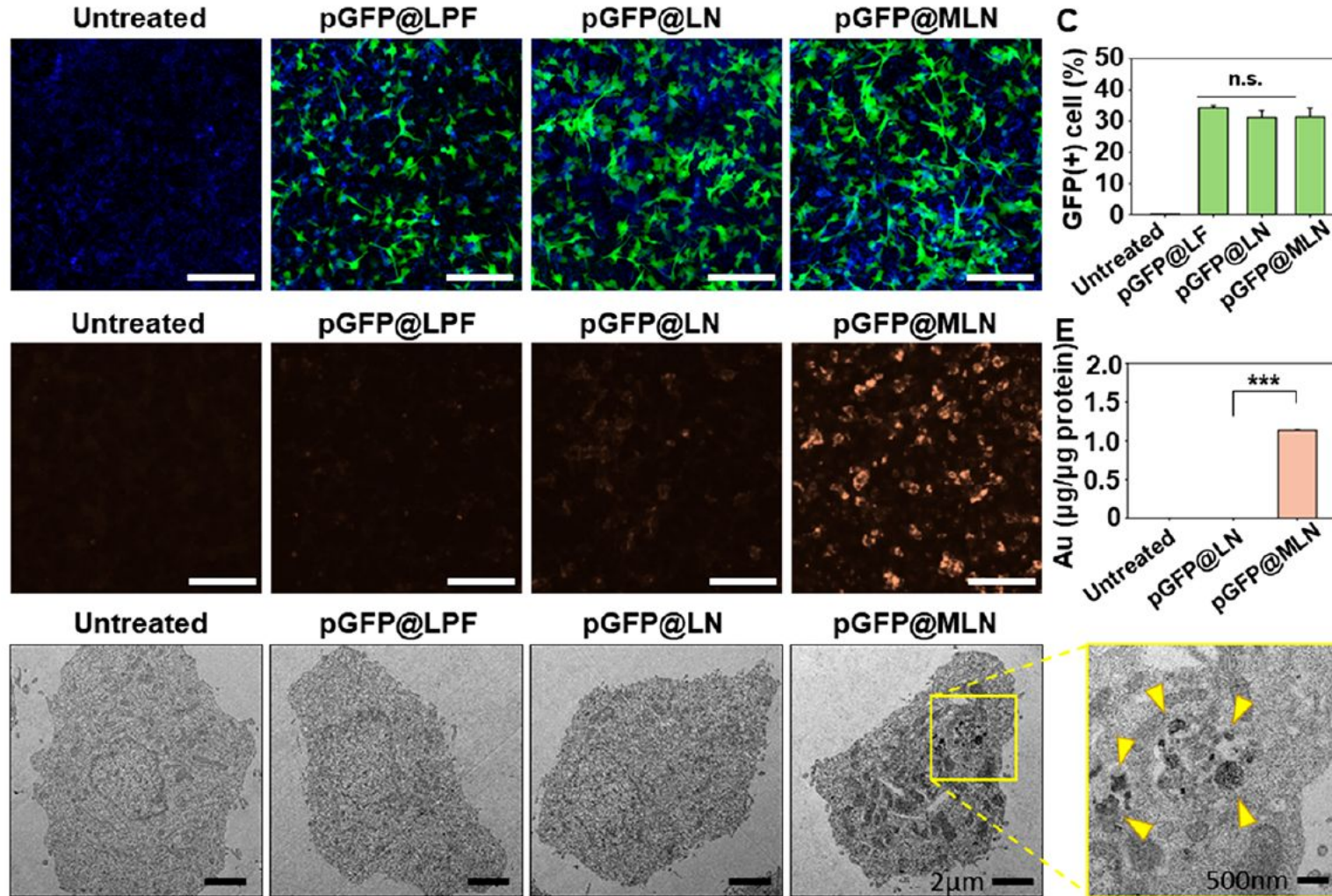
ACS Nano 2021

Metal-lipid hybrid nanoparticles for gene editing delivery and phototherapy



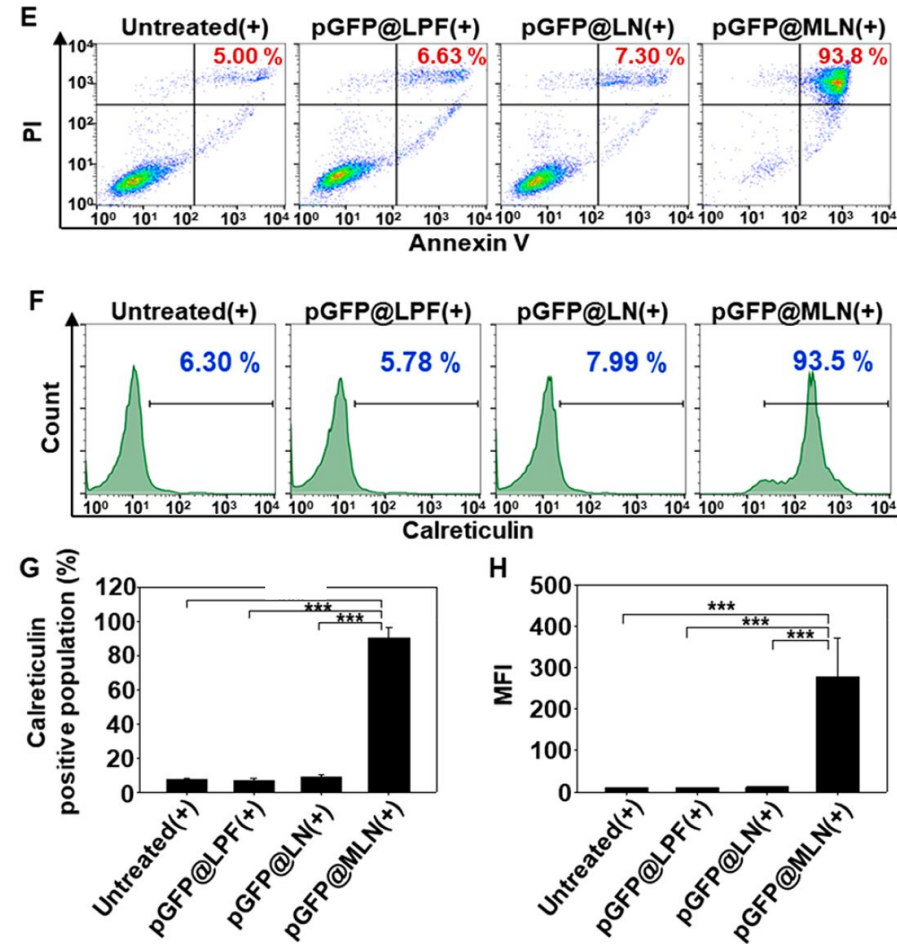
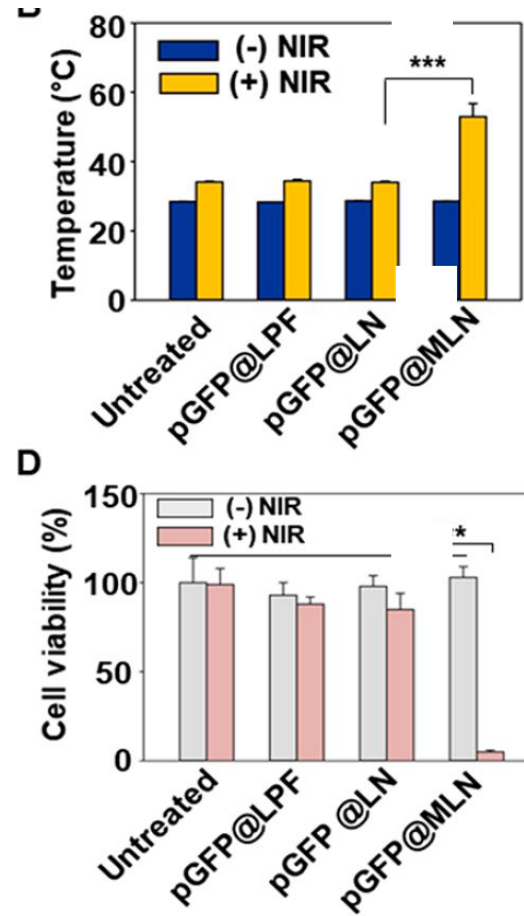
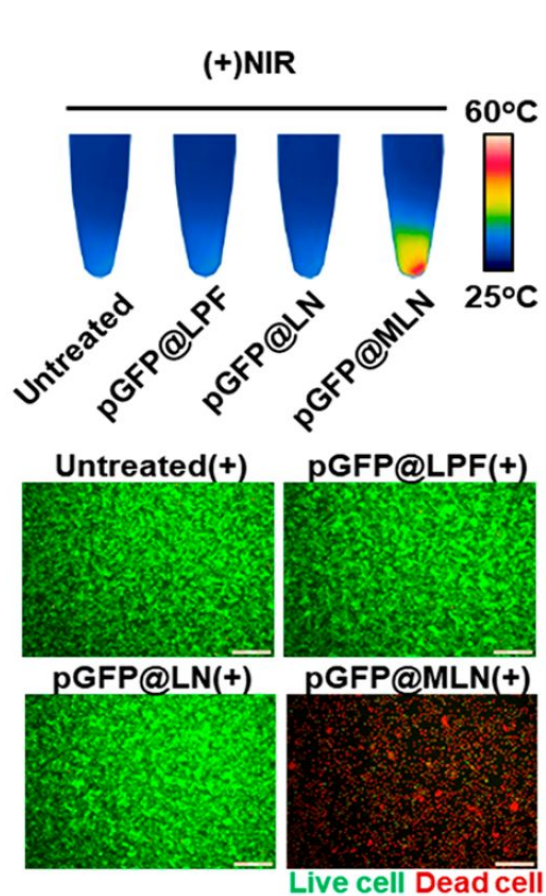
ACS Nano 2021

How to turn Cold tumors Hot?



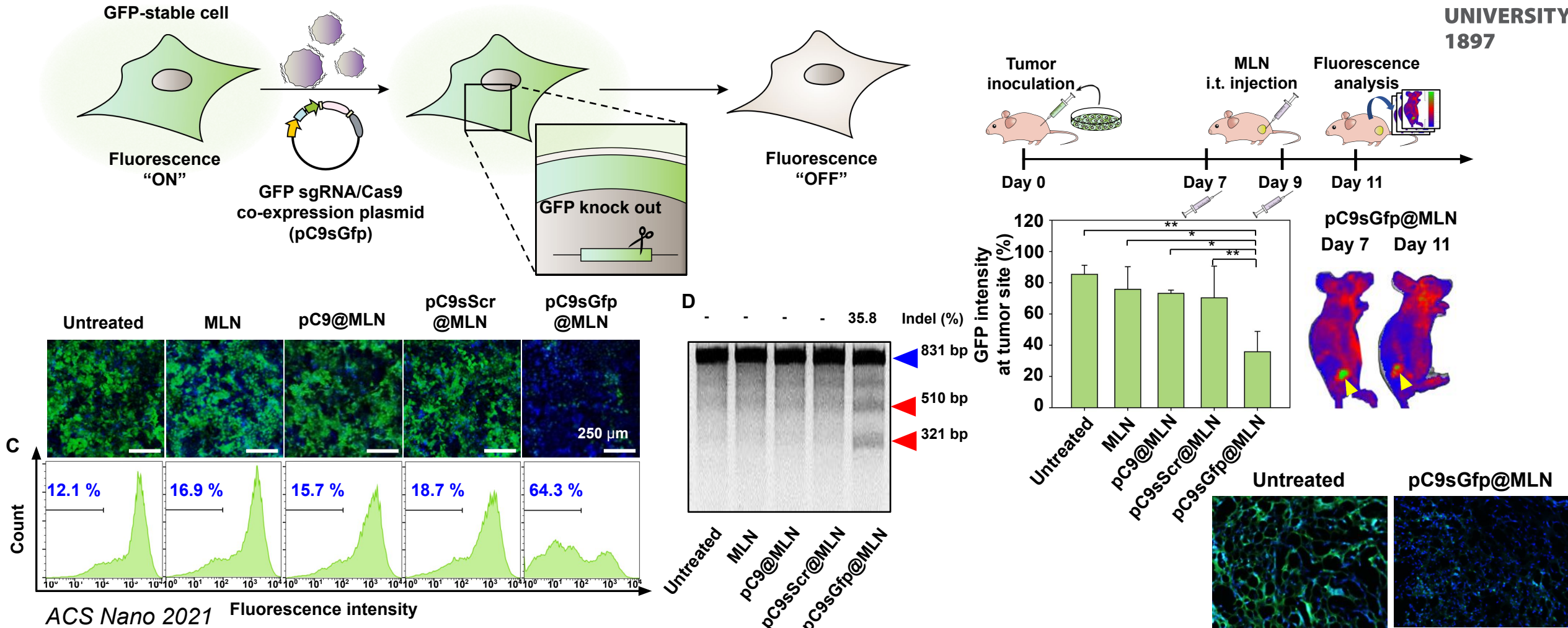
ACS Nano 2021

Phototherapy-mediated immunogenic cell death

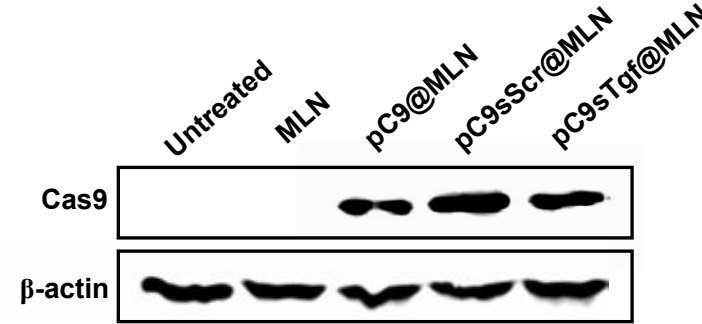
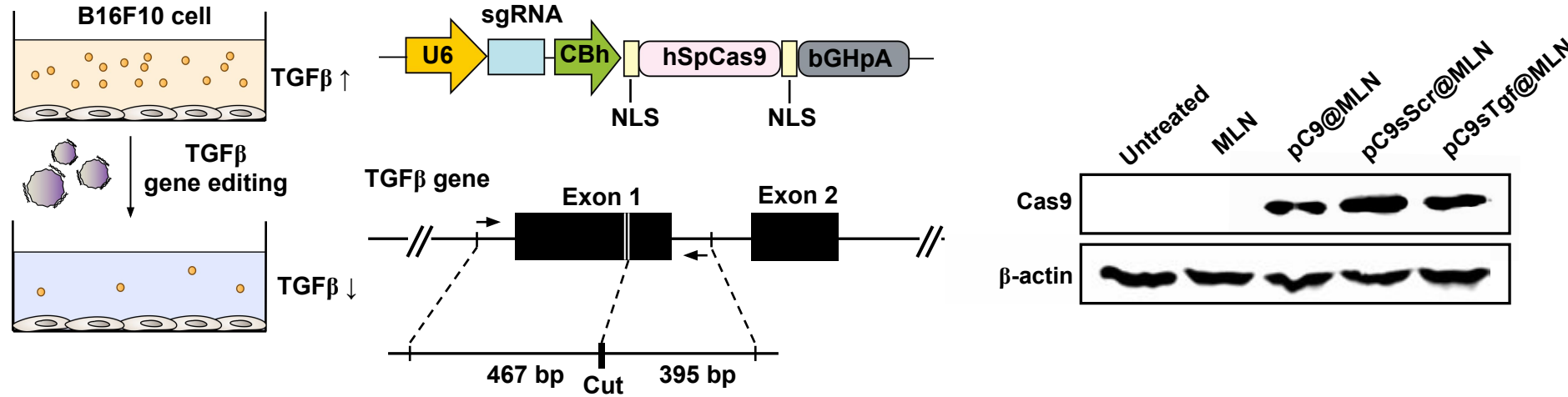


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Nanoparticles-mediated gene editing in tumor cells



Nanoparticles-mediated TGF- β editing in tumor cells



Target PAM

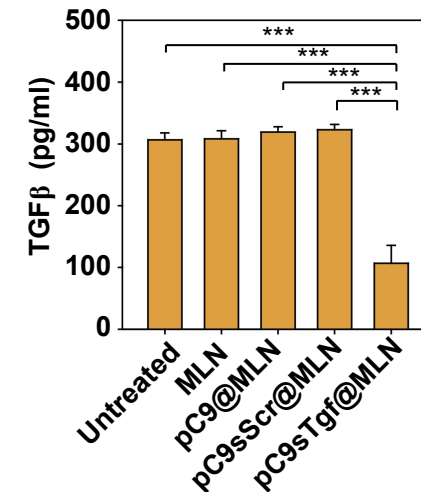
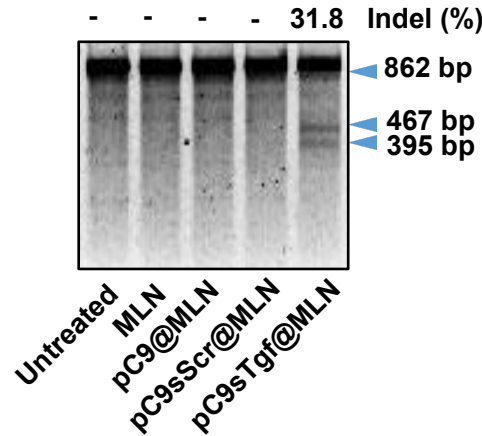
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#1 TCGCTTTGTACAACAGCACCCGC-ACC**GGG**TGGCAGGCCGA

