REACTION BIOLOGY

SubQperior™

the next generation of tumor models

A superior implantation method for cell-line derived tumor models

- Homogeneous tumor growth
- Reproducible study outcome
- Outstanding statistical value

Standard implantation via subcutaneous injection causes frequent ulceration resulting in early abrogation of studies, leaving researchers with too short treatment windows and high heterogenicity with poor statistical value of study results.

To overcome these challenges, we have developed a superior implantation method for standard cell-line derived tumor models.

subQperior™: tumor cell implantation into the mammary fat pad.

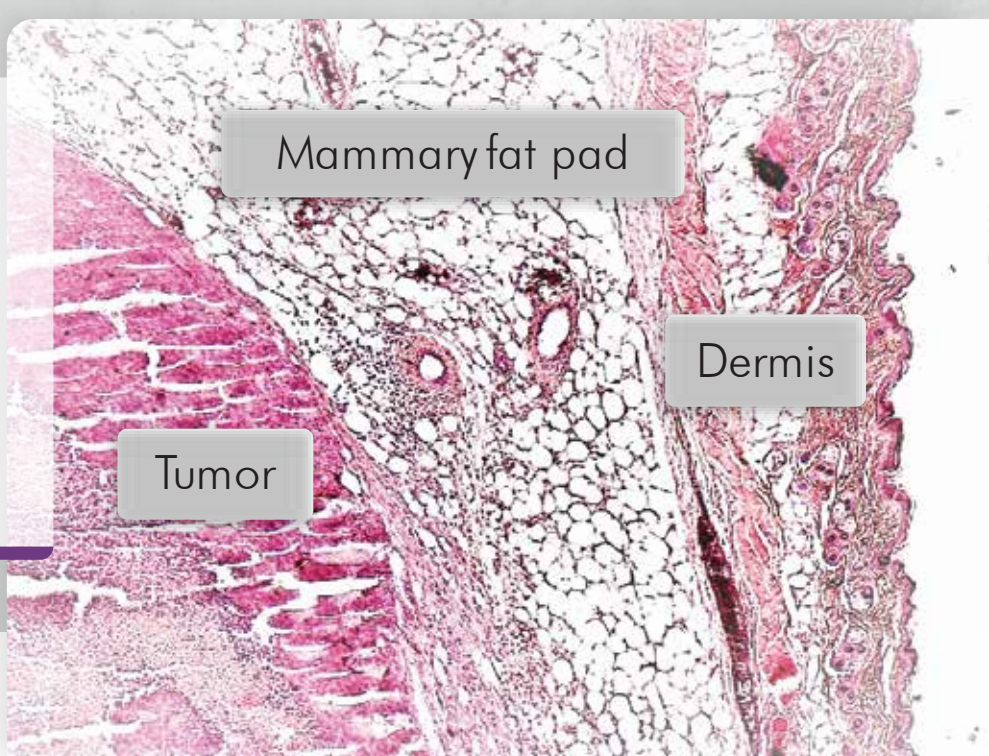
Let's discover together.

The subQperior™ advantage

1. SubQperior™ implantation results in larger tumors.
2. Homogenous and reliable growth yields study outcomes with outstanding statistical value.
3. Tumors are measured via caliper making the handling as easy and inexpensive as for subcutaneous models.
4. Homogeneous tumor growth of subQperior™ models allows to reduce the number of mice per arm.

Tumor cell implantation in the mammary fat pad allows for tumor growth in tissue with the tumor cells being surrounded by stroma.

The mammary fat pad serves as buffer zone between tumor and dermis restricting ulceration and allowing superior growth of tumors in comparison to subcutaneous implantation.



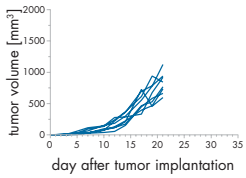
Let's discover together.

