Myeloid				
Marker	**Color**	**Company**	**Clone**	**Dilution**
CD45	APC cy7	Biolegend	30-F11	1:250
CD11c	bv 786	BD Biosciences	HL3	1:150
CD19	PE Cy5	Biolegend	6D5	1:500
F4/80	APC	Biolegend	BM8	1:250
Ly6G	bv 711	Biolegend	1A8	1:250
MHC II	bv 510	Biolegend	M5/114.15.2	1:500
DAPI	UV	ThermoFisher	n/a	1:500
CD11b	PE Cy7	Invitrogen	M1/70	1:150

T cell				
Marker	**Color**	**Company**	**Clone**	**Dilution**
CD45	APC Cy 7	Biolegend	30-F11	1:250
CD11c	bv 786	Fisher Sci	HL3	1:150
CD3	PE Cy7	Biolegend	145-2C11	1:500
CD8a	bv 711	Biolegend	53-6.7	1:250
MHC II	bv 510	Biolegend	M5/114.15.2	1:500
CD80	PE Cy5	Invivogen	B7-1	1:500
CD4	APC	BD Biosciences	RM4-5	1:500
DAPI	UV	ThermoFisher	n/a	1:500

OVA tetramer				
Marker	**Color**	**Company**	**Clone**	**Dilution**
OVA tetramer	PE	NIH Tetramer Core	n/a	1:100
OVA	FITC	n/a	n/a	n/a
CD8a	PE Cy7	Biolegend	53-6.7	1:250
CD11c	bv 786	BD Biosciences	HL3	1:150
DAPI	UV	ThermoFisher	n/a	1:500
CD4	APC	BD Biosciences	RM4-5	1:500

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Supplementary Table 1: Flow cytometry antibody panels. Antibodies used for flow cytometry to evaluate myeloid, T cell and tetramer populations.

Score	Liver	Kidney	Fibrotic capsule
0	normal liver, no lesions or hepatocellular damage noted	normal kidney, no nephritic or inflammatory cell infiltrates noted	normal subcutaneous tissue, no inflammatory cell infiltrates noted outside of capsule
1	rare portal and parenchymal infiltrates but no necrosis	rare inflammation in interstitium without necrosis	rare inflammation in inflammation without necrosis
2	moderate parenchymal or portal infiltrates but no necrosis	moderate inflammation or hyalinization of glomeruli but no necrosis	moderate inflammation or evidence or inflammatory cell infiltrates or chronic inflammation but no necrosis
3	frequent and/or large portal or parenchymal infiltrates with occasional isolated islands of coagulative necrosis	frequent and/or large inflammation or cellular infiltrates with occasional islands of necrosis	frequent and/or large inflammation and/or evidence of giant calls with occasional islands of necrosis
4	extensive areas of inflammation with bridging coagulative necrosis	extensive areas of inflammation and glomerular hyalinization with necrosis	extensive areas of inflammation and and/or many giant cells with thick fibrotic capsule

Supplementary Table 2: Histopathological analysis criteria. Histopathological scoring criteria for assessing inflammation and toxicity in H&E stained slides of liver, kidney and subcutaneous tissues.

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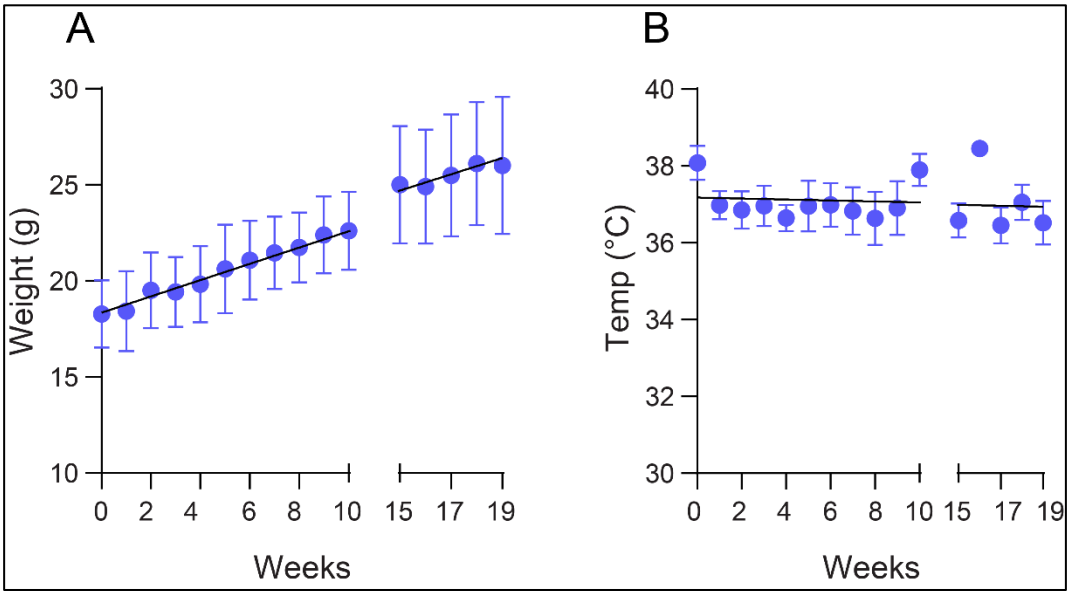