#2 TCGCTTTGTACAACAGCACCC-**A**GACC**GGG**TGGCAGGCCGA

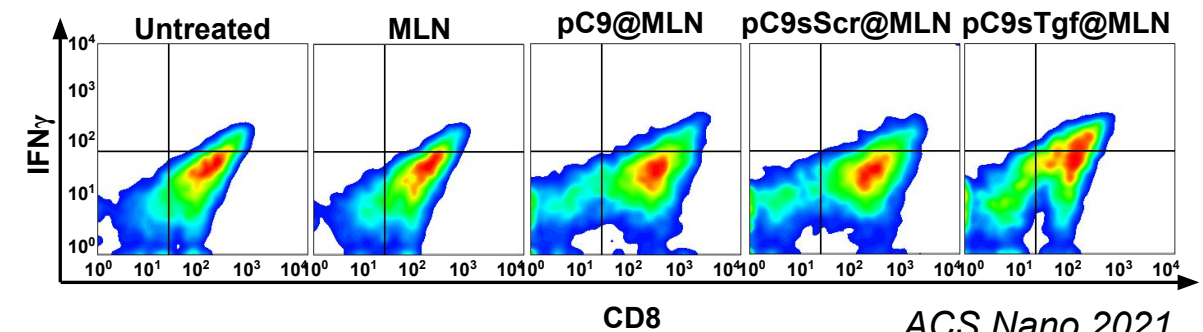
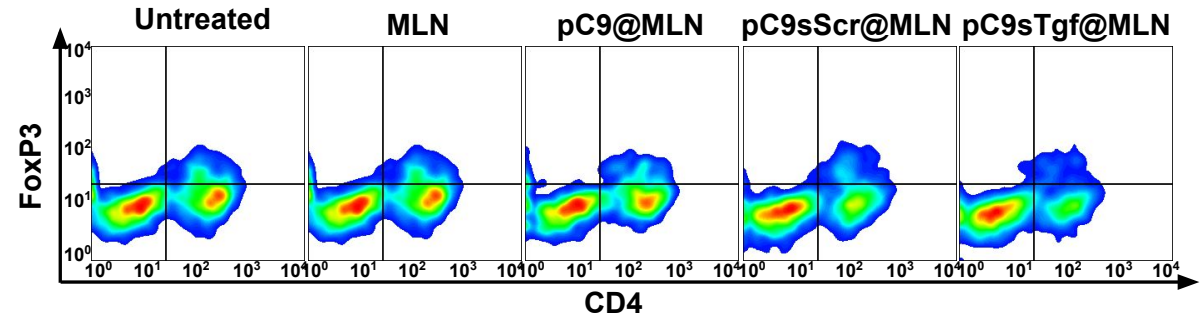
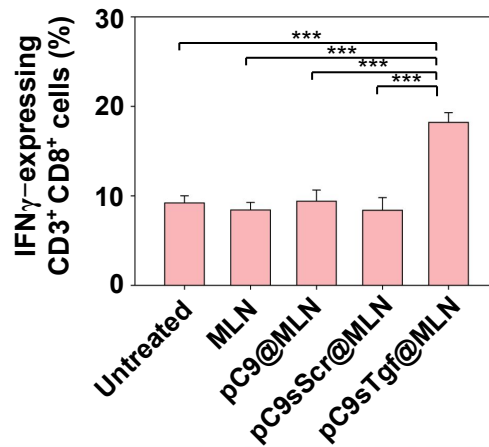
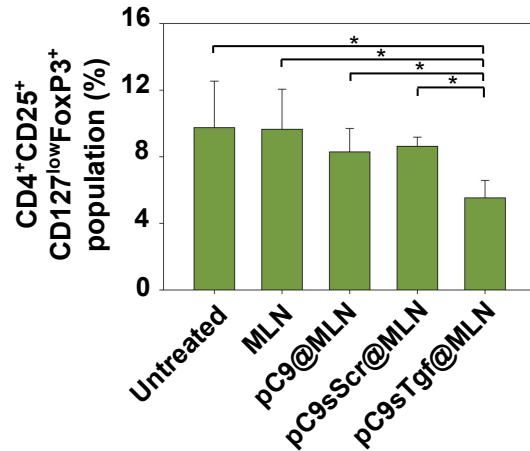
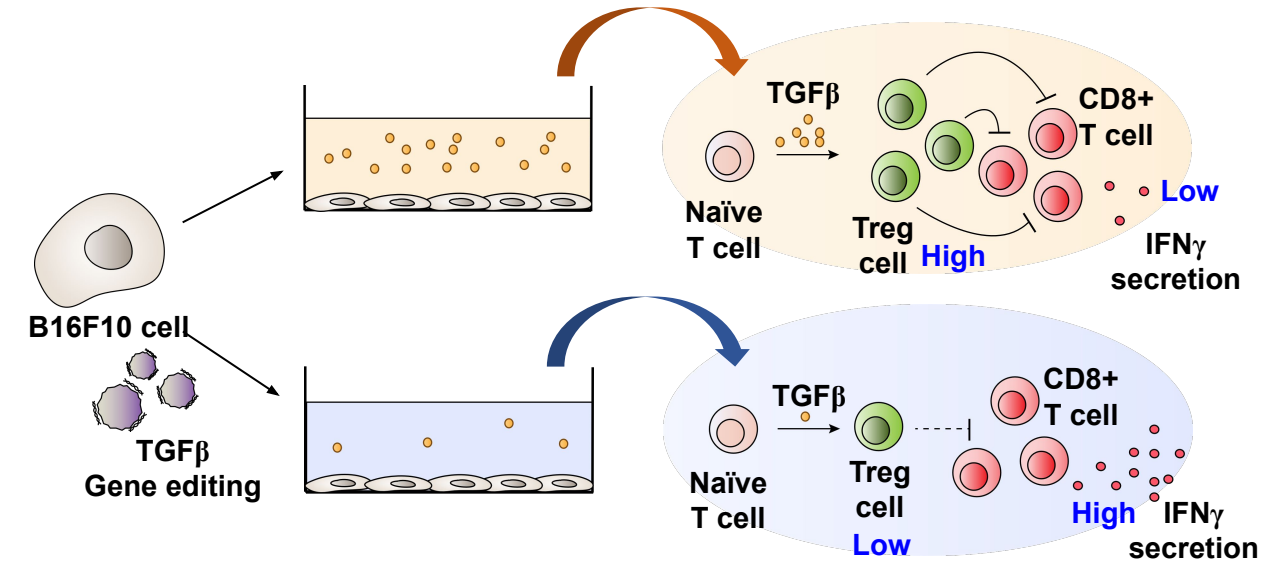
#3 -----ACC**GGG**TGGCAGGCCGA

#4 TCGCTTTGTACAACAGCACCCGC-----



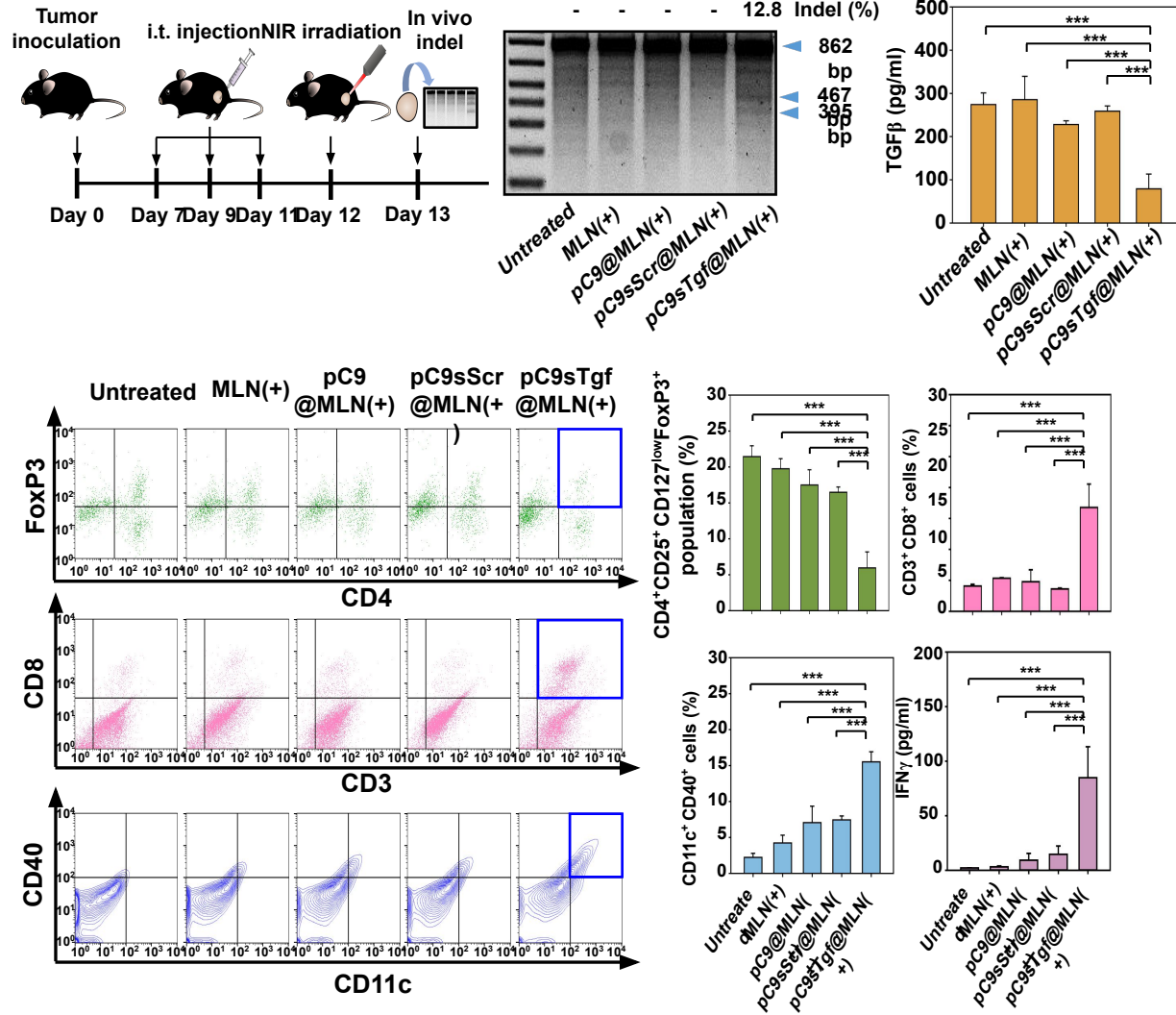
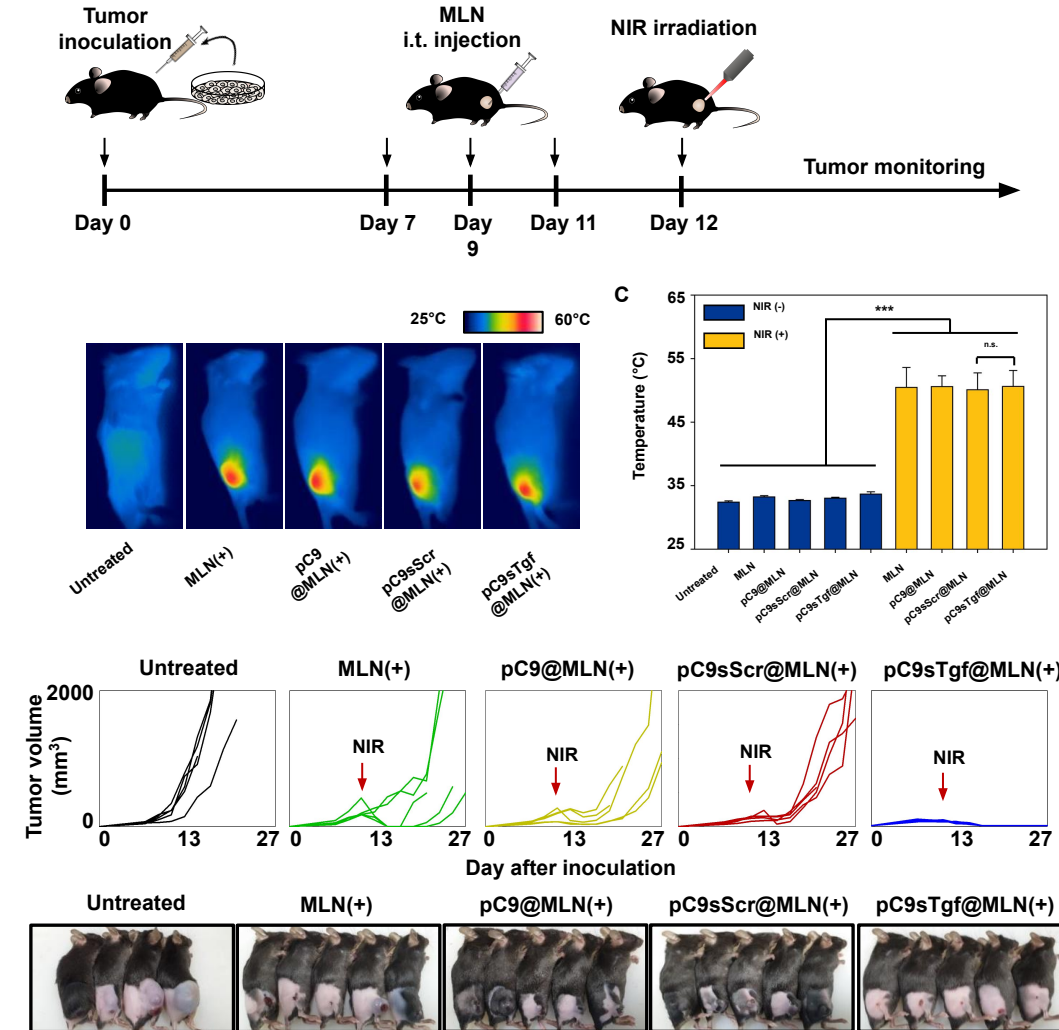
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T cell differentiation after TGF- β editing in tumor cells

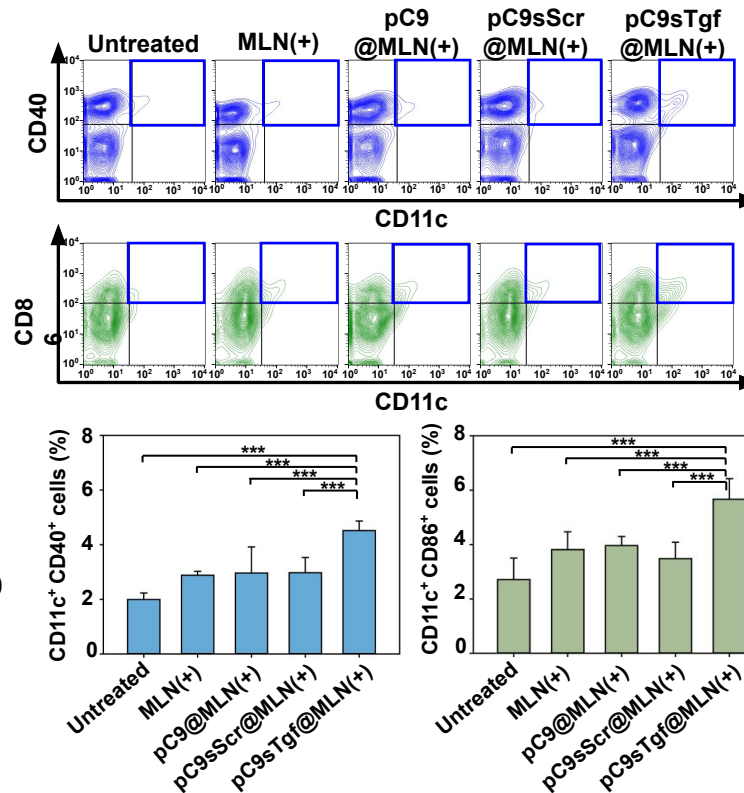
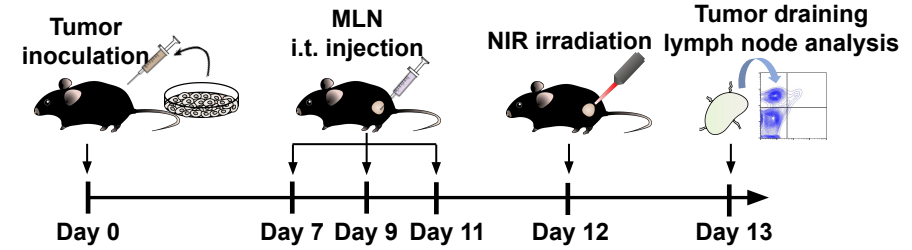
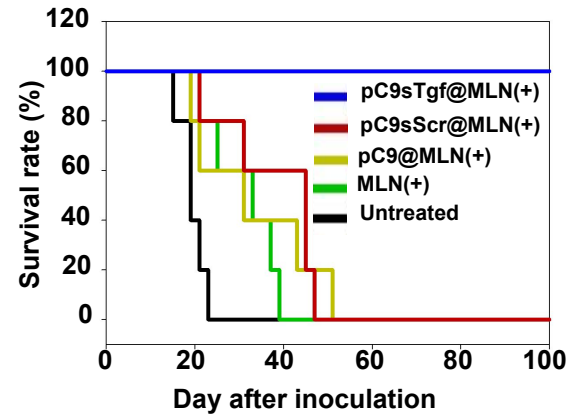
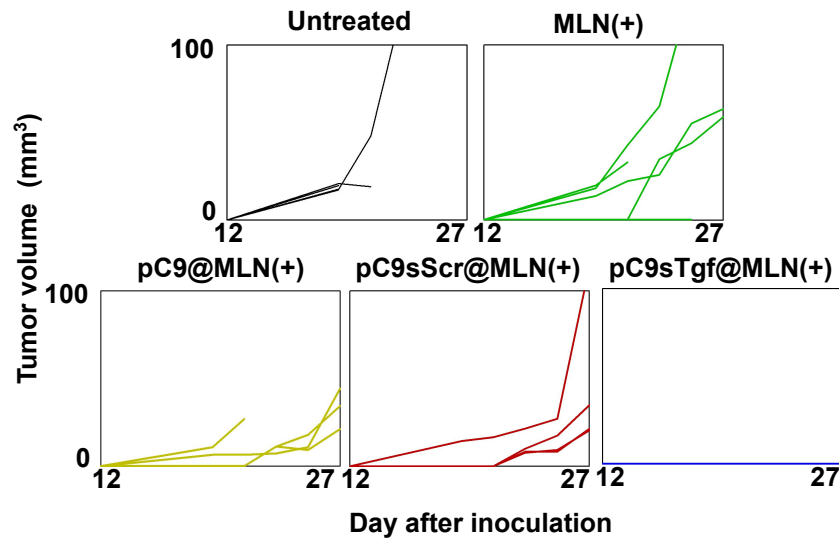
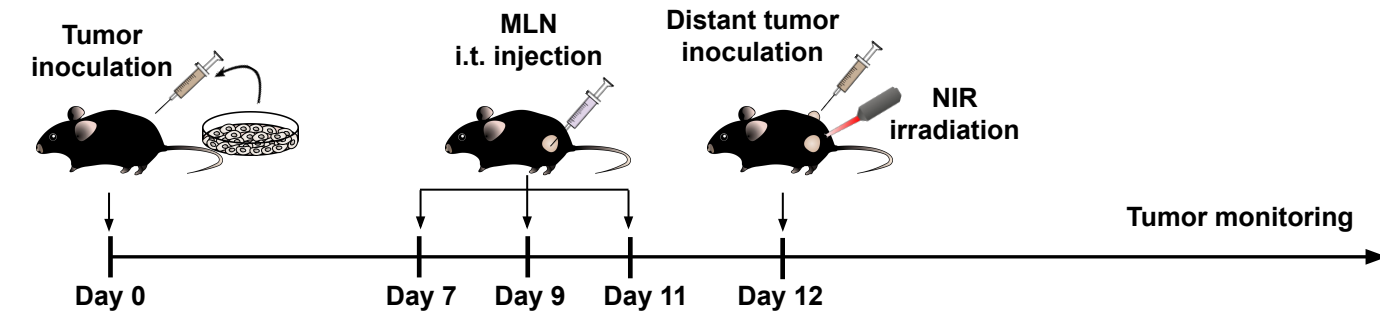


