

Priming Drugs for Success

We specialize in preclinical testing using mouse disease models with humanized therapeutic targets

Humanized Targets

TNFR1
IL17A
IL12B
IL23A
TNF
RANKL
TL1A

CRO Preclinical Services

- In vivo efficacy studies
- In vitro screening
- Ex vivo testing
- PK/PD studies

Our Competitive Advantage

- Unique mouse disease models
- Wide expertise in preclinical testing
- Standardized procedures
- SPF animal breeding facilities
- Team of experienced researchers
- Customized solutions
- Scientific consultation



WHO WE ARE



In vitro and *in vivo* preclinical drug evaluation services



Proprietary mouse models of human disease



Standardized procedures

Scientific Consultation

Expert team of scientists



OUR MISSION



Customer and quality-oriented, process-driven approaches tailored to meet individual customer needs.

Arthritis | Intestinal Inflammation | Lupus | Fibrosis |
Acute Inflammation | Psoriasis | Multiple sclerosis |
Infectious Diseases | Spondyloarthritis |
Osteoporosis | Cancer

OUR

CLIENTS AROUND THE GLOBE

20 years of collaboration with pharma and biotech industry



 **SANDOZ**

 **Generium**
Science


Viron
Therapeutics Inc.


Zyngenia


apidel
www.apidel.com


AstraZeneca


AVESTHAGEN


YUHAN
CORPORATION


TAISHO PHARMACEUTICAL


高雄醫學大學
Kaohsiung Medical University


elasmogen

Our clients around the globe

Since 2006 we have executed over 400 contracts and we have collaborated with over 130 pharmaceutical and biotech companies



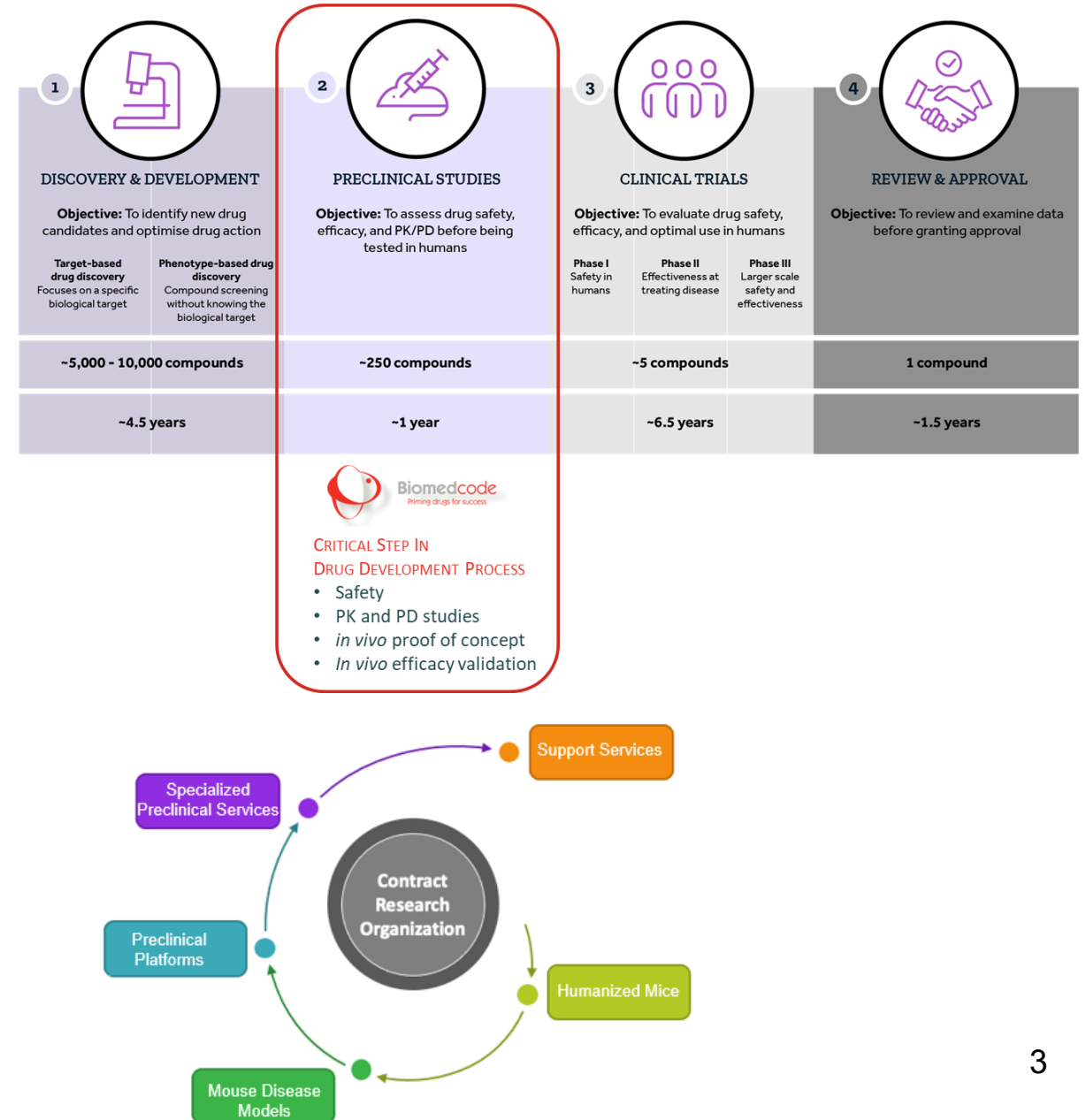
Company Overview

Biomedcode's Niche in the Drug Development Process

Biomedcode is a **Contract Research Organization (CRO)** that since 2006 specializes in providing high-quality, translational **in vivo preclinical efficacy evaluation services** for pharmaceutical and biotechnology companies developing novel biologics, biosimilars and small molecules. We support drug development from early proof-of-concept through advanced preclinical validation, generating robust data that enable informed go/no-go decisions and accelerate the path toward clinical success.