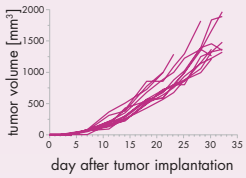
Comparison of subcutaneous and subQperior™ tumor models

subcutaneous | subQperior™ | subcutaneous | subQperior™

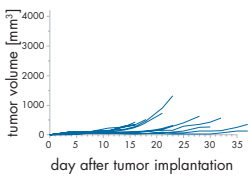
Homogenous Growth

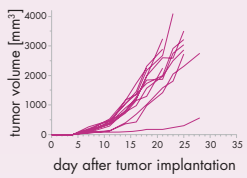
4T1





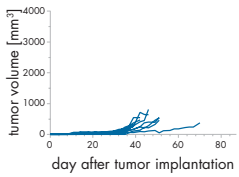
MC38-CEA

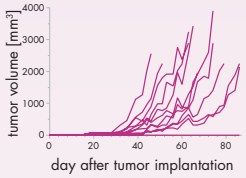




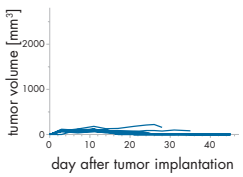
Improved growth of notoriously difficult tumor models

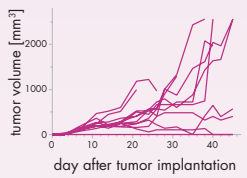
AB12





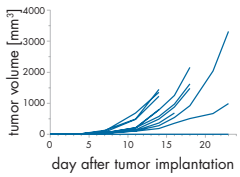
HEPA 1-6

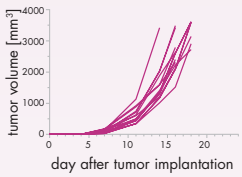




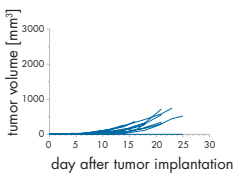
Longer therapy window

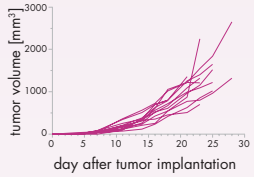
B16-F10





RENCA



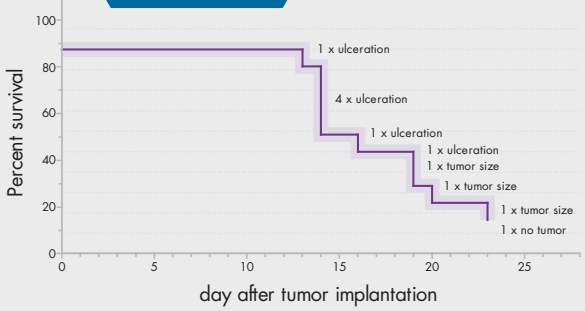


Tumor cells were implanted subcutaneously or subQperior™ in the respective mouse strain of tumor origin. Tumor growth was monitored via calipering. Mice were sacrificed at their individual termination time points.

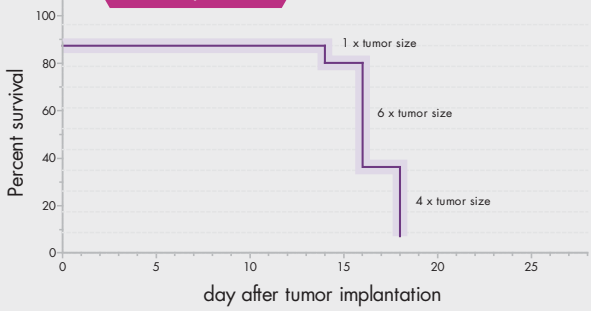
Larger tumor sizes + Homogeneous growth + Reproducible results = **Efficacy studies with outstanding statistical value**