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Antitumor efficacy in TGF- β edited tumor

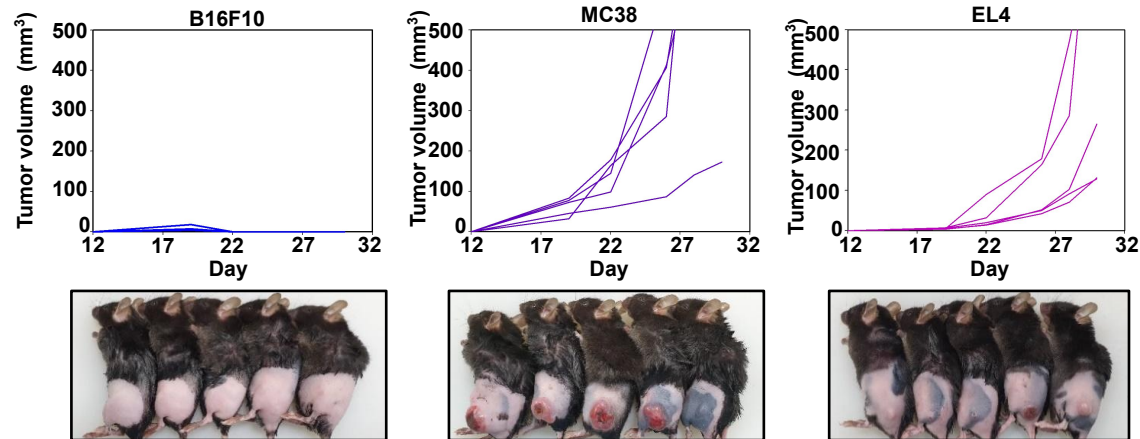
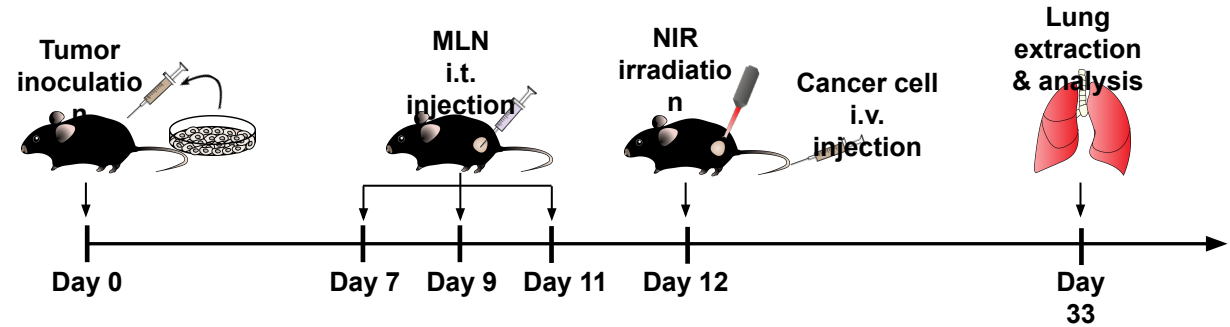
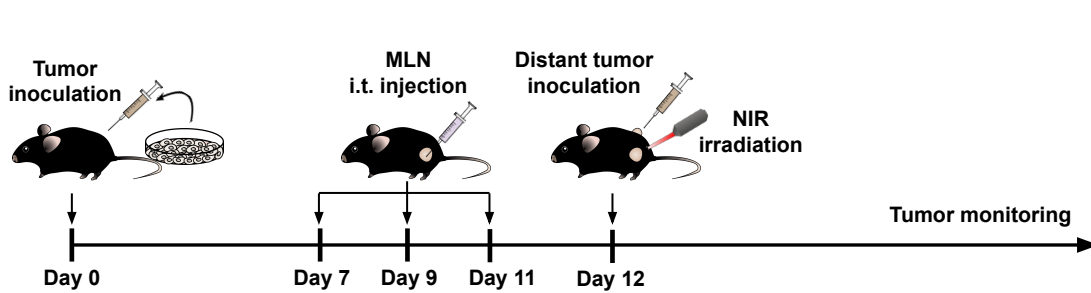


Adaptive antitumor immunity after TGF- β editing

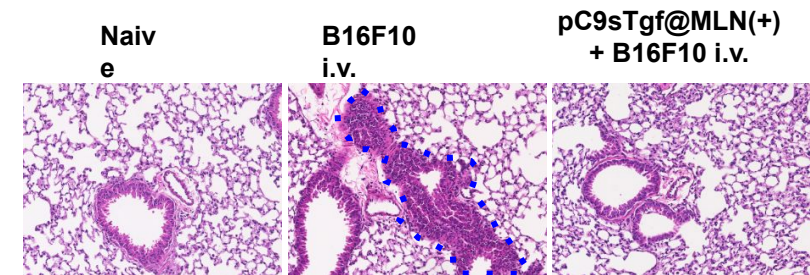
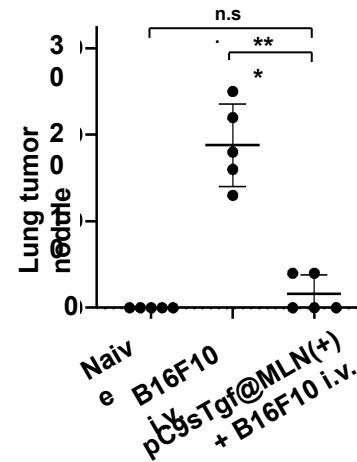


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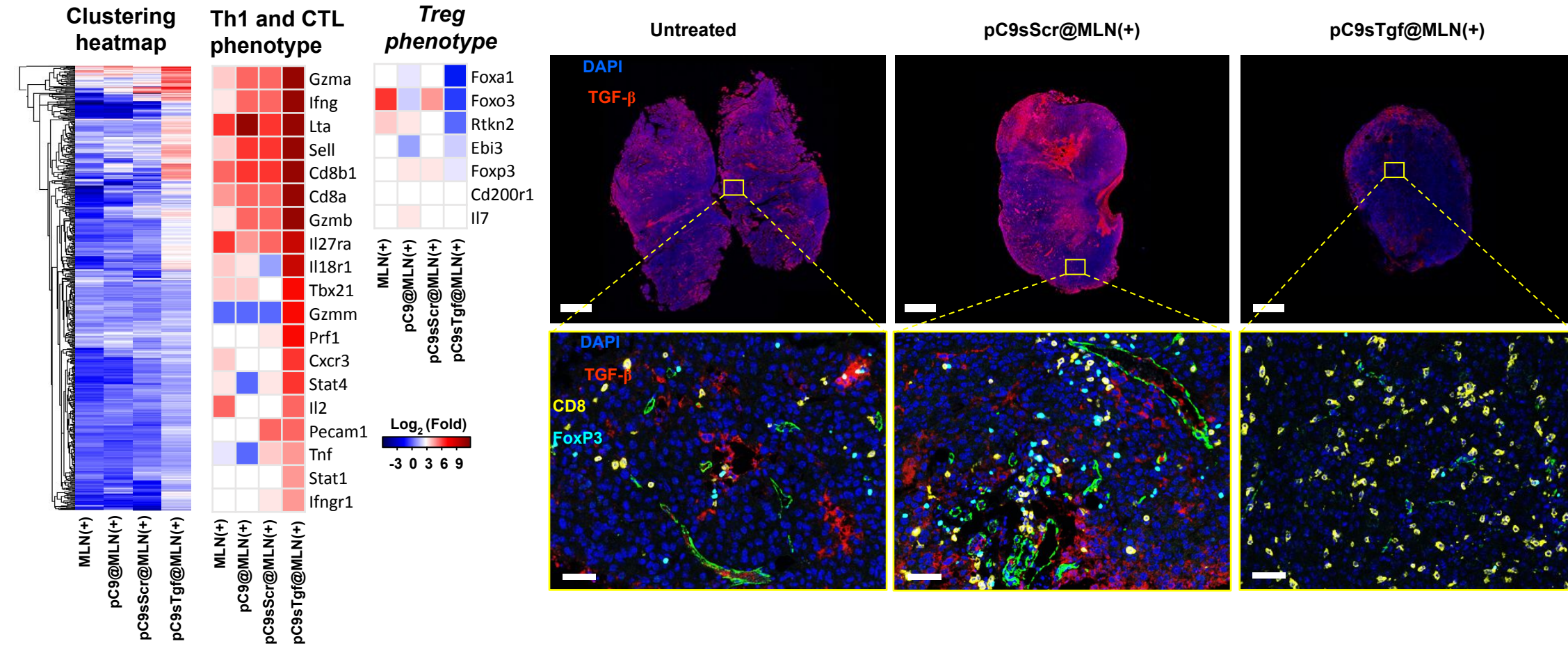
How to turn Cold tumors Hot?



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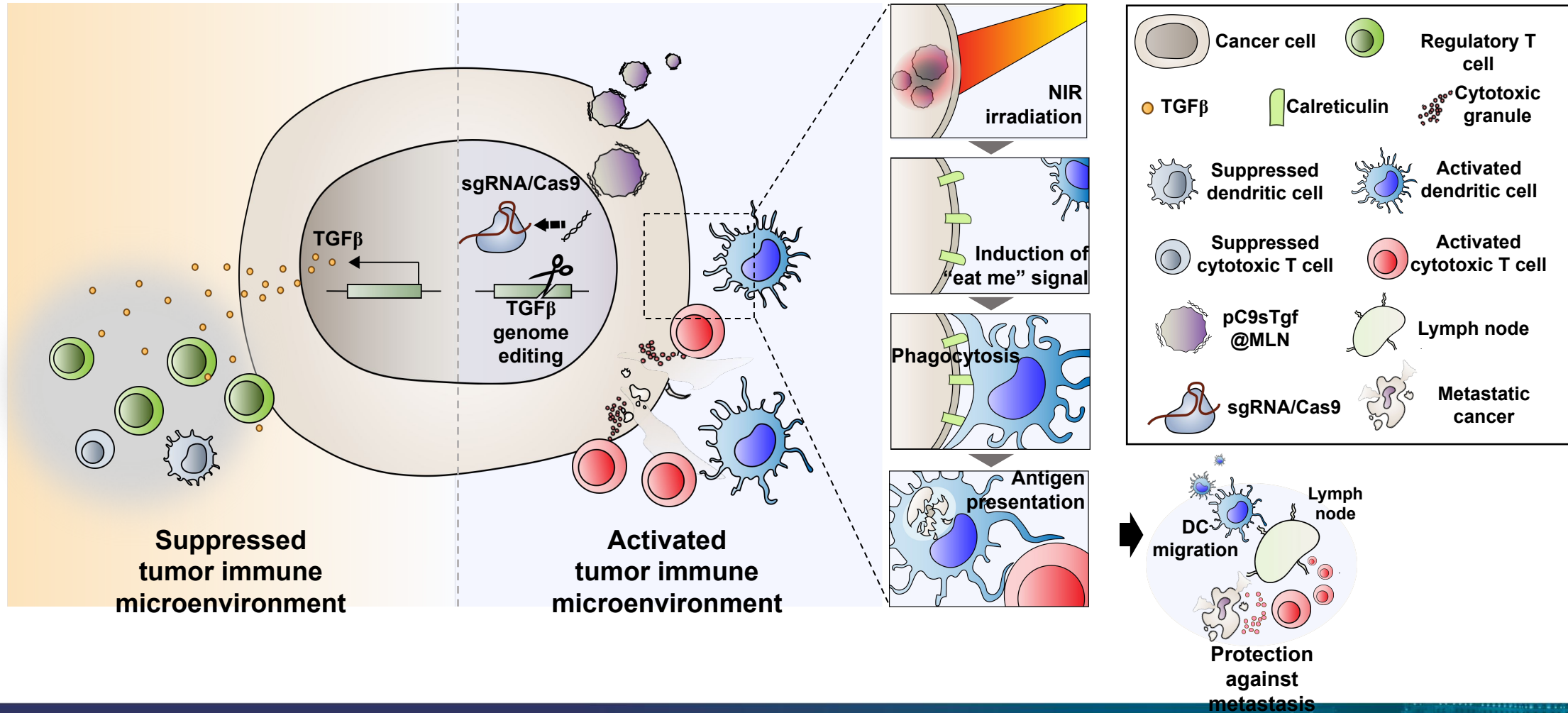


Transcriptome and immunohistochemical analysis



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Enhanced adaptive antitumor immunity in TGF- β -edited tumor microenvironment



Metabolic pathway of gold nanoparticles

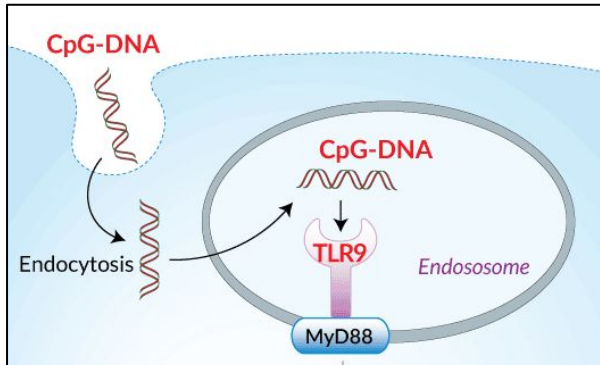
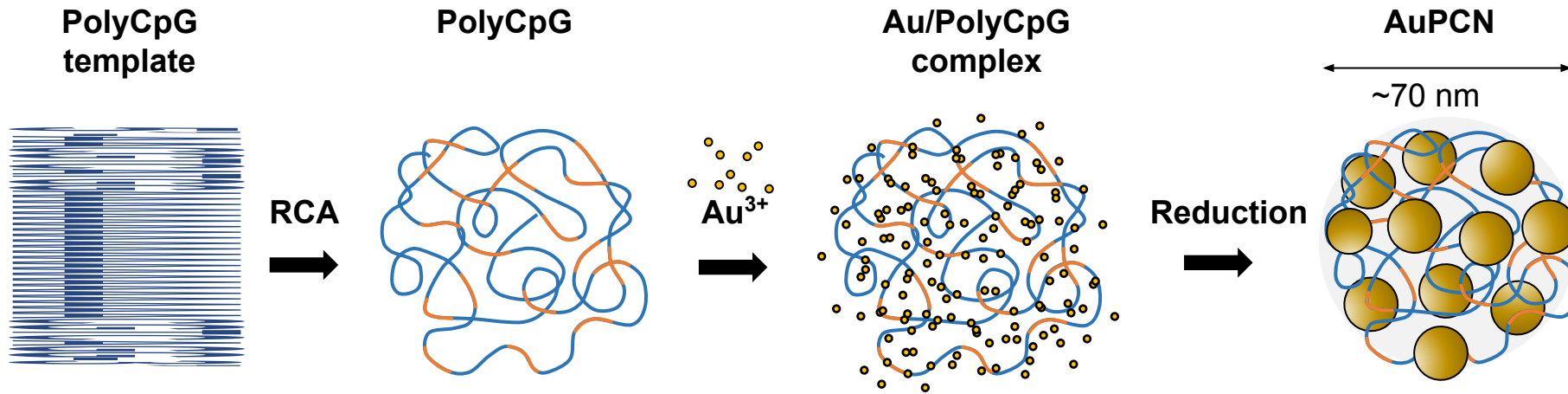