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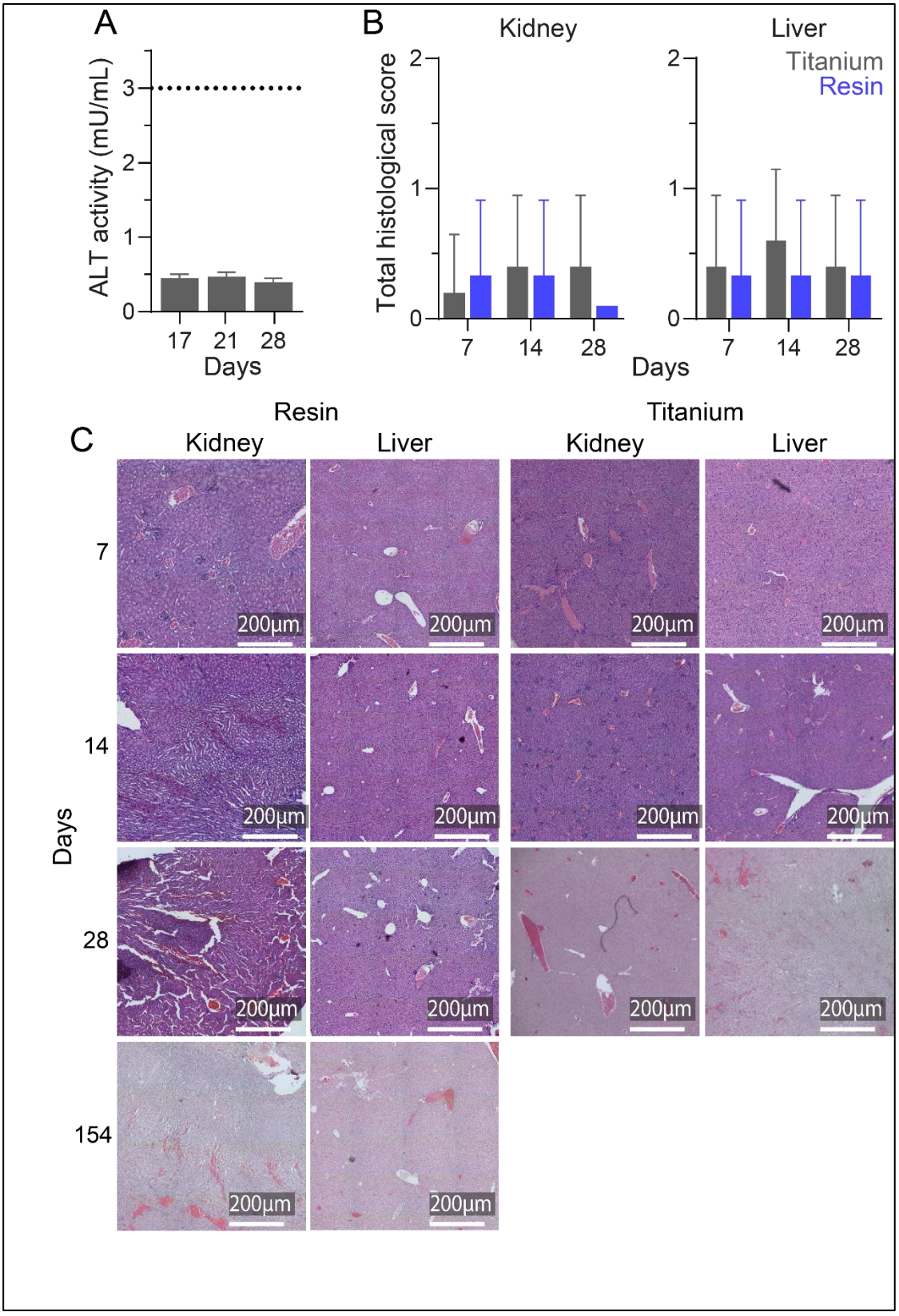
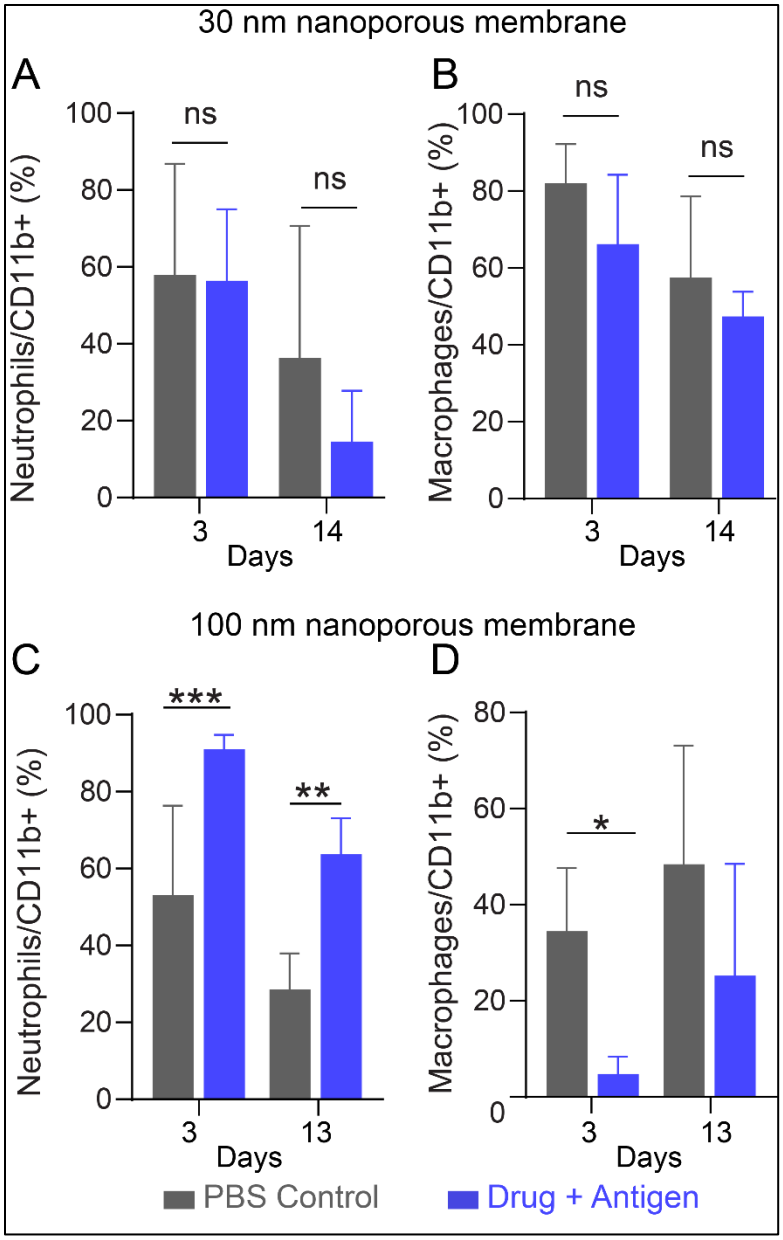
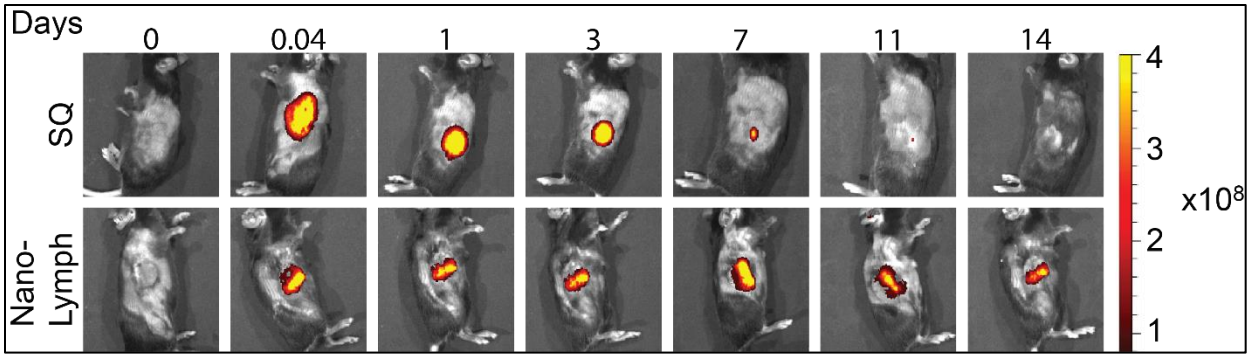
Supplementary Figure 1: Extended NanoLymph Implantation. (A) Mice weight over 19 weeks post-implantation. (B) Mice temperature over 19 weeks post-implantation. Graphs are plotted as mean ± SD.