Our **integrated preclinical platforms** are built around a unique portfolio of well-characterized mouse disease models that closely replicate human pathophysiology and incorporate clinically relevant humanized therapeutic targets, including TNF, TNFR1, IL-23p19, IL-23p40, IL-17, TL1A and RANKL. These validated models provide predictive efficacy assessment across **inflammatory** and **autoimmune diseases, fibrosis** and **oncology**. Complementing our in vivo expertise, we are now expanding our capabilities with **mouse-derived lung and intestinal organoid platforms** for early-stage **ex vivo drug screening**.

Biomedcode is a trusted partner to major pharmaceutical and biotechnology companies across Europe, the United States and Asia, with a proven track record of supporting IND-enabling development programs. Through long-term collaborations with global industry leaders, we deliver high-quality, translationally relevant preclinical research that helps de-risk and accelerate the development of innovative therapeutics.



Our Solution and Our Competitive Advantage



Extensive list of **proprietary transgenic and mutant** mouse models with **Humanized Targets**:

- TNF
- TNFR1
- IL17
- RANKL
- IL23p19
- IL23p40
- TL1A

Extensive list of **validated** mouse preclinical models that recapitulate **human disease complexity**:

- Rheumatoid Arthritis
- Interstitial Pulmonary Fibrosis
- Scleroderma
- Crohn's Disease
- Colitis
- Systemic Lupus
- Spondyloarthritis
- Osteoporosis
- Psoriasis
- Multiple Sclerosis
- Cancer
- Acute inflammation
- Infectious Diseases

Validated **Preclinical Platforms**:

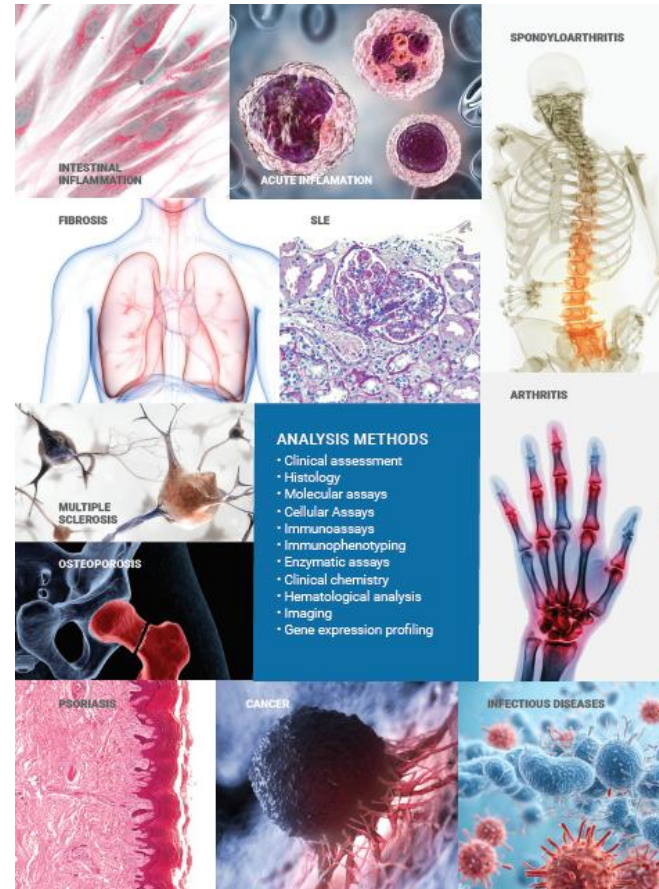
- Standardized study design
- Historical data with positive and Negative Controls
- Optimized therapeutic window

Integrated Services:

- Scientific Consultation → Study Design → Ex vivo and In vivo Efficacy → In Vivo Monitoring → Sample collection, processing and analysis → Data Analysis → Reporting

Track Record:

- Extensive track record of Successfully supporting multiple IND applications



HUMANIZED MOUSE MODELS

Biomedcode offers mice humanized for the following targets:

TNF

TNFR1

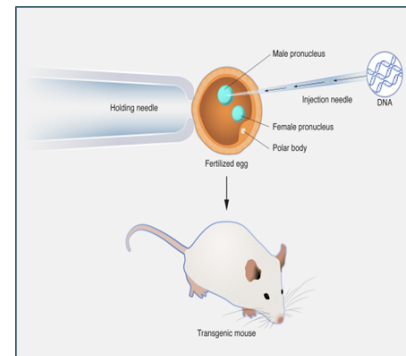
IL17

RANKL

IL23p19

IL23p40

hTL1A



Transgenic/Mutant Mouse Model Development

- Select a druggable human protein/gene target
- Design the transgene/mutation
- Generate the mice carrying the mutation
- Altered expression of the gene/protein usually leads to spontaneous pathology