Advanced Materials (2019)

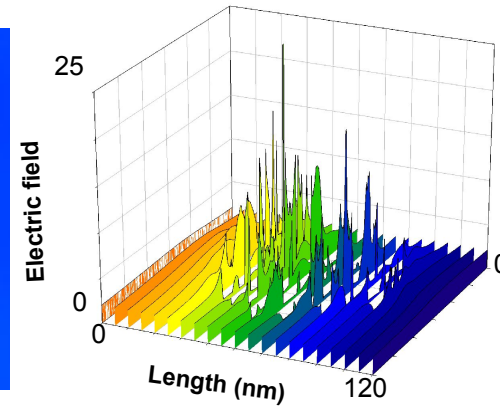
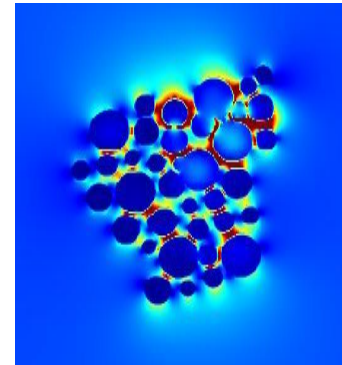
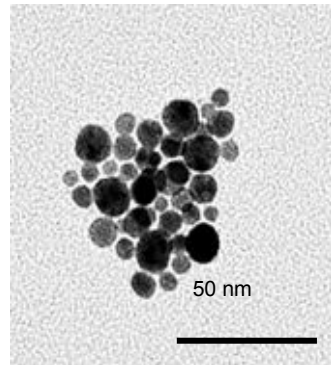
Retention of gold nanoparticles

- Oxidative stress
- Inflammation
- Tissue damage

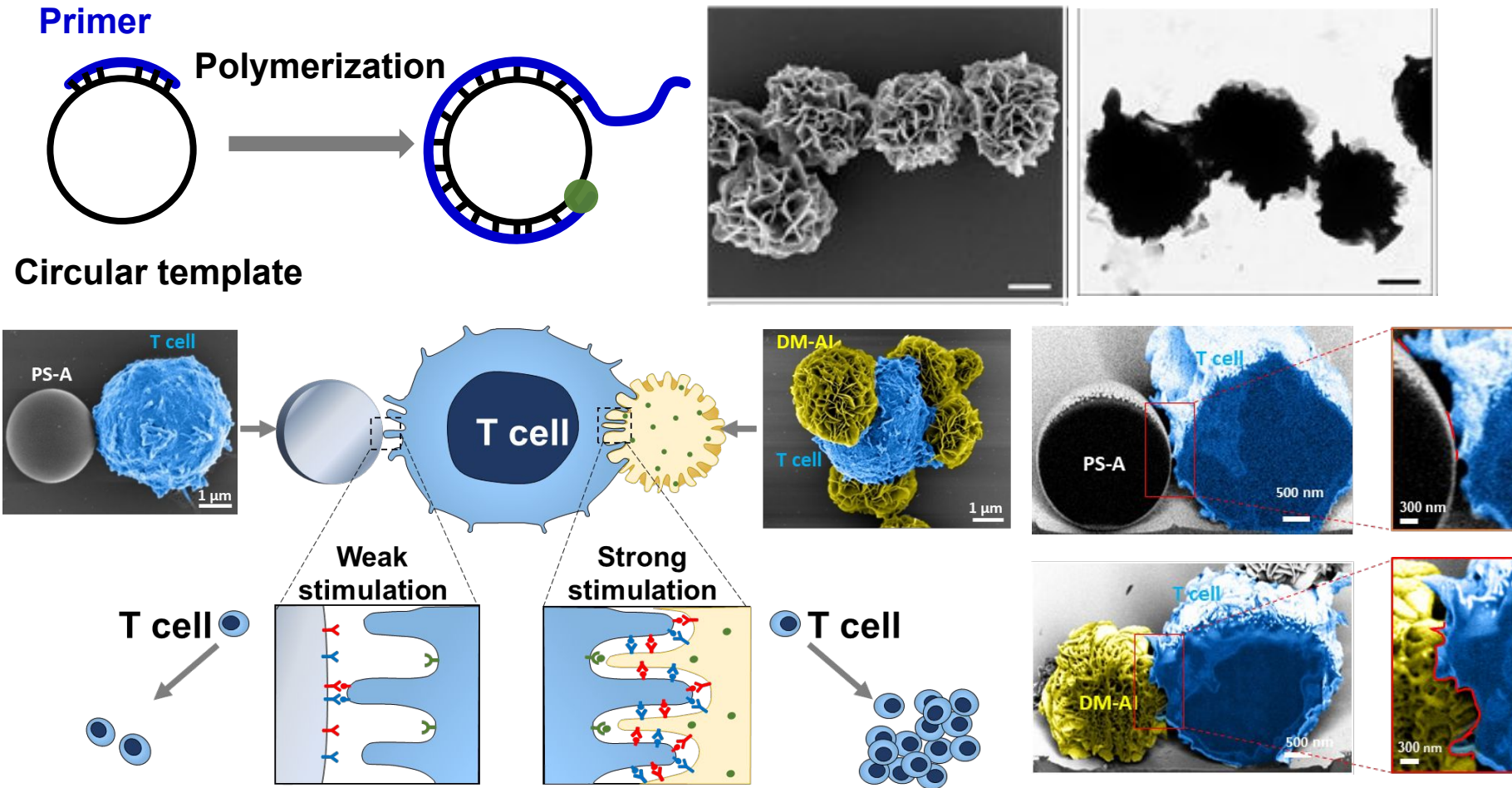
PolyCpG-supported gold nanocluster



Biomaterials 2022

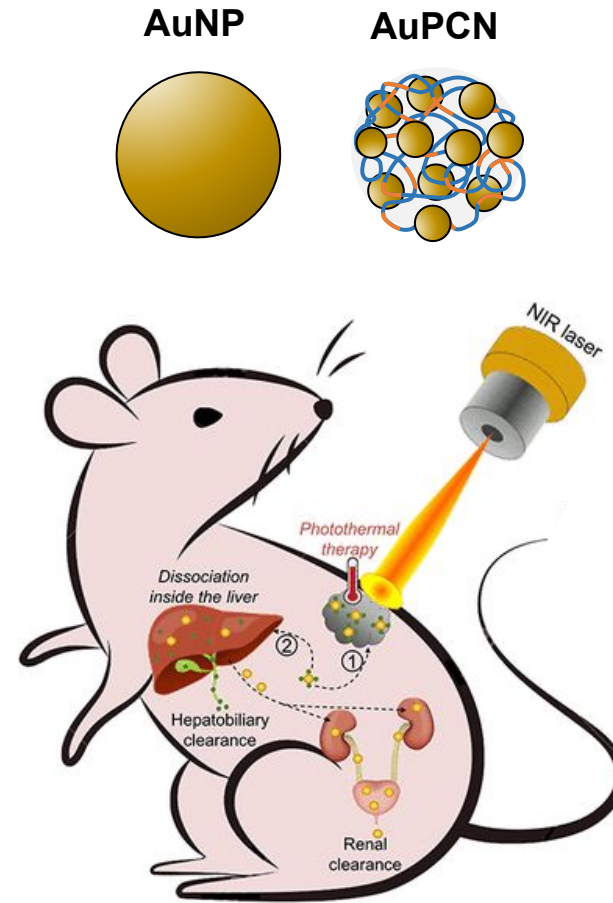
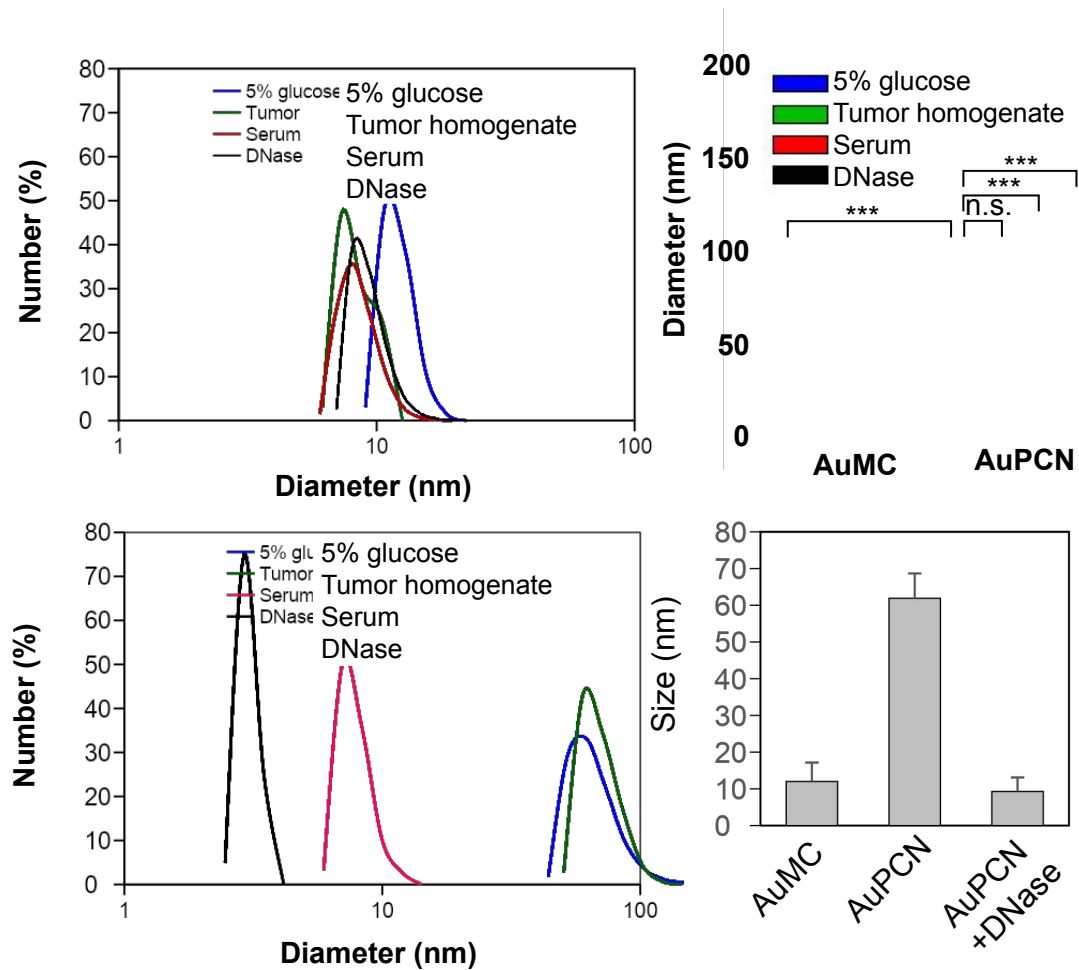


Enzymatic process generating long ssDNA from circular template



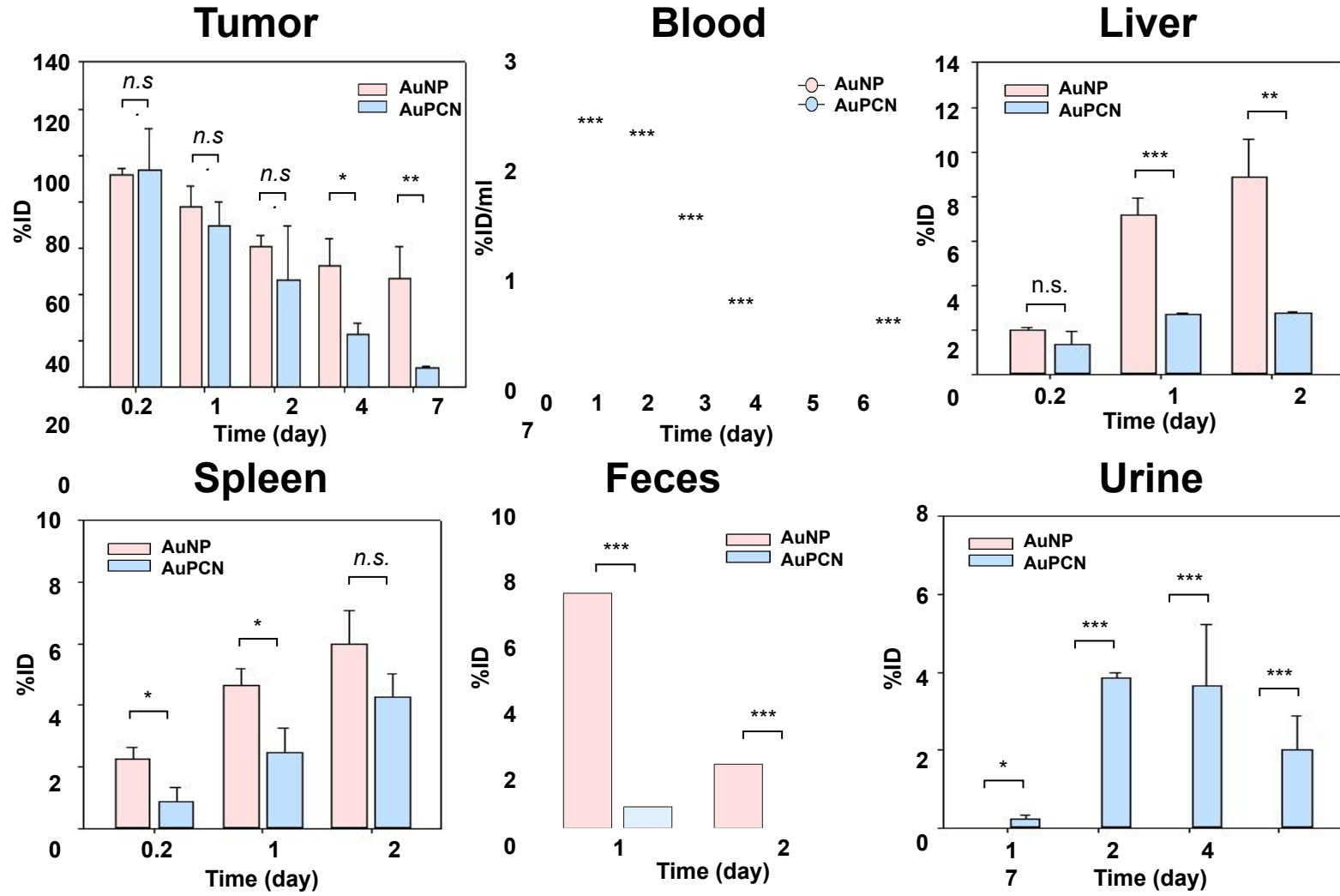
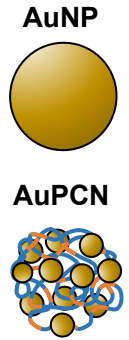
Bioactive Mater 2022