A
ALT activity (mU/mL)
3
2
1
0
17
21
28
Days
B
Kidney
Liver
Titanium
Resin
Total histological score
2
1
0
7
14
28
Days
C
Resin
Titanium
Kidney
Liver
Kidney
Liver
Days
7
14
28
154
200µm

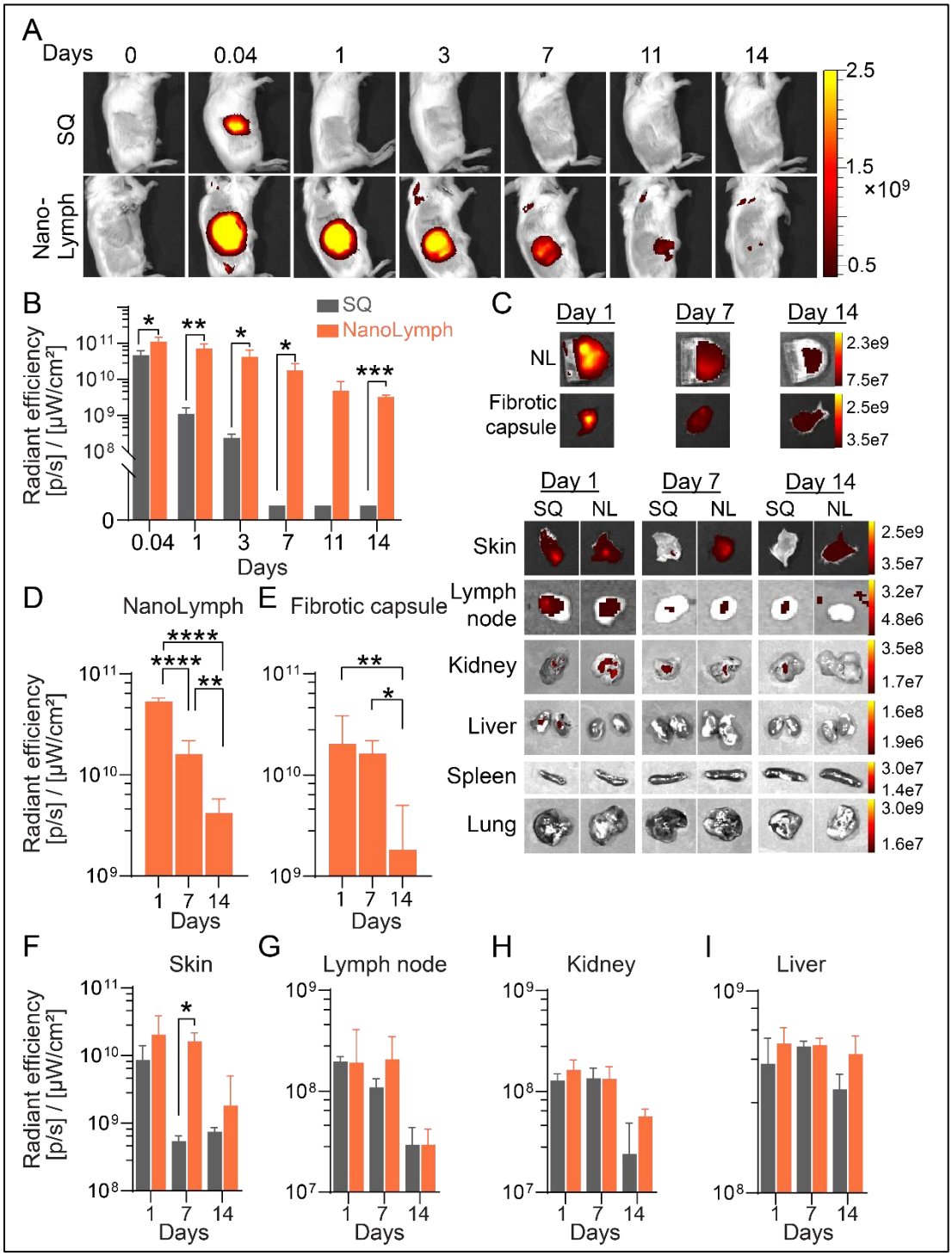
Supplementary Figure 2: Evaluation of NanoLymph induced toxicity. (A) ALT liver enzymes in serum of implanted mice. Dotted line indicates value of positive control. (B) Pathological scoring of histological sections of kidney and liver. (C) Hematoxylin and Eosin (H&E) stained kidney and liver at 7, 14, 28 and 154 weeks post-implantation with NanoLymph versus titanium control. Resin in gray, titanium in blue. Scale bar 200 µm. Graphs are plotted as mean ± SD. Statistical significance determined via one-way ANOVA. *P ≤ 0.05, **P ≤ 0.01 and ***P ≤ 0.001.