Offering Comprehensive Preclinical Research Solutions



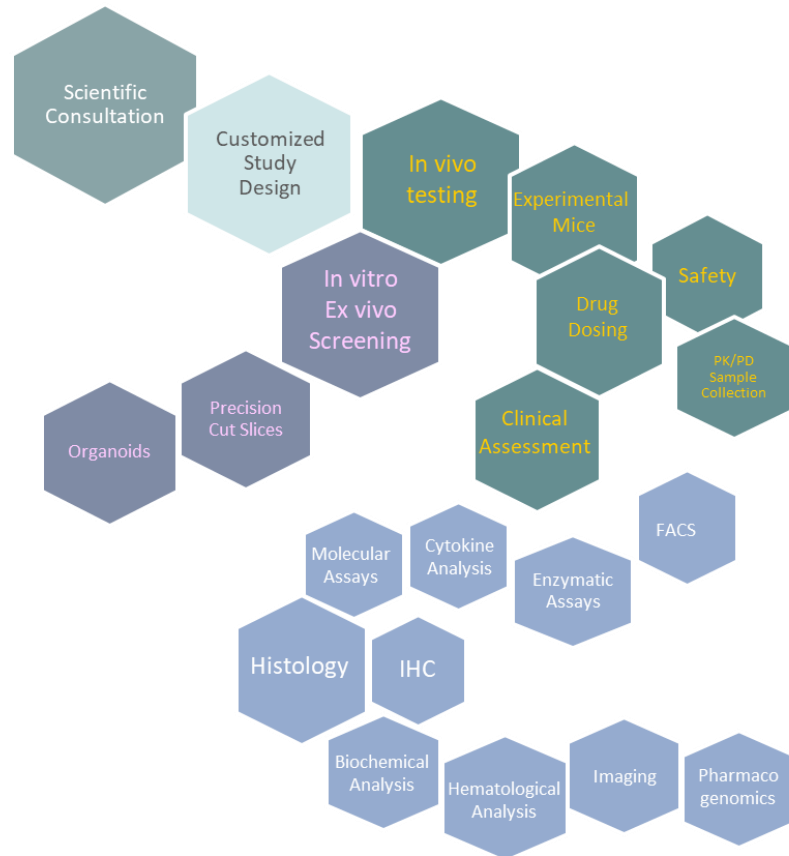
Biomedcode
Priming drugs for success

In vivo pharmacology: PK/PD Sample Collection, Safety Assessment, Method Development, Efficacy drug evaluation

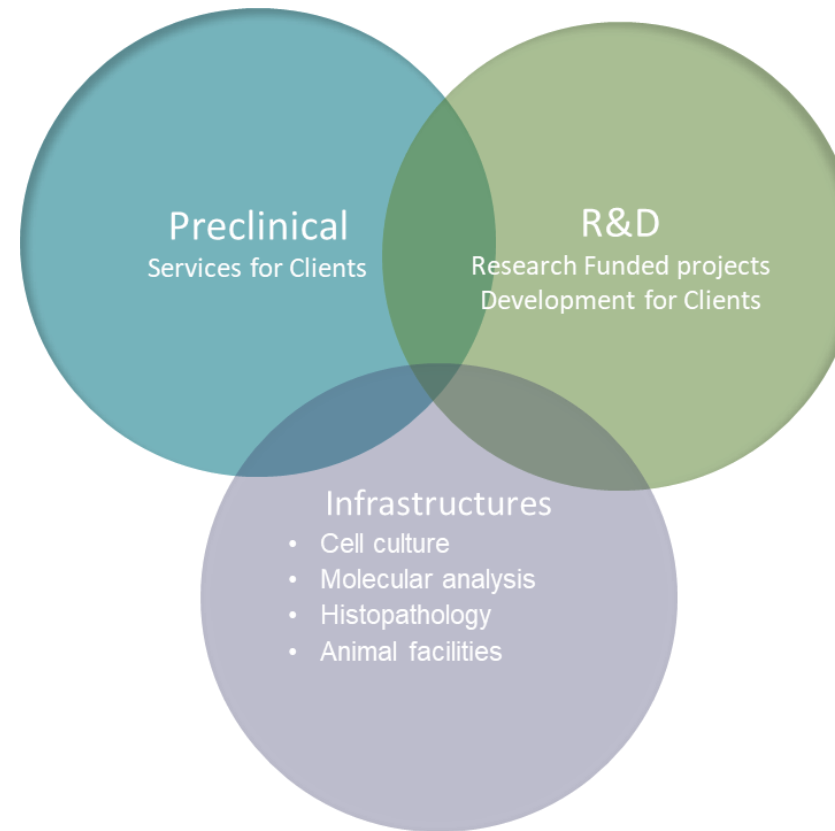
In vitro/ex vivo studies: Mechanistic studies in 2D cell cultures, Precision Cut Tissue Slices, Organoids

Read Outs: Pathology & Histology, Molecular Assays, Gene Expression Profiling, FACS, Imaging