Nuclease-declustering gold nanoparticles

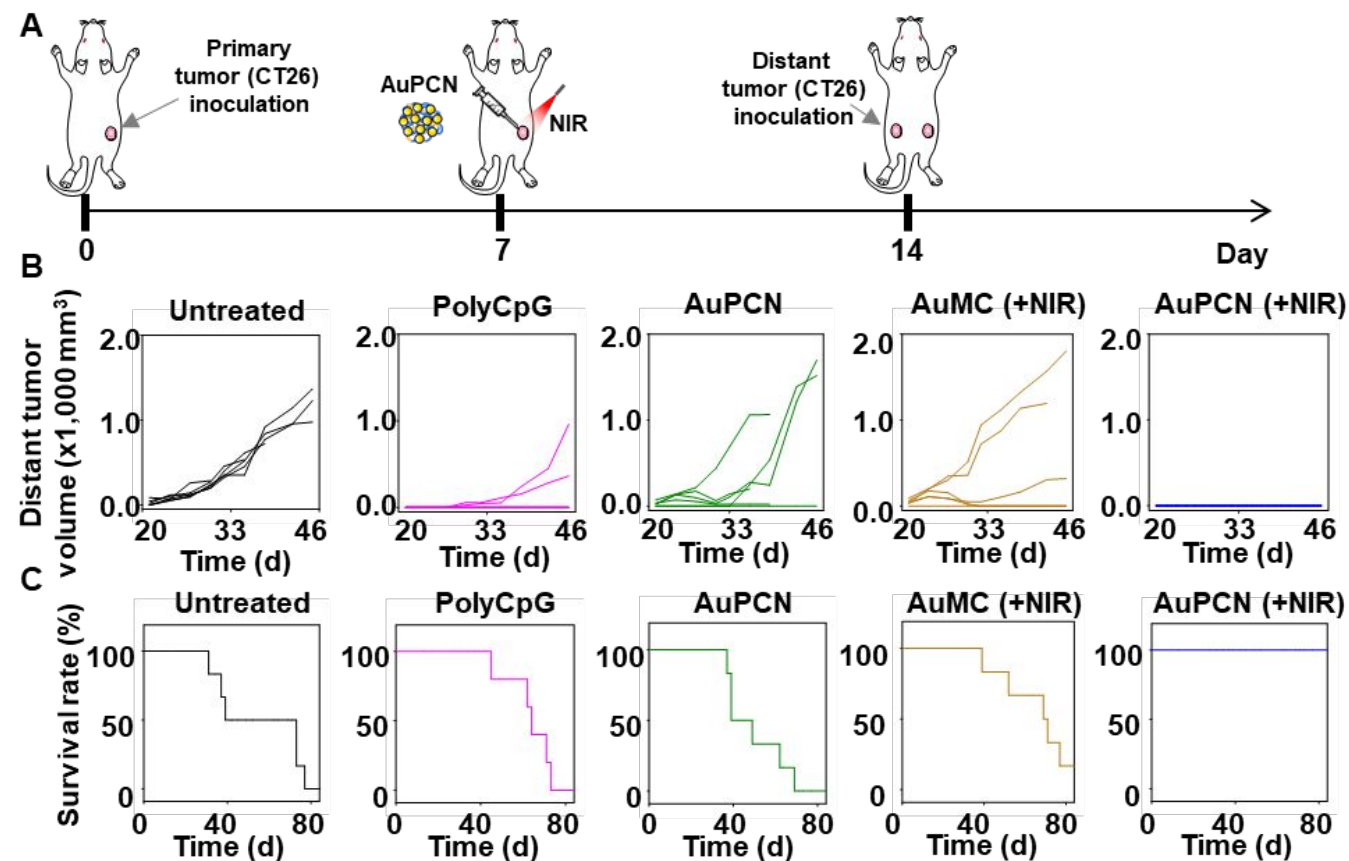
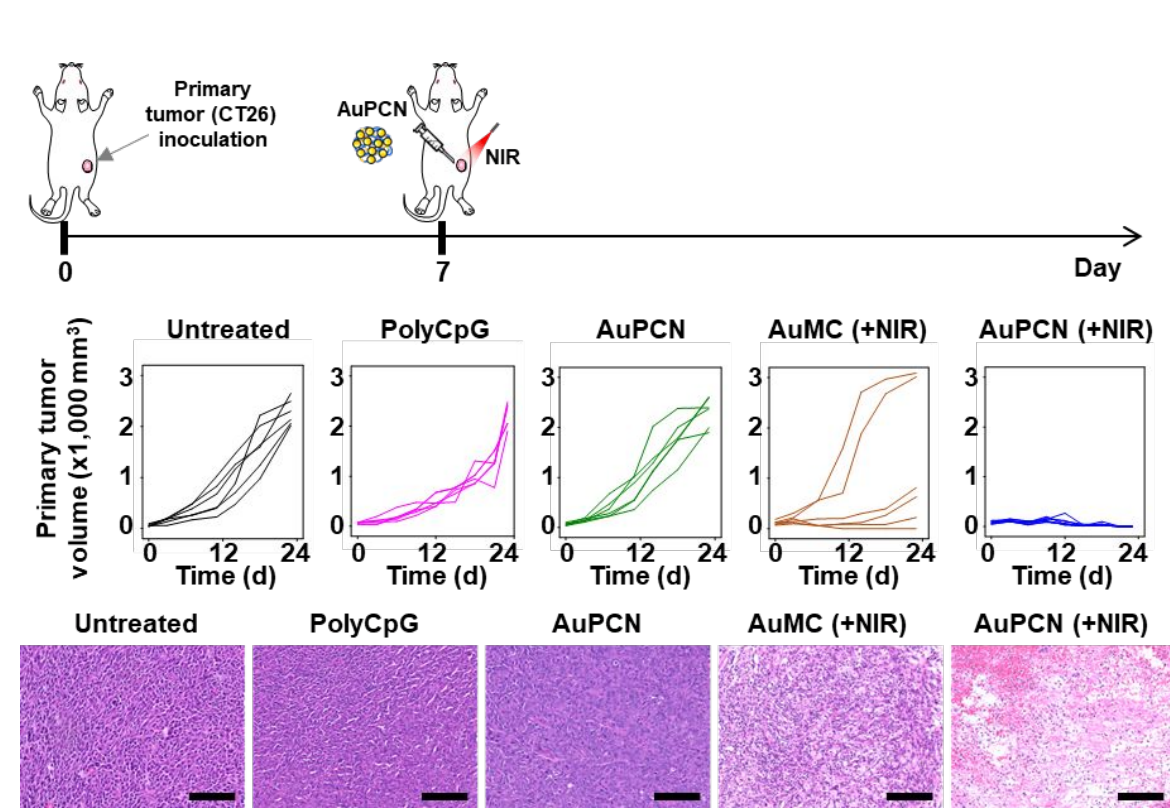


Biomaterials 2022

In vivo fates, pharmacokinetic, and excretion



Antitumor effects against rechallenged tumors

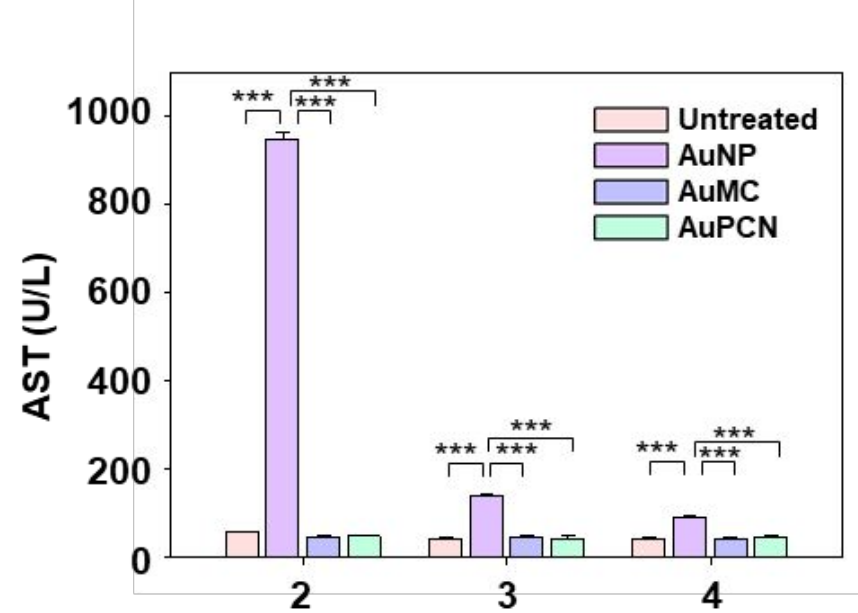
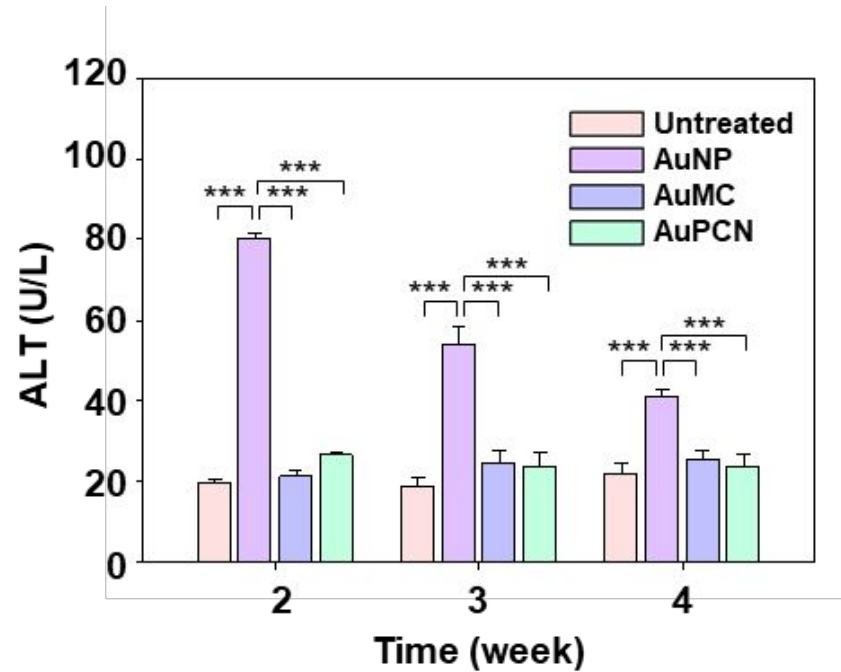
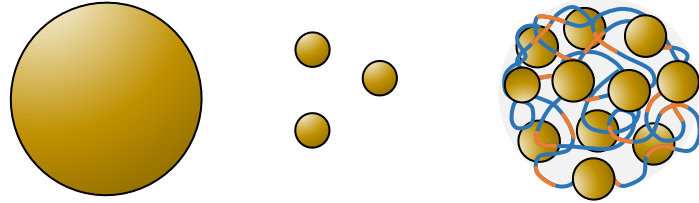


In vivo evaluation of safety

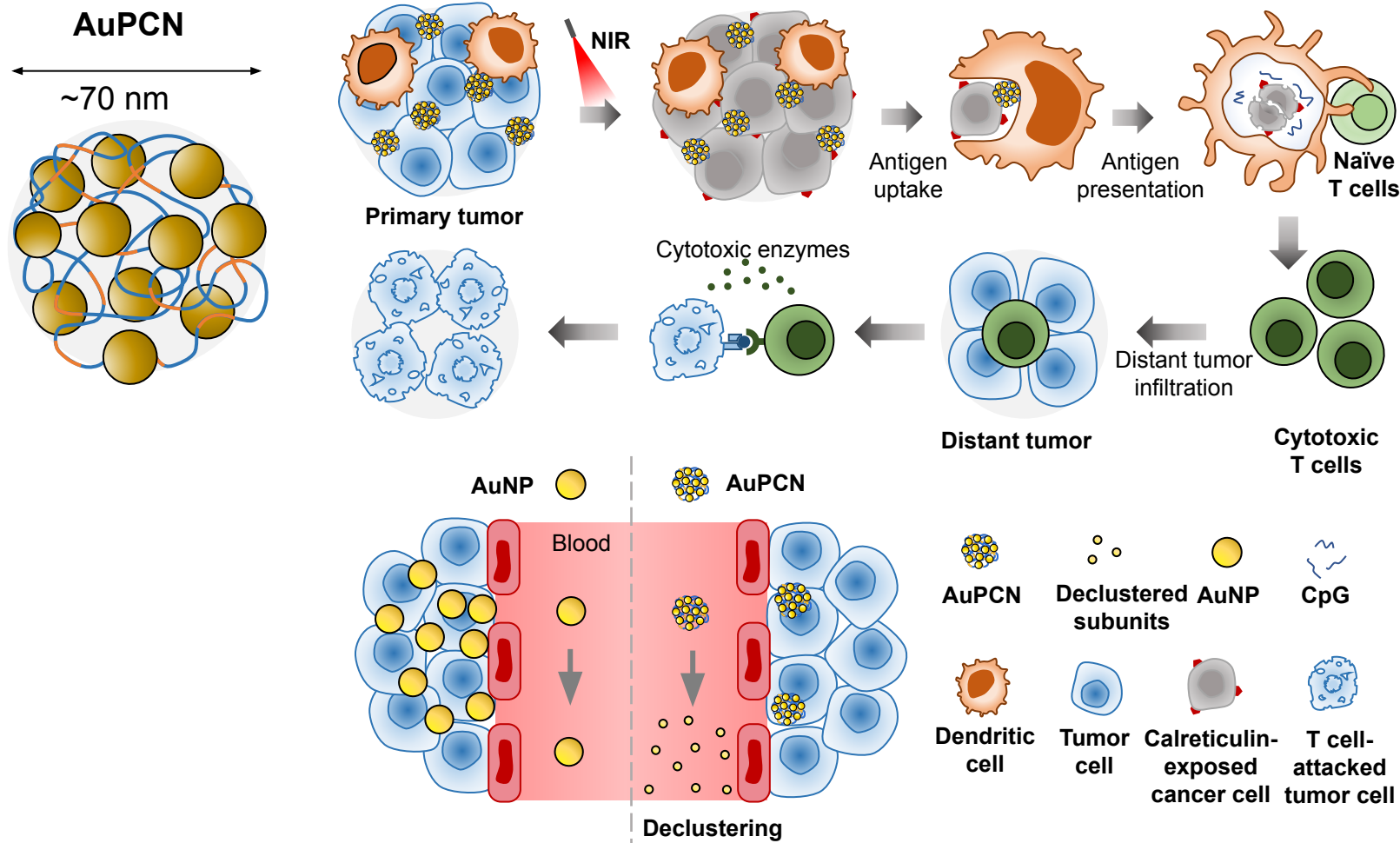
AuNP

AuMC

AuPCN



Concatemeric DNA-assisted metal nanoclusters for immunophototherapy



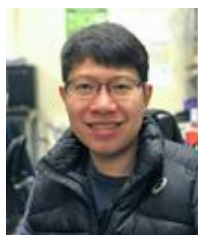
Acknowledgements



Seoul National University
College of Pharmacy



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Faculty of Pharmacy

ACS Nano 2019
Dr. Quoc-Viet Le



Soongsil University
School of
Systems Biomedical Science



ACS Nano 2021

Dr. Dongyoon Kim
Yina wu



Bioactive Mater 2022
Biomaterials 2022

Dr. Jaiwoo Lee
Dr. Junho Byun



Sungtaek Kang
Jeong Gil Sun
Jaeseong Lee
Hyeseon Park
Ji Young Min
Jeong Min Lee



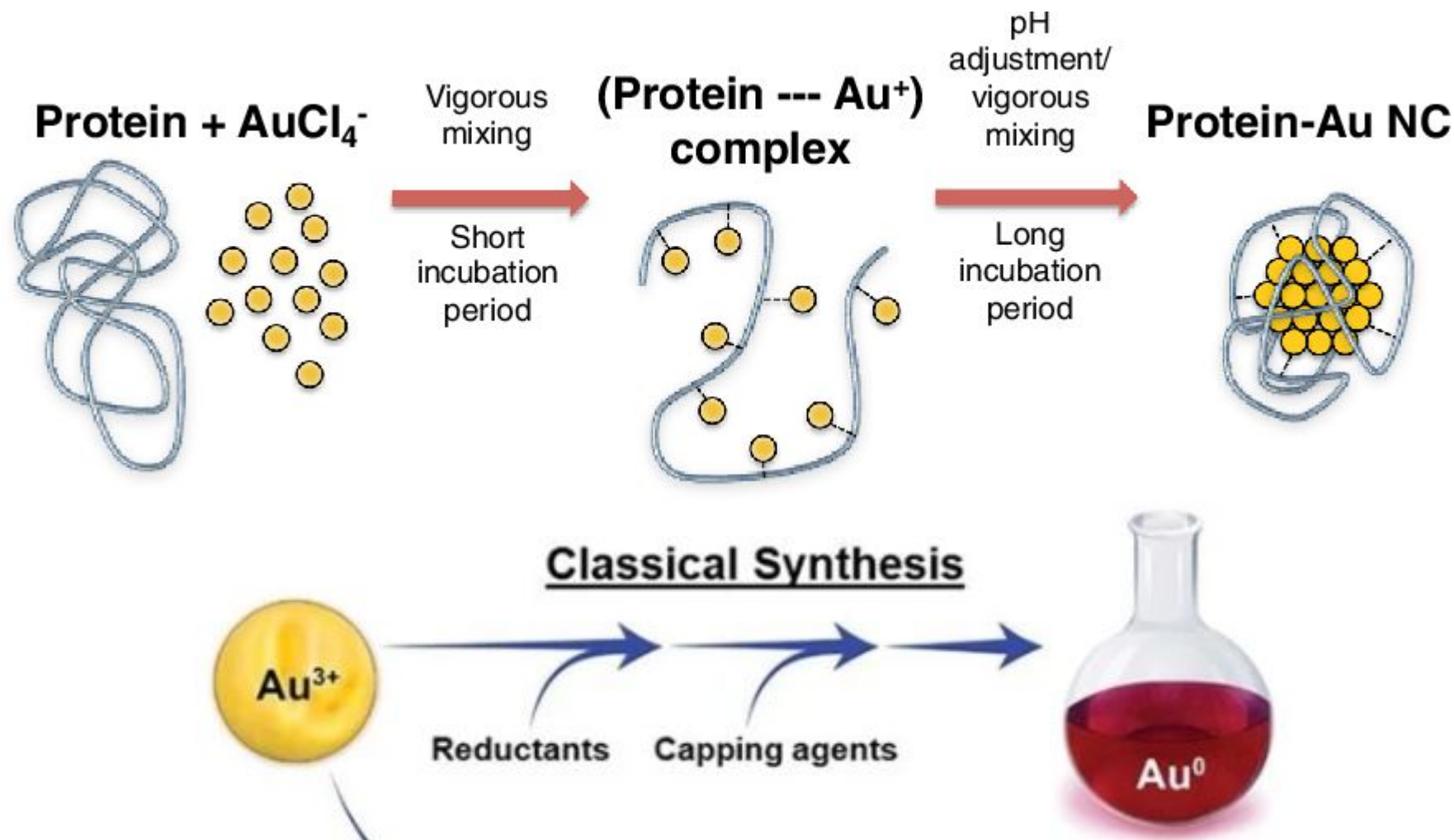
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JULY 24-28, 2023 **Paris Hotel » Las Vegas, NV, USA**