SubQperior™ tumor implantation overcomes ulceration as the main cause of study termination

subcutaneous

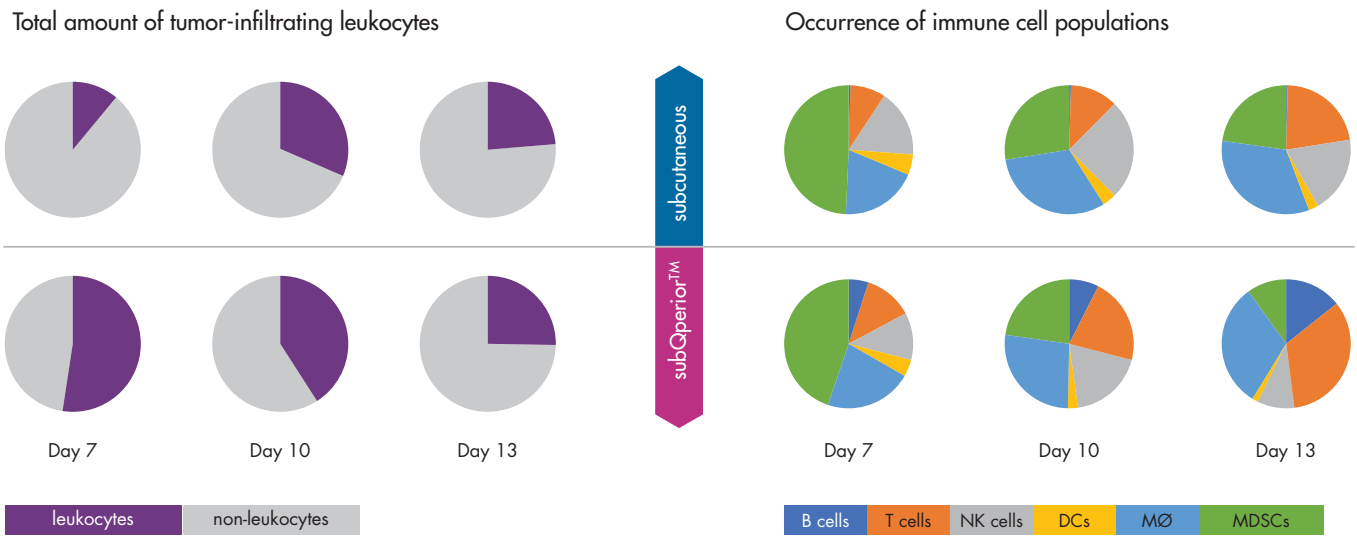


subQperior™



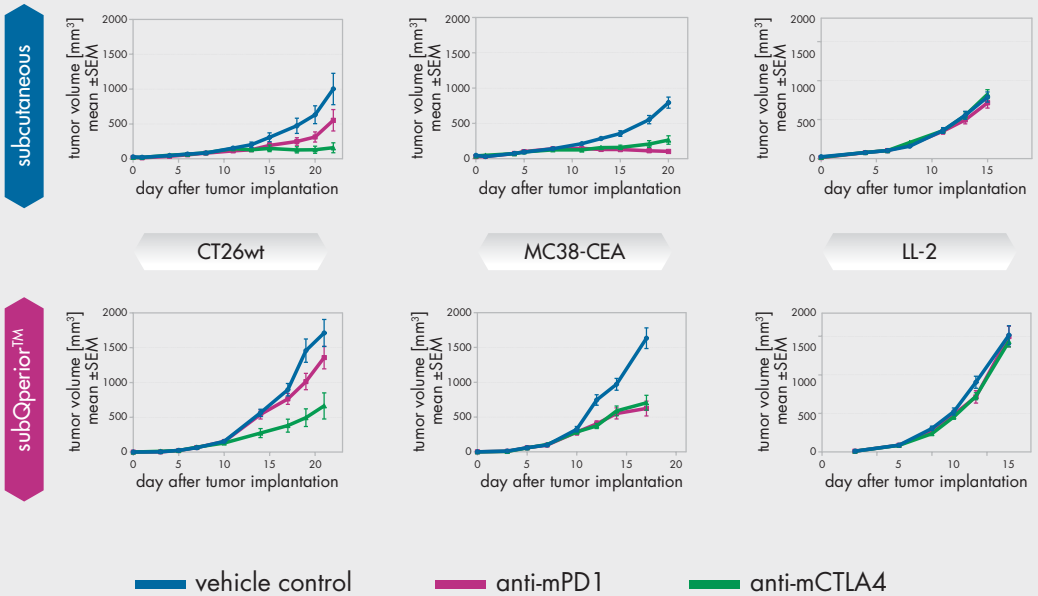
Kaplan-Meier plot showing the causes of death of mice bearing B16-F10 tumors after subcutaneous or subQperior™ implantation. Tumor ulceration is the cause of termination for 7 animals after subcutaneous implantation. In contrast, all animals with subQperior™ tumor implantation were taken down because tumors reached maximum allowed size.