Reporting and Data interpretation



Standard Operating Procedures

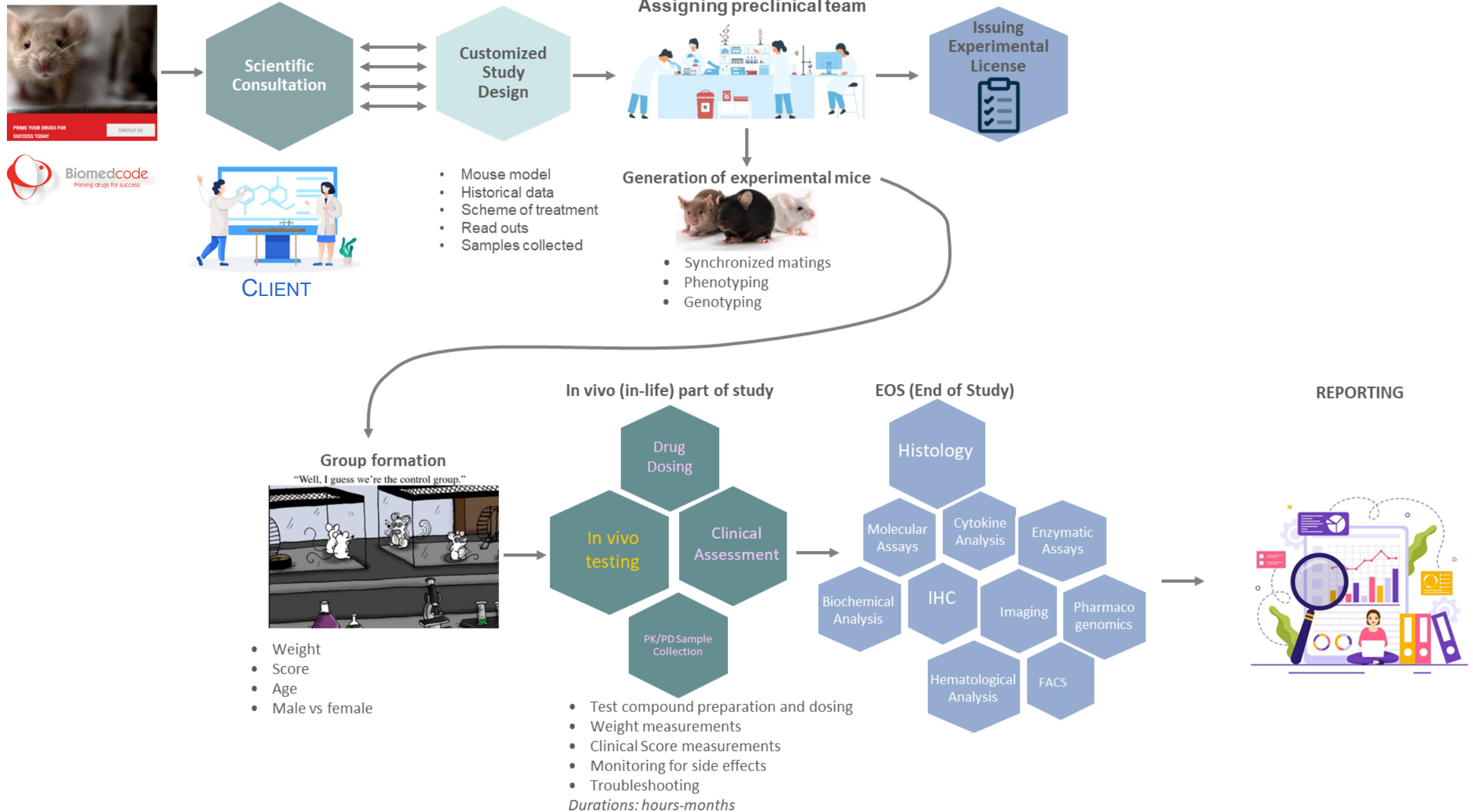


Generation of novel humanized mouse models
Novel disease model development
Novel assay development



Customized Services for Clients
Participation in funded research projects/networks
Collaborative drug discovery activities

Our Pipeline



Offering Reliable, Ethical and Reproducible Science



Biomedcode has integrated in its mode of operation:

- Quality Management System
- Experimental Licenses, ethical compliance
- Customized Study Design
- SOP-driven processes
- Documentation Forms
- Program Management
- Calibrated equipment
- QA checkpoints at different project phases
- Archiving
- Audits



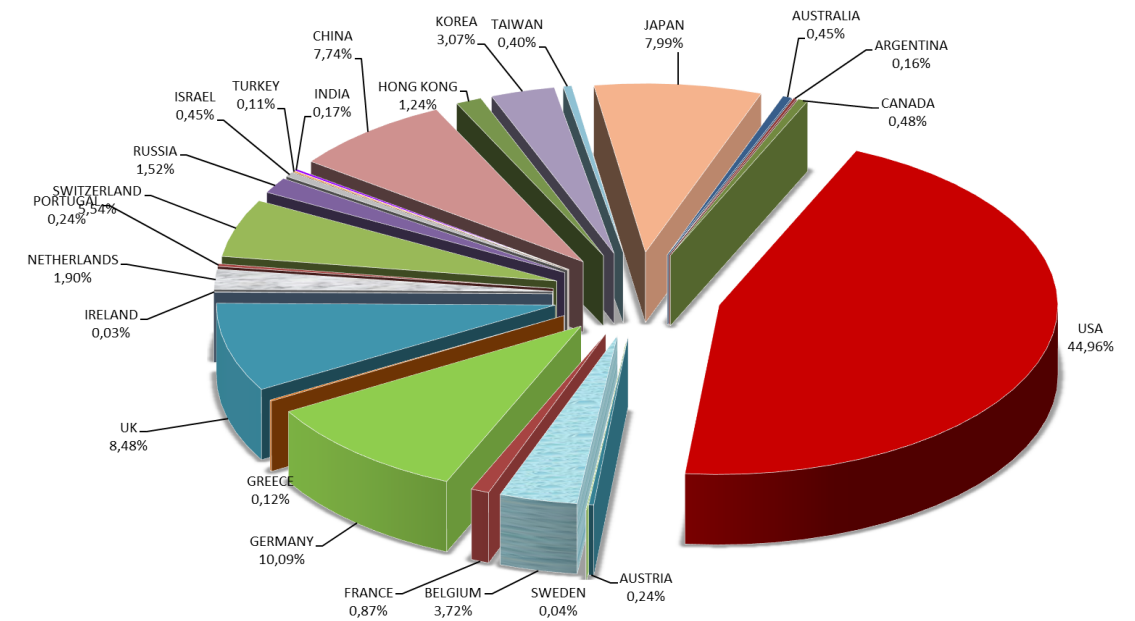
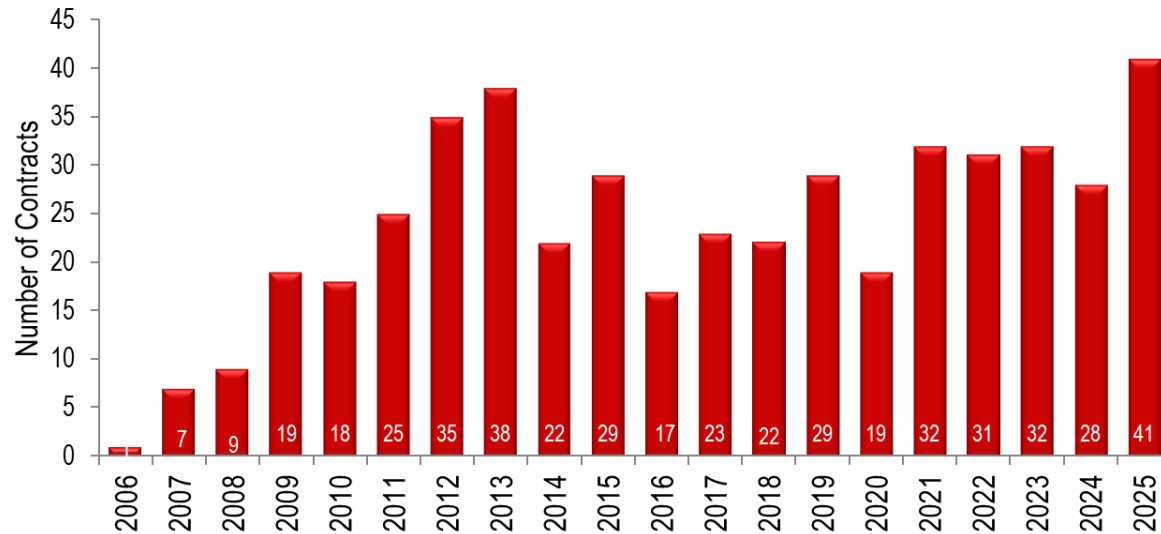
Biomedcode is a Partner of Choice for leading Pharma and Biotech partners