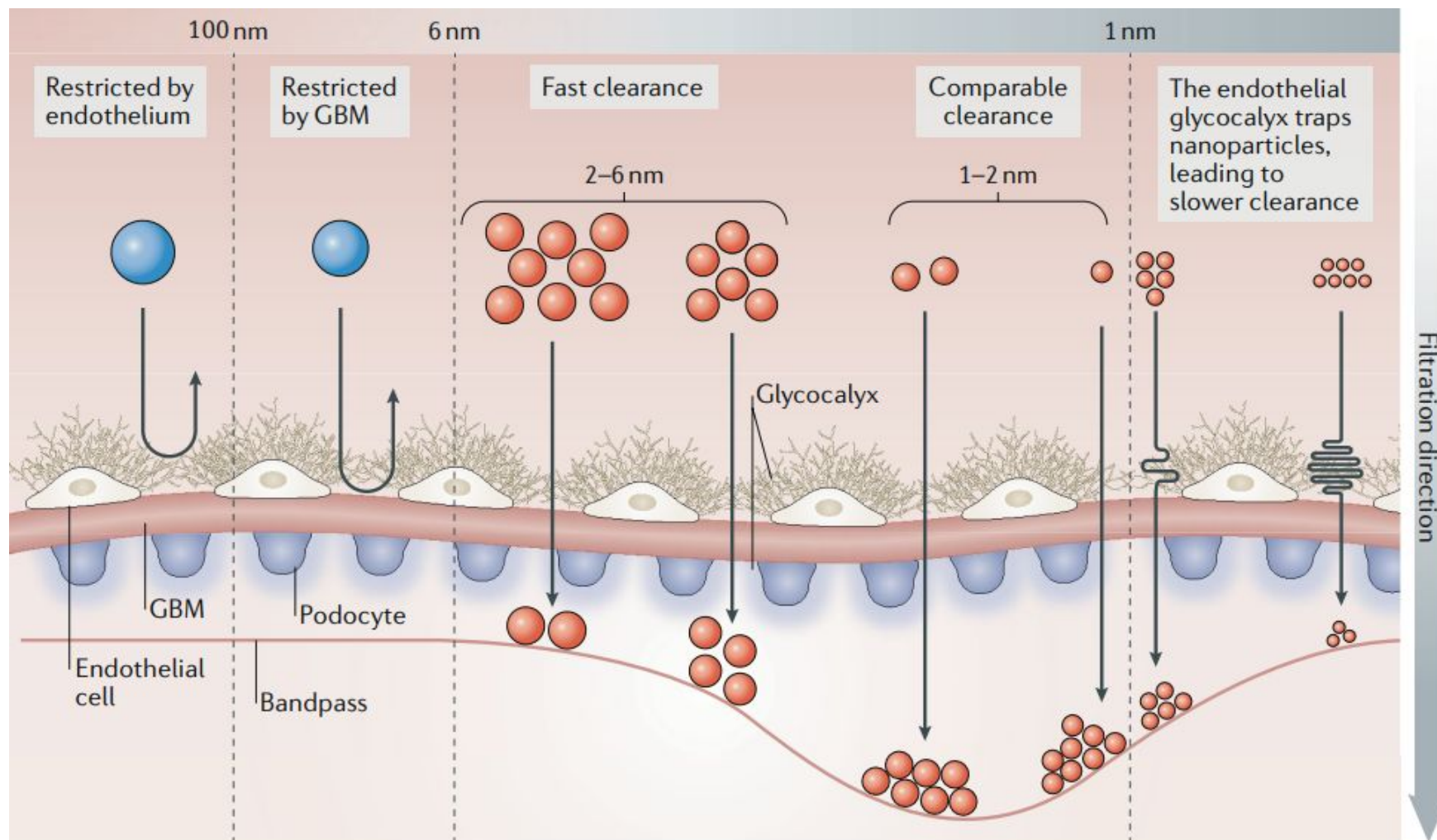
THE FUTURE OF DELIVERY SCIENCE

Supplementary Information

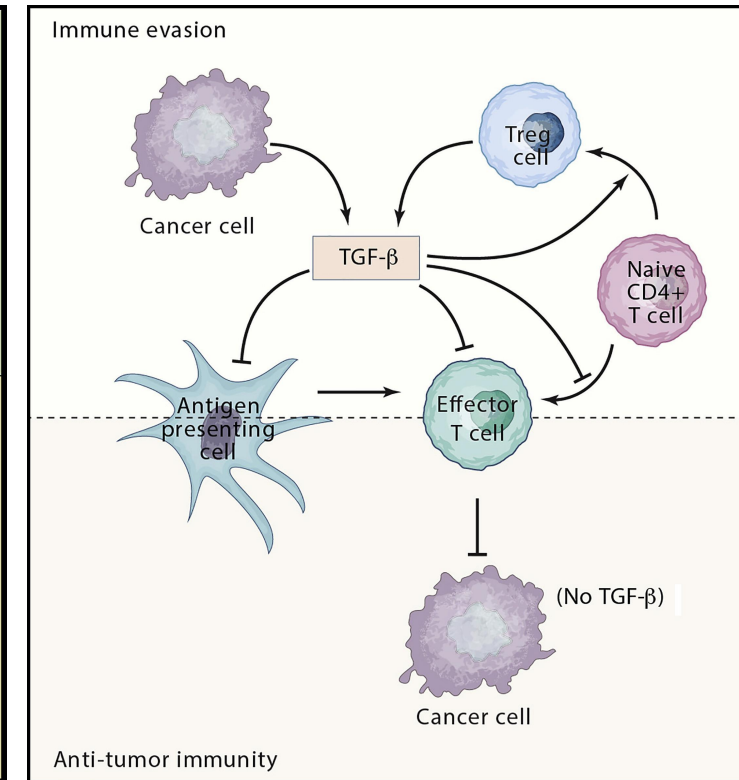
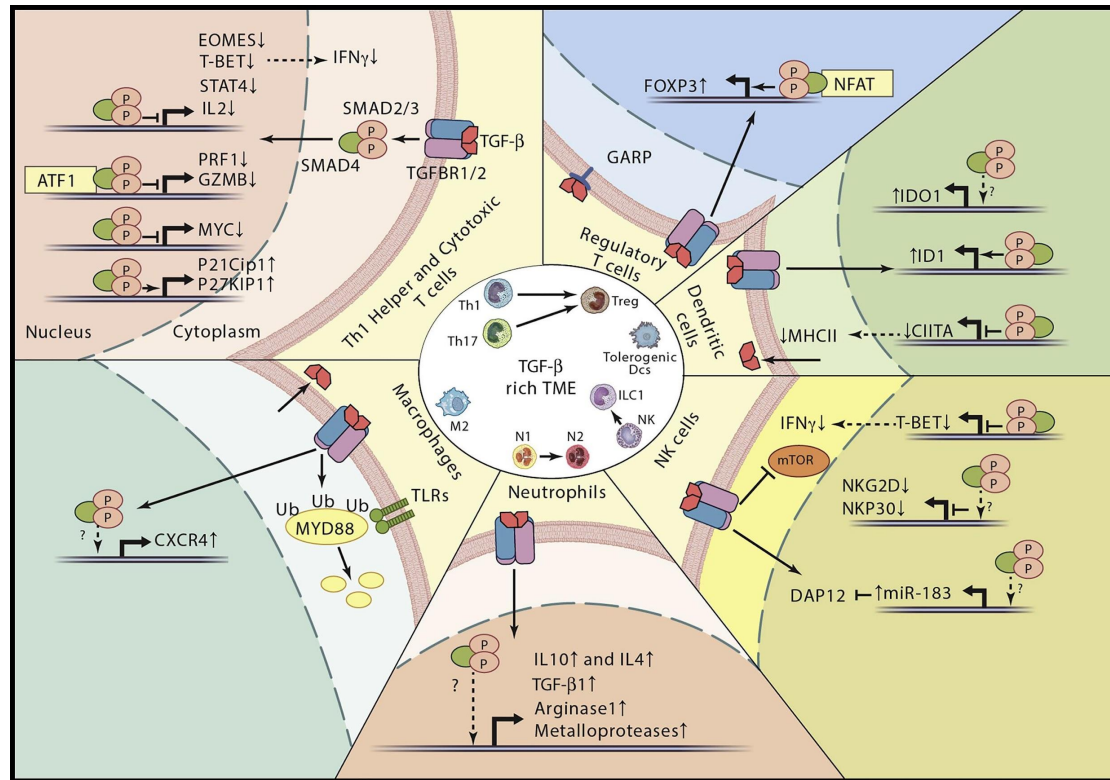
Preparation of gold nanoclusters



Glomerular filtration of nanoparticles

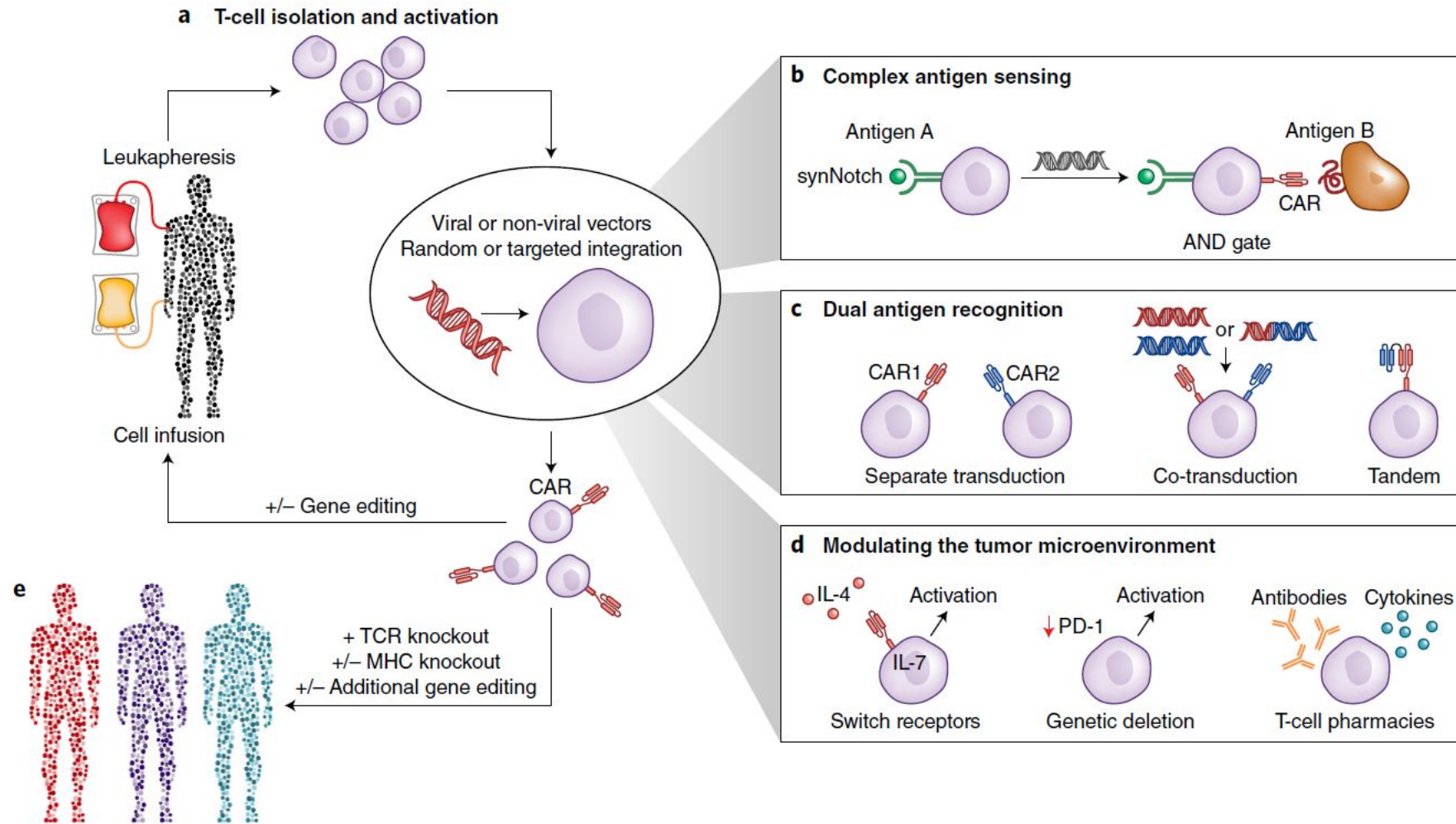


Turn-off TGF- β for effector T cell activation



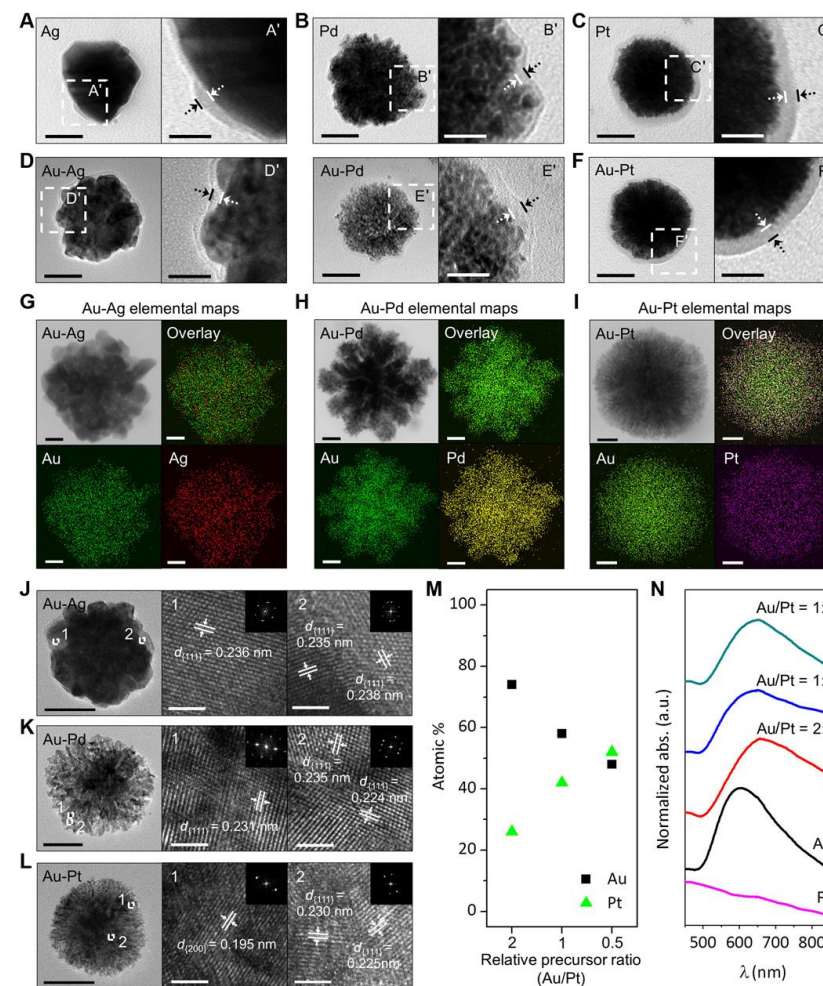
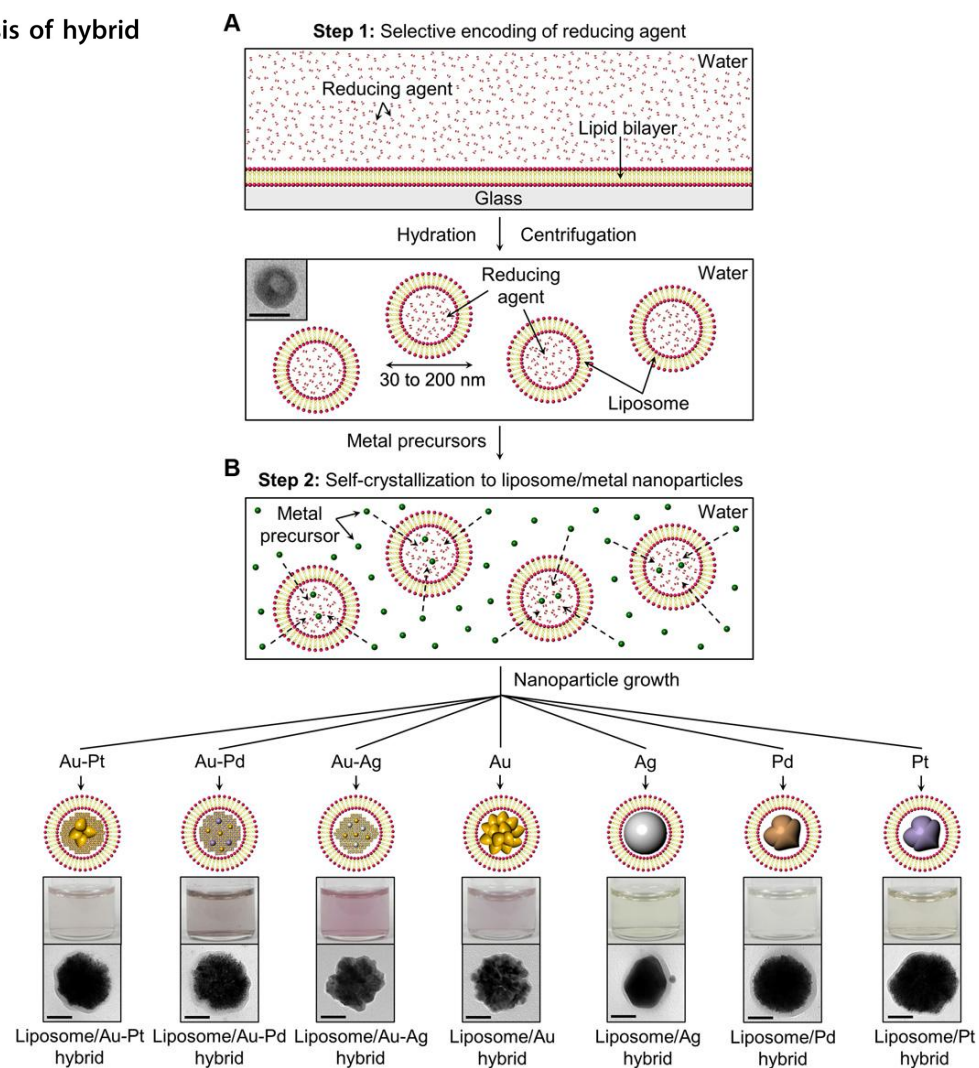
Immunity (2019)