Immune cells infiltrating subQperior™ and subcutaneous CT26wt tumors



Syngeneic CT26wt colon tumor cells were implanted subcutaneously and subQperior™, respectively. On day 7, day 10 and day 13 after implantation, five animals were euthanized and the tumors were harvested for flow cytometry analysis. The tumor was disrupted, erythrocytes removed and up to 3 x 10^6 single cells dispensed per well. Cells were stained for live/dead and the antigens CD3, CD4, CD8a, CD45, CD25, CD11b, Ly6C, Ly6G, F4/80, CD11c, MHC class II, CD206, CD335, CD49b, B220 and FoxP3. The samples were analyzed by flow cytometry using a LSR Fortessa (Becton Dickinson).

Immune Checkpoint Inhibitor treatment show similar responses for subcutaneous and subQperior™ tumor models



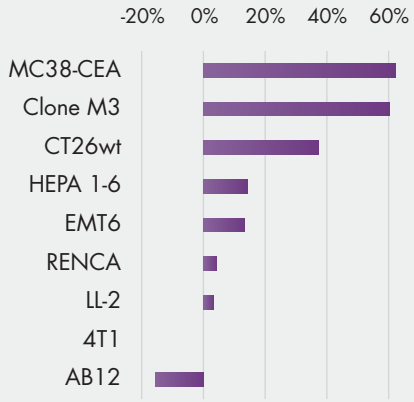
Tumor cells were implanted subcutaneously or subQperior™ in the respective mouse strain of tumor origin.

Tumor growth was monitored via calipering. After randomization, mice were treated with vehicle, anti-mPD1 or anti-mCTLA4 antibody, each at 10 mg/kg, three treatments, intra-peritoneally.

subQperior™ tumor models superior to subcutaneous

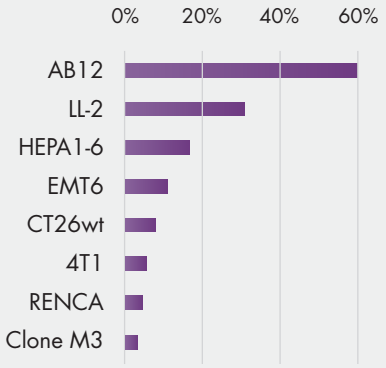
SubQperior™ tumor models show a variety of immune phenotypes

Response to anti-PD1 treatment [% tumor growth inhibition]



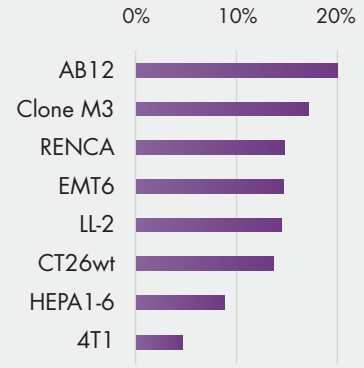
SubQperior™ tumor models were investigated for their response to anti-mPD1 antibody treatment (10 mg/kg, three treatments, intra-peritoneally). Tumor growth inhibition (TGI) is shown in percent as compared to vehicle control.