Since 2006

480 Preclinical Contracts
12 Out-licensing Agreements
134 Clients
27 Countries



Global distribution of our Clients
2006-2026



Biomedcode is a partner of choice in European and National Funded Research Consortia

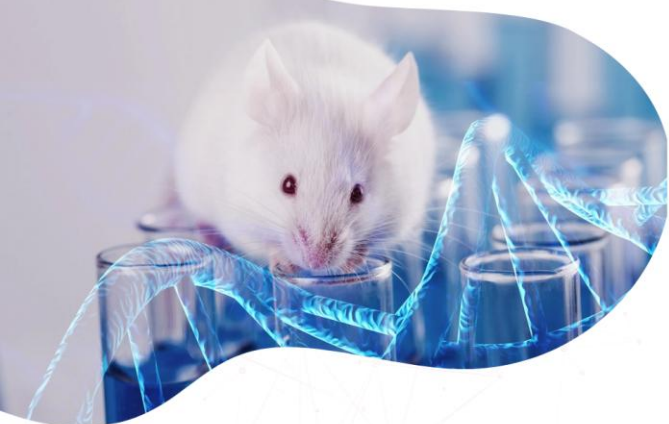


Participation in National Funded Projects

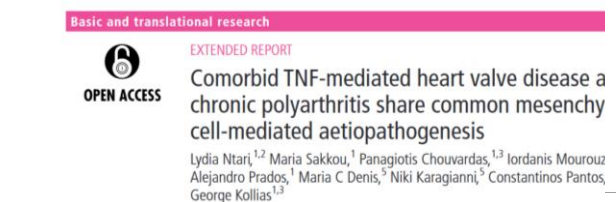
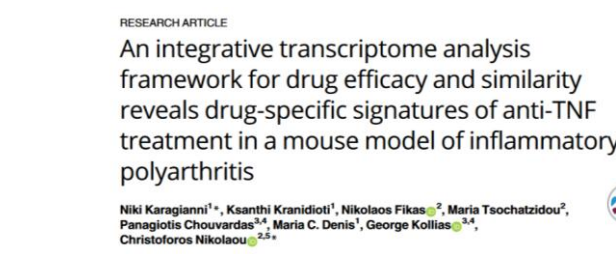
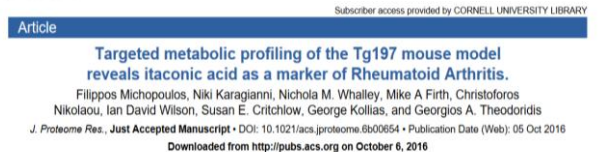
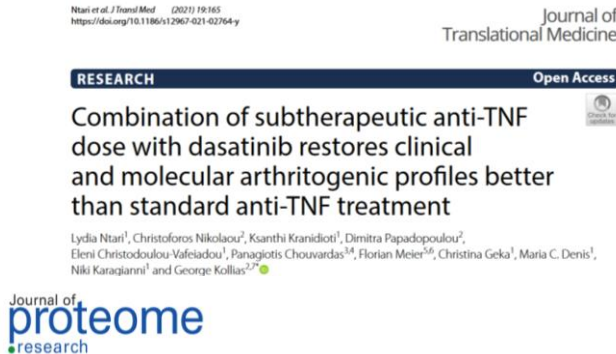
- **BreastCaRANKL**: Development of breast cancer mouse models
- **HUPLA**: Humanized mice for IL17 and IL23 pathogenic pathways
- **SEPIA**: Integration of imaging approaches in preclinical platforms
- **DrugArt**: Development of novel small molecule therapeutics
- **BioOnChip**: Development of tumor on chip for preclinical testing
- **THERALEAD**: Development of arthritis therapeutics