T-cell immune-editing strategies

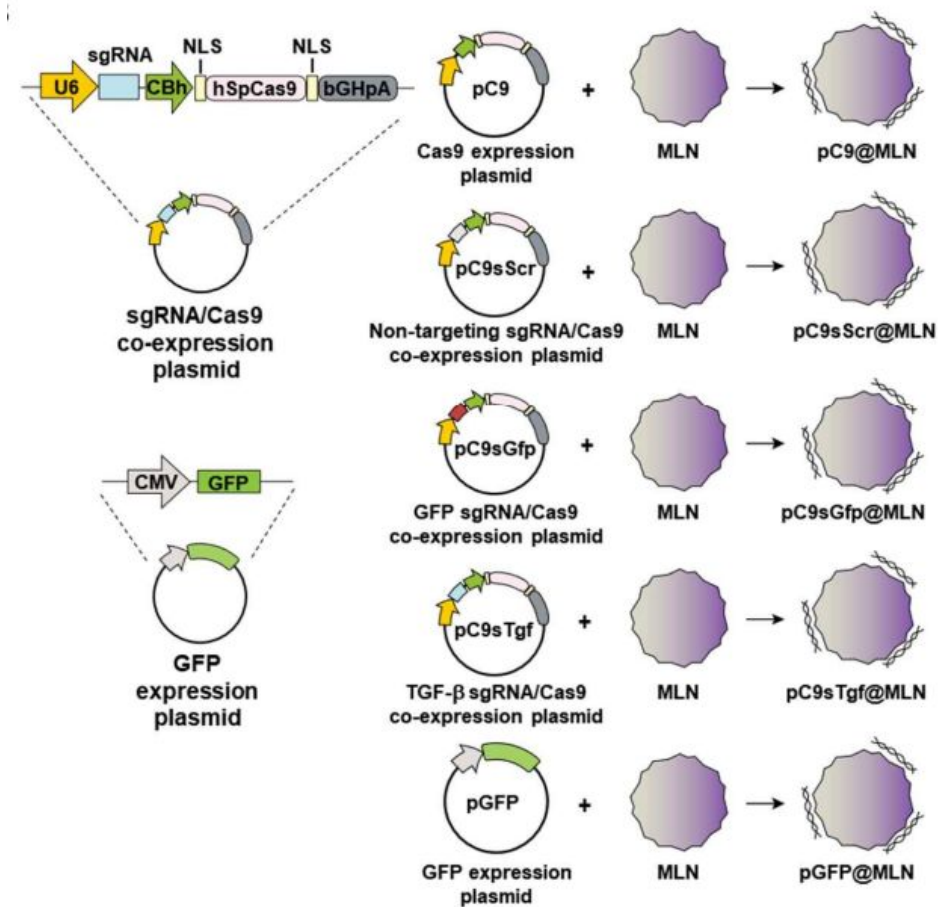
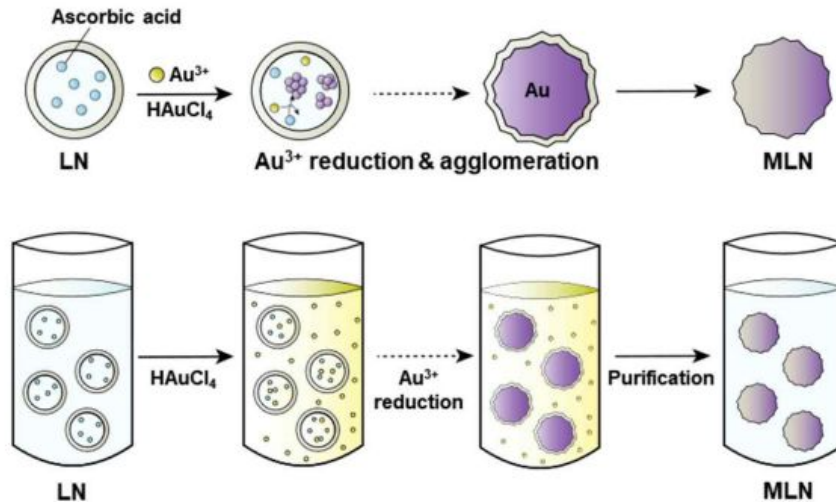


Nat Biotechnol
(2019)

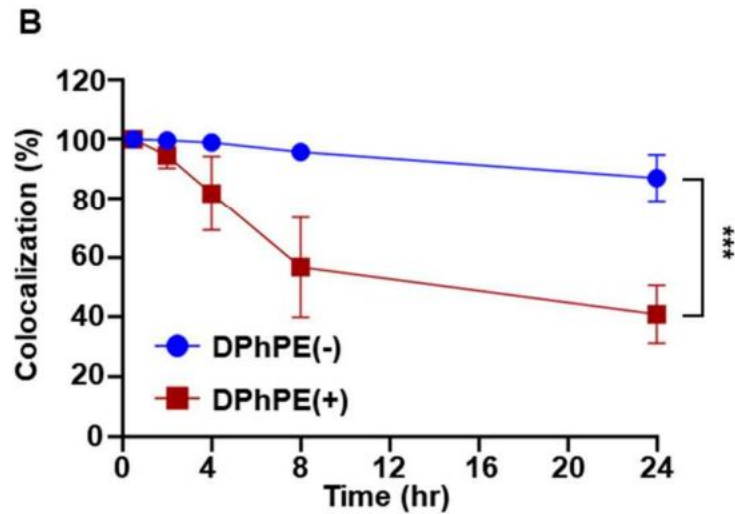
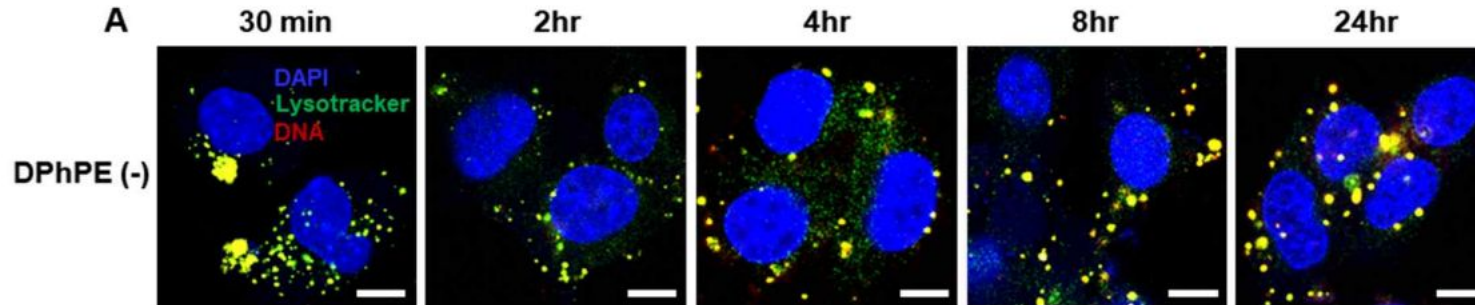
General and programmable synthesis of hybrid liposome/metal nanoparticles



Metal-lipid hybrid nanoparticles

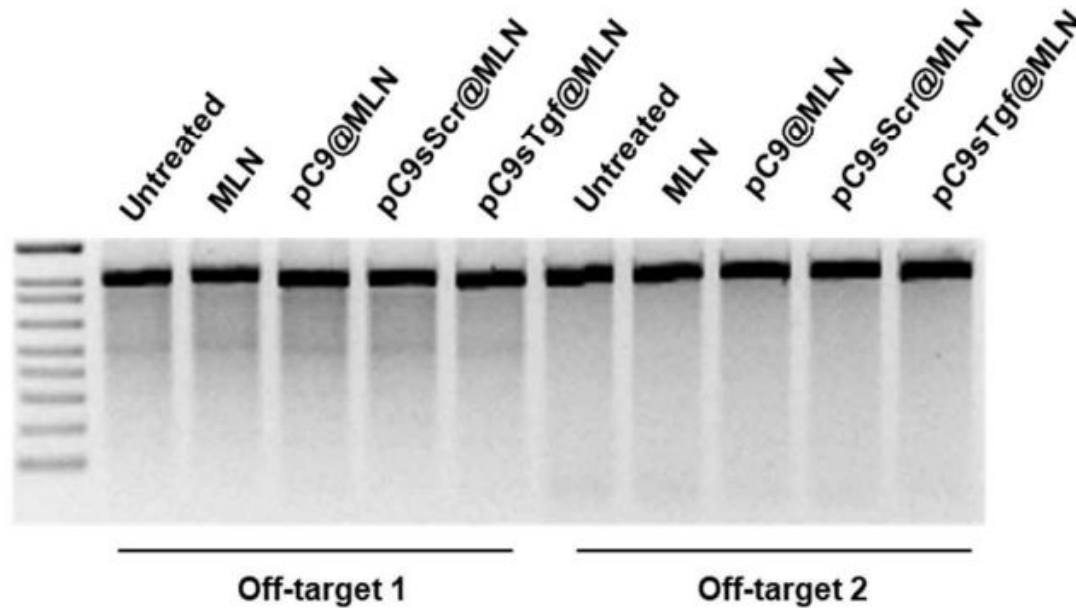


Effect of MLN composition



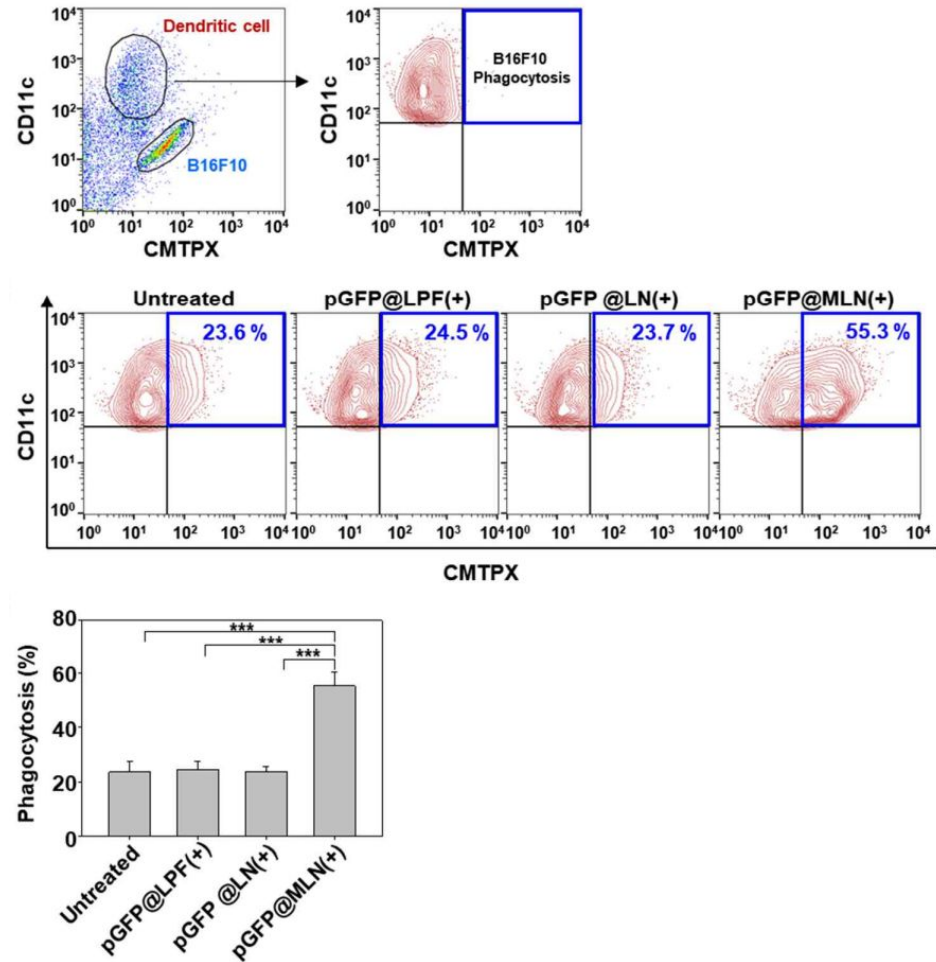
Off-target effect

TGF- β sgRNA target (Ch 7) : GTACAACAGCACCCGCGACC
Off-target 1 (Ch 18) : CTGCA^GCAGCACCCGCGACC
Off-target 2 (Ch 4) : GTCCAACAGCACCCG^TGACT

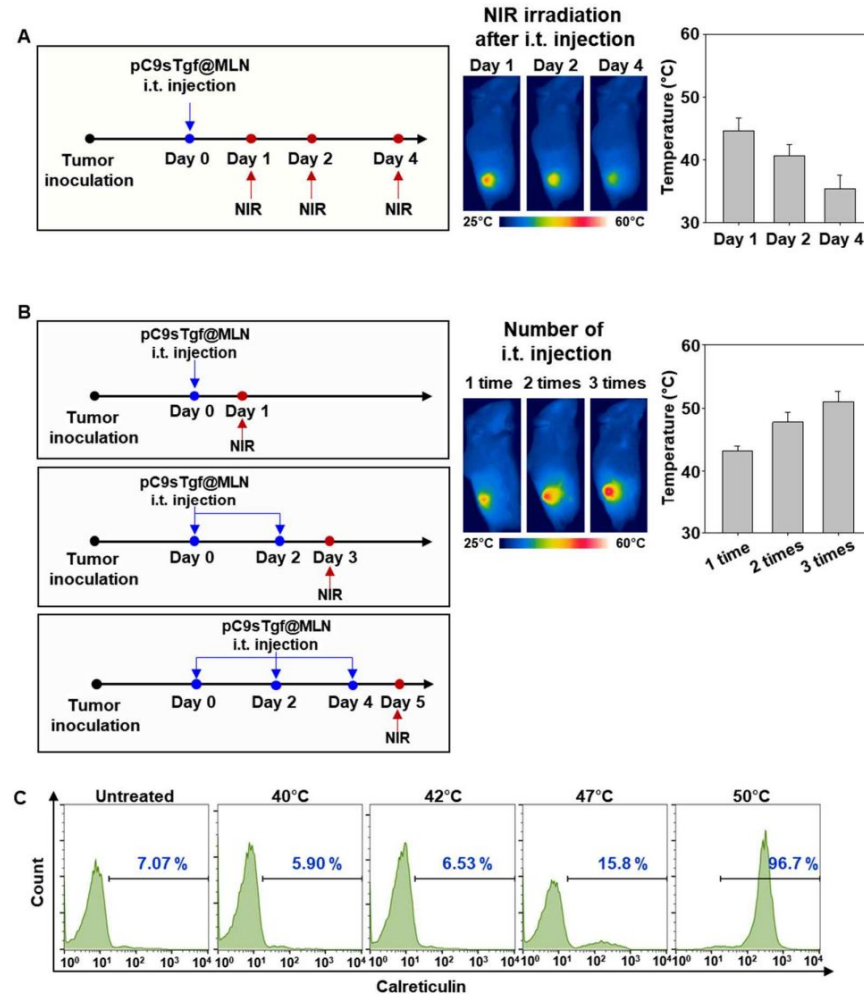


Wellcome Sanger Institute Genome editing website
(<https://wge.stemcell.sanger.ac.uk/>)

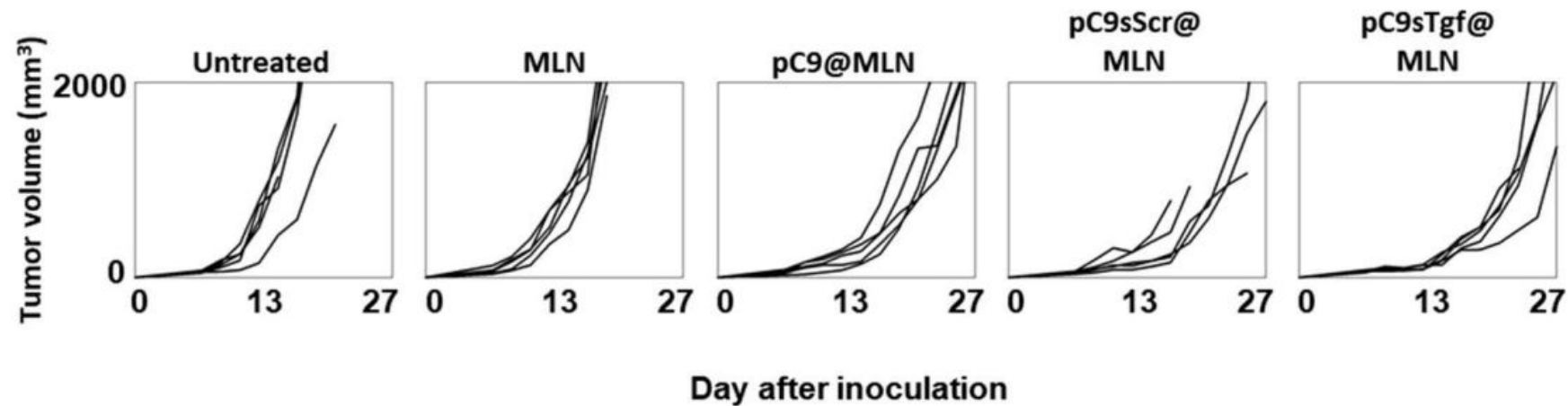
Phagocytosis of B16F10 cells by dendritic cells