Leukocyte frequency in tumors of total events [%]



Tumors were isolated at endpoint and investigated with the All-In-One flow cytometry panel comprising 17 markers. Leukocytes (CD45+, live, single) are depicted in relation to total events of tumor single cell suspension.

T cell frequency in tumors [%]



T cell frequency (CD45+, CD3+, CD11b-, live, single) is shown in % of total leukocyte population in terminally collected tumors.

Representative examples of subQperior™ study results. Data points are derived from one study only and do not account for biological variation.

SubQperior™ panel screen - quarterly

Every three months, Reaction Biology offers a panel screening option to evaluate the efficacy of client compounds on 6 tumor models with fast turnaround.

Choose 6 out of 8 tumor models

CT26wt	MC38-CEA	Clone M3	B16.F10	4T1	RENCA	EMT6	LL/2

We share data of vehicle and anti-PD1 treatment groups with all clients participating at no cost:

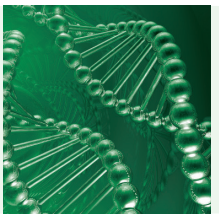
Pay for 1 group and get results from 3 groups

vehicle control	α-mPD-1 treatment	your compound

ask for a quote today!

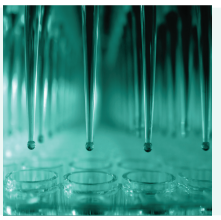
OUR SERVICES AND PRODUCTS

Recombinant Proteins



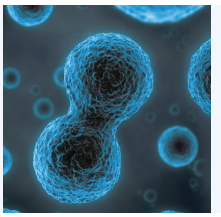
Kinases • Epigenetic Proteins Apoptosis-related Proteins • PARPs • Substrates Custom-tailored Protein Production
Cloning and Mutagenesis

Target-specific Assays



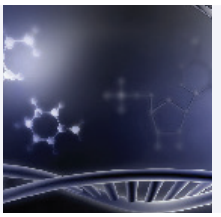
780+ Kinase Assays • 160+ Epigenetic Assays
Target Protein Degradation Assays • RAS Pathway Assays
Ion Channels • GPCRs • Proteases • Phosphatases
DUBs • Metabolic Enzymes • Apoptosis-related Proteins

Cell-based Assays



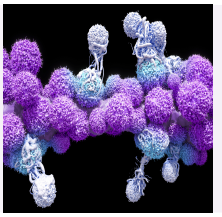
Cell Proliferation and Viability Assays • Cell Panel Screening
Soft Agar Assays • Drug Combination Testing
3D Tumor Spheroid Assays • Migration and Invasion Assays
Angiogenesis Assay • Custom Assay Development

Biophysical Assays



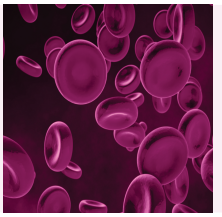
Surface Plasmon Resonance • Thermal Shift
Isothermal Titration Calorimetry
Microscale Thermophoresis
Custom-tailored Assay Development

In Vivo Pharmacology



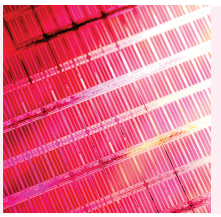
In Vivo Hollow Fiber Model
Xenograft Models • Syngeneic Models
Orthotopic Models • Metastasis Models
Proprietary Models

ADME & Safety



Cardiac Safety Panel • PK/PD Studies
Maximum-tolerated Dose Determination

Biomarker Discovery



Immunophenotyping • Multiplex Immunoassays
Tissue Mircoarray Analysis • qPCR Service
Flow Cytometry Service • Western Blot Service

Let's discover together.

REACTION BIOLOGY

Reaction Biology
USA • Germany

requests@reactionbiology.com
+49.761.769996.0 • +1.610.722.0247
www.reactionbiology.com