Participation in European Funded Projects

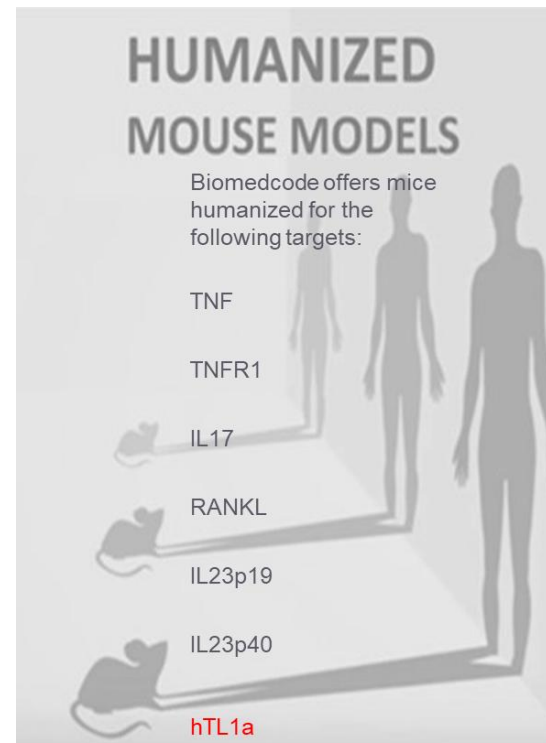
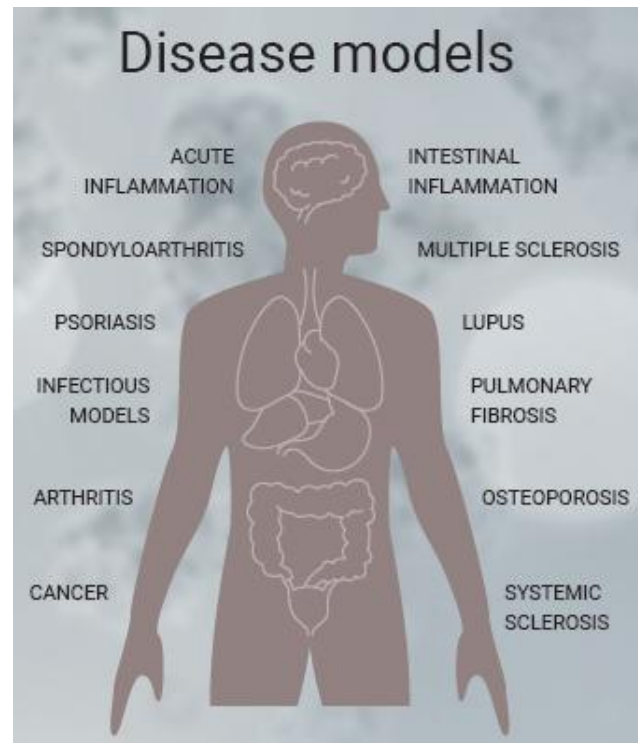
- **PRIMTECH3R (2025-2028)**: Drug screening using organotypic cultures
- **INFRAPLUS (2024-2027)**: Lung and Intestine organotypic cultures
- **Infrafrontier2020**: Specialized Phenotyping Pipelines
- **aDDress**: Progeria and inflammation
- **CodeAge**: Progeria and inflammation
- **TARKINAid**: Src kinase inhibition in arthritis
- **TARKINAid**: Src kinase inhibition in arthritis
- **Infla-Care**: Intestinal Inflammation and Cancer
- **Masterswitch**: Pathogenic pathways in arthritis Pharmacogenomics & Metabonomics
- **MUGEN**: Pathogenic pathways in arthritis



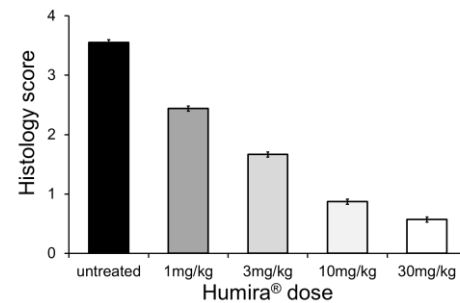
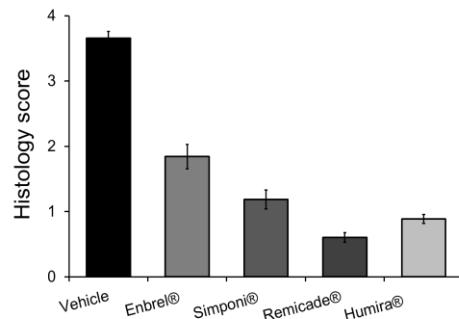
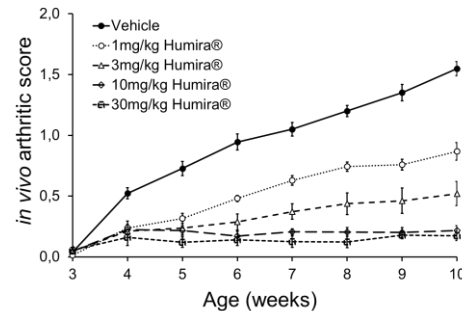
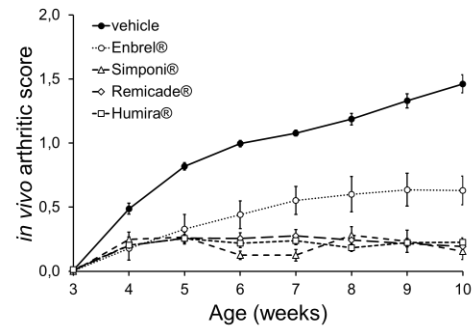
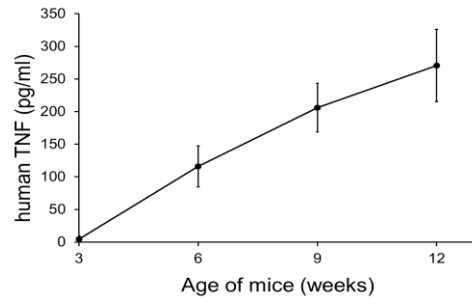
Advancing Scientific Knowledge Through Research and Publication



Biomedcode's Portfolio of preclinical mouse models



Our first Case Study/Success Story: Predicting Clinical Success



Tg197: A human TNF expressing mouse spontaneously developing arthritis. The cornerstone model for Biomedcode, used extensively by the Pharma industry to support the development of multiple anti-hTNF biologics and biosimilars.