Supplementary Figure 3: NanoLymph with smaller nanoporous membranes induce minimal inflammatory cell infiltrate. NanoLymph mounted with 30nm nanoporous membranes, recruitment of (A) neutrophil and (B) macrophages at 3 and 13/14 days. NanoLymph mounted with 100nm nanoporous membranes, recruitment of (C) neutrophil and (D) macrophages at 3 and 13/14 days. Control NanoLymph in gray, Drug/Antigen NanoLymph in blue. *P ≤ 0.05, **P ≤ 0.01 and ***P ≤ 0.001. Graphs are plotted as mean ± SD. Statistical significance determined via two-way ANOVA.



Supplementary Figure 4: NanoLymph refillability and drug retention in vivo after long-term implantation. IVIS analysis of Qdot 705 injected SQ or within NanoLymph at various time points in age-matched mice implanted with NanoLymph for 22 weeks.


A
Days 0 0.04 1 3 7 11 14
SQ
Nano-Lymph
2.5
1.5
×10⁹
0.5
B
SQ
NanoLymph
Radiant efficiency [p/s] / [μW/cm²]
Days
C
Day 1
Day 7
Day 14
NL
Fibrotic capsule
2.3e9
7.5e7
2.5e9
3.5e7
SQ NL SQ NL SQ NL
Skin
Lymph node
Kidney
Liver
Spleen
Lung
2.5e9
3.5e7
3.2e7
4.8e6
3.5e8
1.7e7
1.6e8
1.9e6
3.0e7
1.4e7
3.0e9
1.6e7
D
NanoLymph
E
Fibrotic capsule
F
Skin
G
Lymph node
H
Kidney
I
Liver

Supplementary Figure 5: Antigen retention within NanoLymph. (A) IVIS analysis of ovalbumin conjugated to Alexa Fluor 647 (OVA-AF647) in the antigen reservoir in implanted NanoLymph compared to injected subcutaneous (SQ) control. (B) Relative radiance analysis by IVIS of OVA-AF647comparing SQ (grey) to NanoLymph drug reservoir (orange) across time points in vivo. (C) Ex vivo IVIS images of OVA-AF647 in organs comparing NanoLymph (NL) to bolus injected SQ. Relative radiance analysis by IVIS of OVA-AF647 in (D) NanoLymph and (E) fibrotic capsule and (E) skin surrounding implant. (F) Relative radiance analysis by IVIS of OVA-AF647 in (G) inguinal lymph node, (H) kidney and (I) liver. *P ≤ 0.05, **P ≤ 0.01 and ***P ≤ 0.001. Graphs are plotted as mean ± SD. Statistical significance determined via two-way ANOVA.