Effect of dosing frequency and NIR irradiation regimens

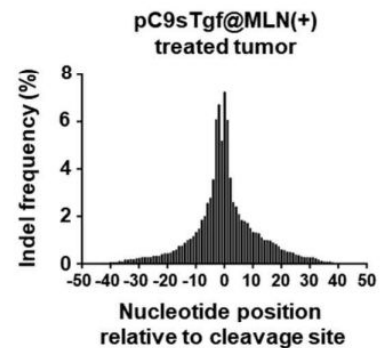


TGF- β editing without NIR irradiation

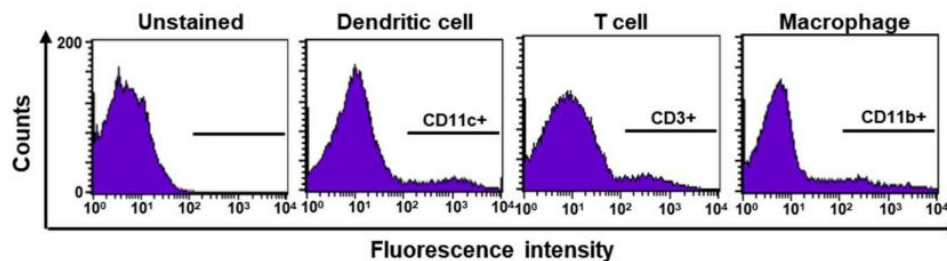


TGF- β editing in immune cells

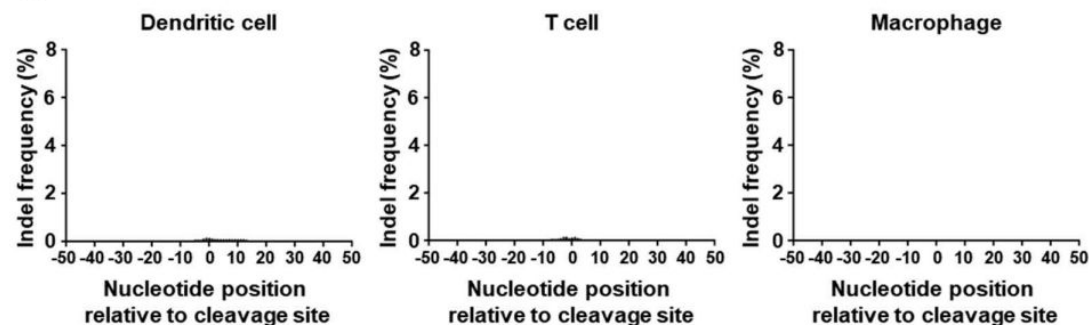
A



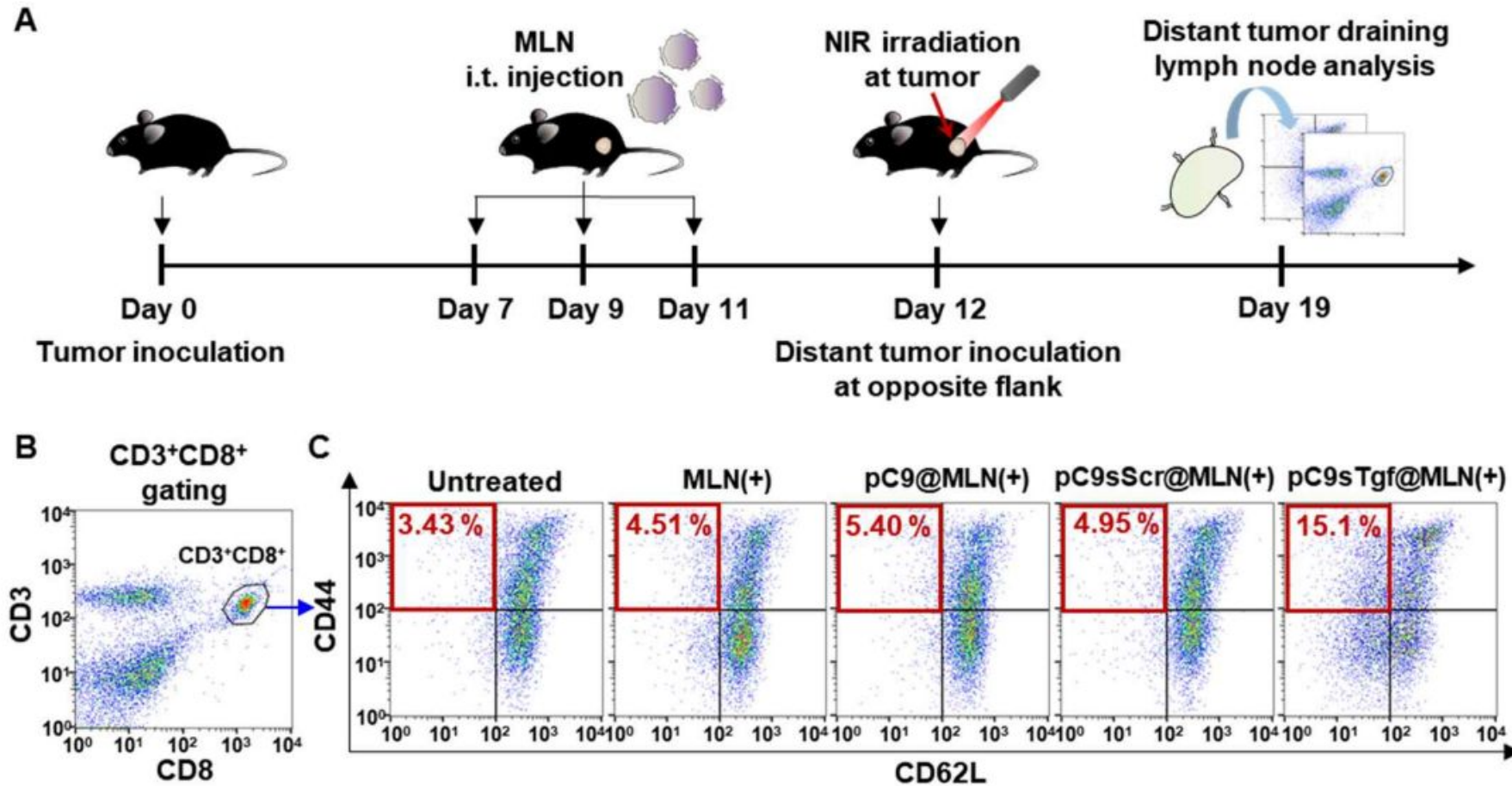
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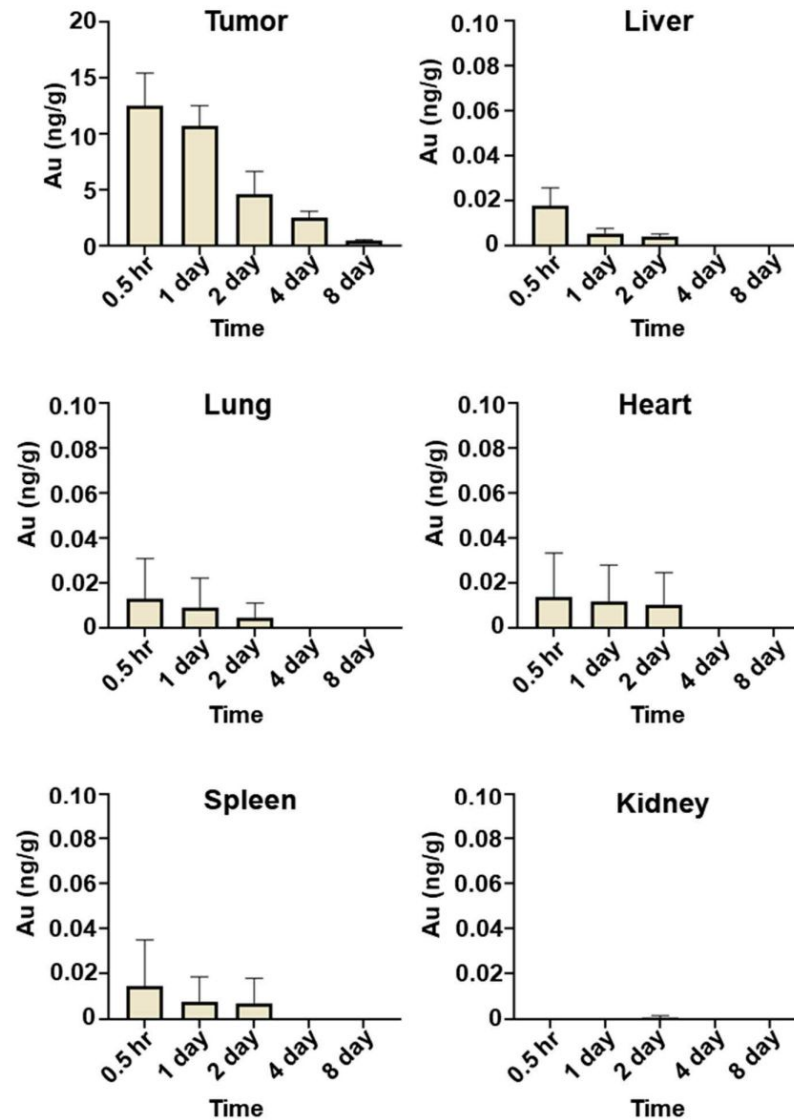
C



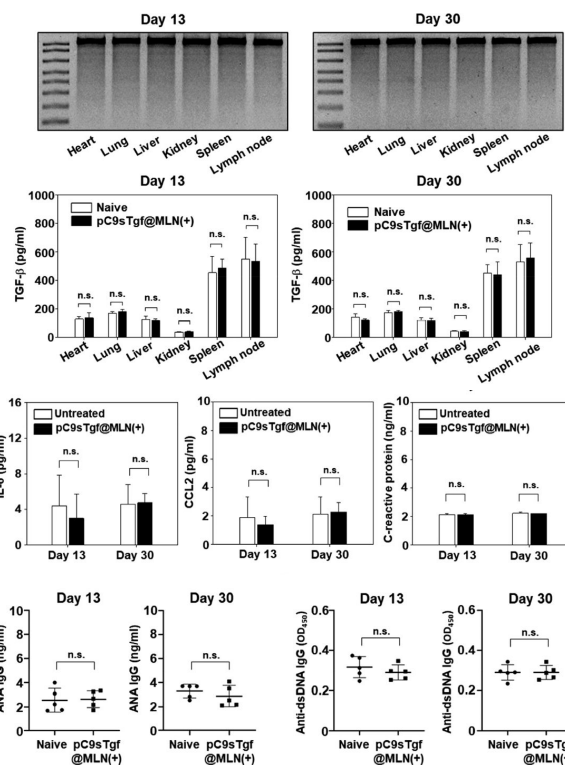
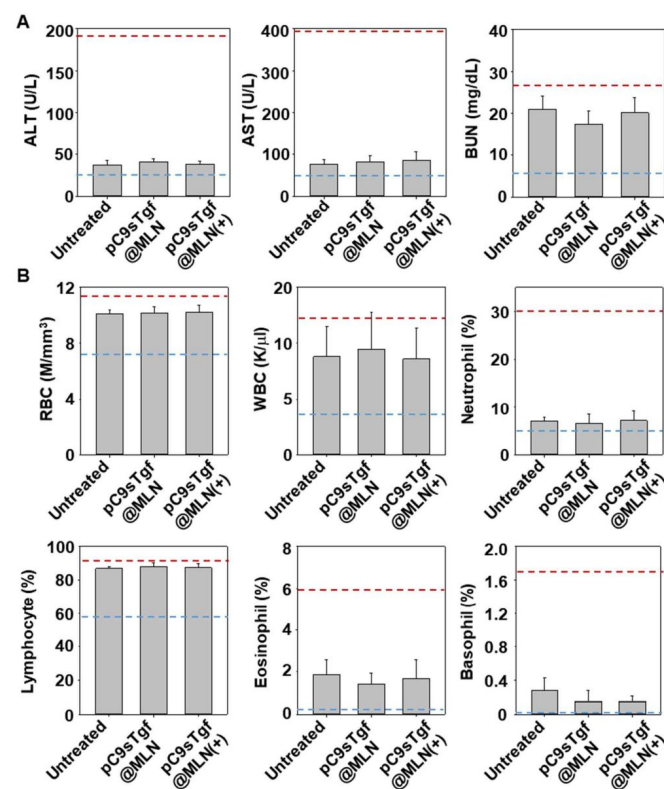
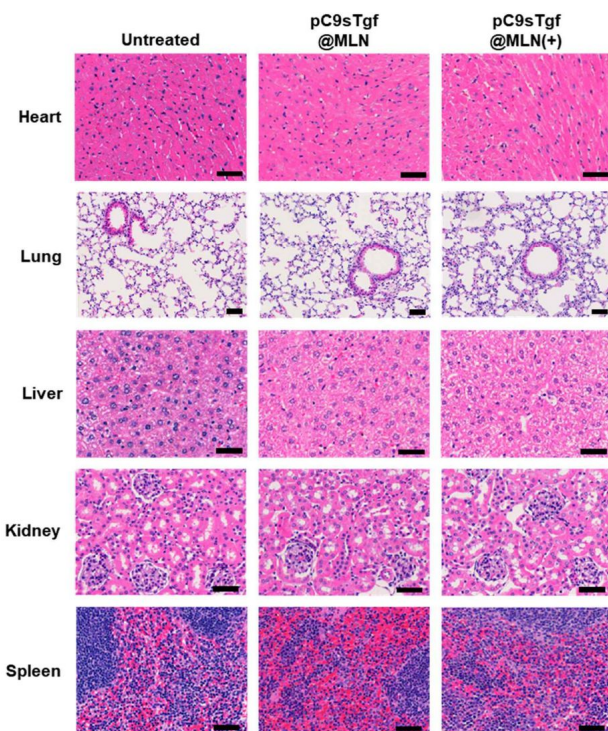
Effector memory T cells

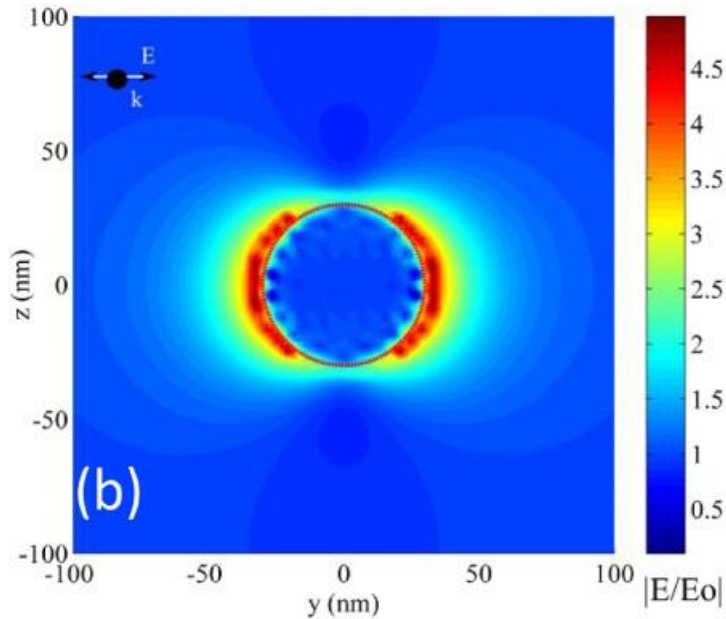
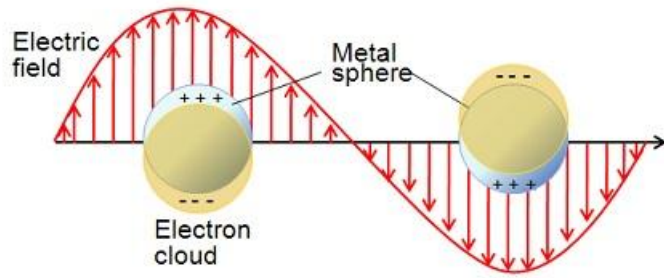


Biodistribution

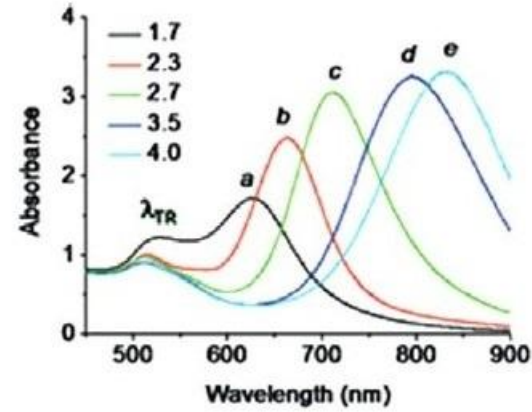


Safety concerns





Simulation of the surface plasma resonance of a spherical particle



Different colors of gold nanoparticles and their respective light absorbance