ORIGINAL RESEARCH
published: 22 March 2019
doi: 10.3389/fimmu.2019.00526



An Anti-hTNF- α Variable New Antigen Receptor Format Demonstrates Superior *in vivo* Preclinical Efficacy to Humira® in a Transgenic Mouse Autoimmune Polyarthritis Disease Model

Obinna C. Ubah^{1*}, John Steven¹, Andrew J. Porter^{1,2} and Caroline J. Bareille¹

¹ Dasmogen Ltd, Aberdeen, United Kingdom; ² Scottish Biologics Facility, School of Medical Sciences, University of Aberdeen, Aberdeen, United Kingdom

EXPERT OPINION ON BIOLOGICAL THERAPY, 2016
<http://dx.doi.org/10.1080/14712598.2016.1217329>



ORIGINAL RESEARCH

Characterization and non-clinical assessment of the proposed etanercept biosimilar GP2015 with originator etanercept (Enbrel®)

Hans-Peter Hofmann^a, Ulrich Kronthaler^a, Cornelius Fritsch^b, Roger Grau^b, Stefan O. Müller^c, Robert Mayer^d, Andreas Seidl^e and Antonio Da Silva^a

^aPreclinical Development, Sandoz Biopharmaceuticals/Hexal AG, Holzkirchen, Germany; ^bExternal Bioassay Support, Novartis Pharma AG, Basel, Switzerland; ^cSandoz Biopharmaceuticals/Hexal AG, Holzkirchen, Germany; ^dPhys. Chem. Characterization, Sandoz GmbH, Langkampfen, Austria; ^eGlobal Analyt. Charact. & Bioanalyt., Hexal AG Oberhaching, Bayern, Germany

mAbs 4:5, 600-613; September/October 2012; © 2012 Landes Bioscience

Simultaneous targeting of TNF and Ang2 with a novel bispecific antibody enhances efficacy in an *in vivo* model of arthritis

Palanisamy Kanakaraj,^{1,*} Bridget A. Puffer,¹ Xiao-Tao Yao,¹ Spandana Kankanala,¹ Ernest Boyd,¹ Rutul R. Shah,¹ Geping Wang,¹ Dimki Patel,¹ Rajesh Krishnamurthy,¹ Shashi Kaithamana,¹ Rodger G. Smith,¹ David W. LaFleur,¹ Carlos F. Barbas III,² David M. Hilbert,¹ Peter A. Klener¹ and Viktor V. Roschke^{1,*}

¹Zyngene, Inc., Gaithersburg, MD USA; ²Department of Chemistry and Molecular Biology, The Scripps Research Institute, La Jolla, CA USA

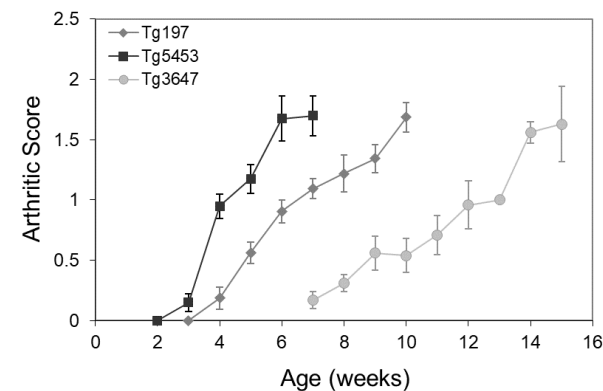


hTNF dependent mouse models of Arthritis (Spontaneous Models)

Spontaneous Arthritis

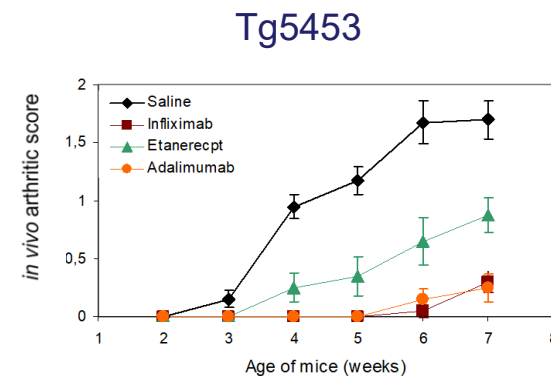
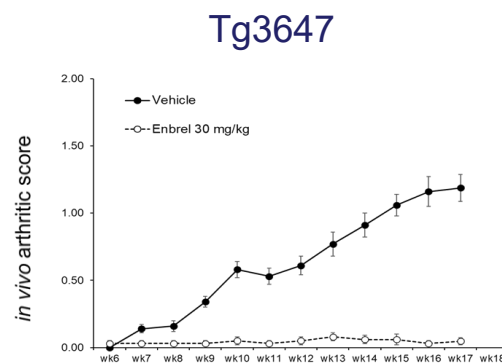
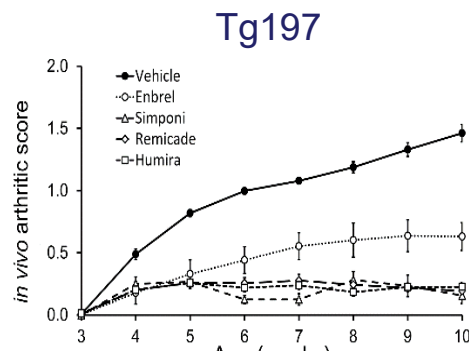
- **Tg197**: hTNF dependent fast progressing pathology
- **Tg3647**: hTNF dependent slow progressing pathology
- **Tg5453**: transmembrane hTNF dependent fast progressing pathology

These are mice that overexpress human TNF and they spontaneously develop arthritis pathology



Models validated with:

Remicade (Infliximab), Enbrel (Etanercept), Humira (Adalimumab), Cimzia (Certolizumab), Simponi (Golimumab)



hTNF/hTNFR1 dependent mouse models

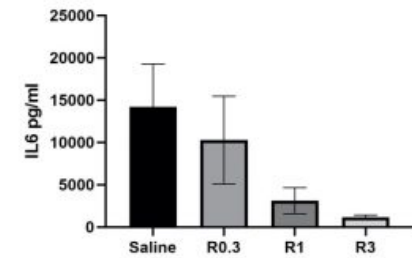
Tg1278TNFKO: transgene expressing normally regulated hTNF in the absence of mouse TNF. These mice do not have a spontaneous phenotype but they overexpress hTNF following induction.

hTNFR1KI: knock-in mice expressing human TNFR1 in the place of mTNFR1

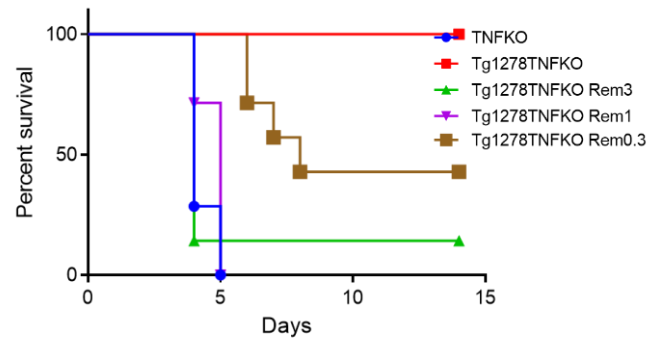
Models validated with: Remicade (Infliximab), Enbrel (Etanercept), Humira (Adalimumab)



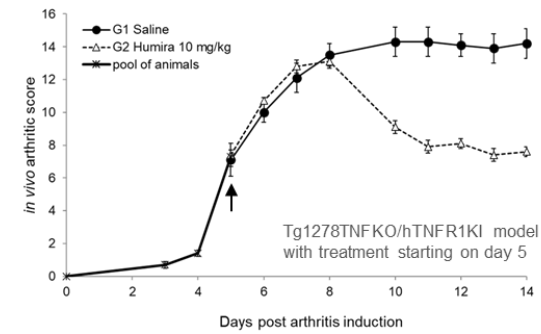
LPS Sepsis Model



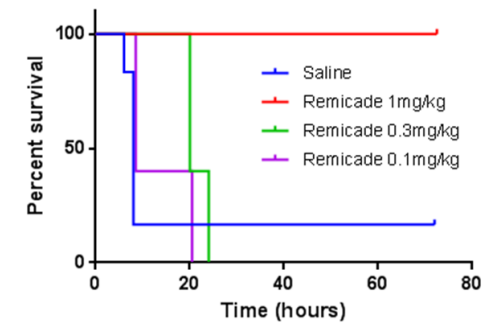
Listeria Infection Model



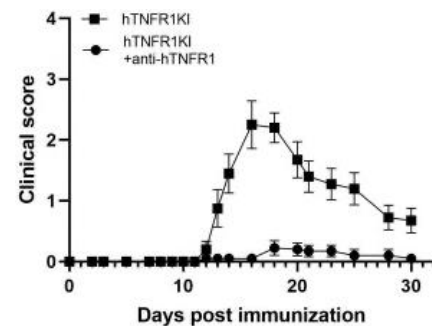
Collagen Antibody Induced Arthritis (CAIA) Model



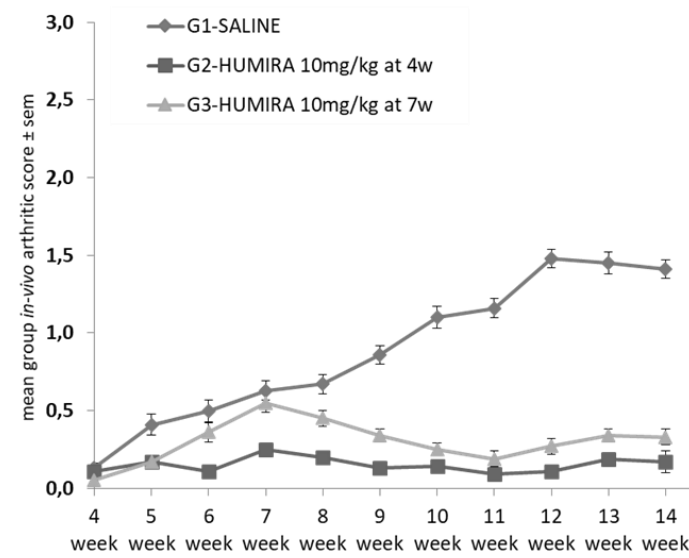
LPS/GaIN Hepatic Failure Model



MOG-induced Experimental Autoimmune Encephalomyelitis (EAE)



Tg197/hTNFR1KI Arthritis

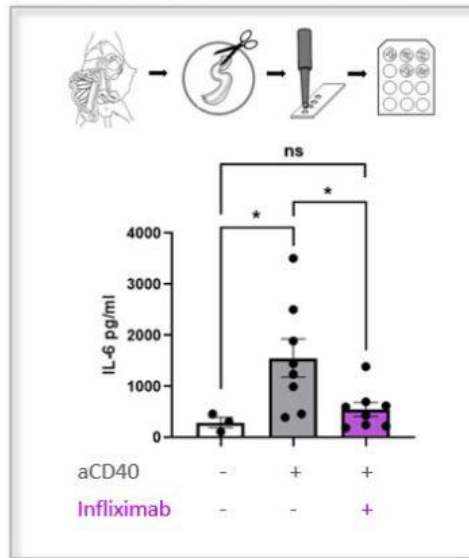


hTNF dependent mouse models of induced colitis

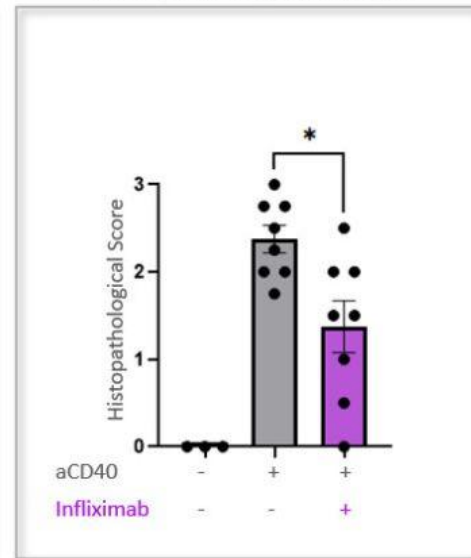
antiCD40-induced Colitis Model



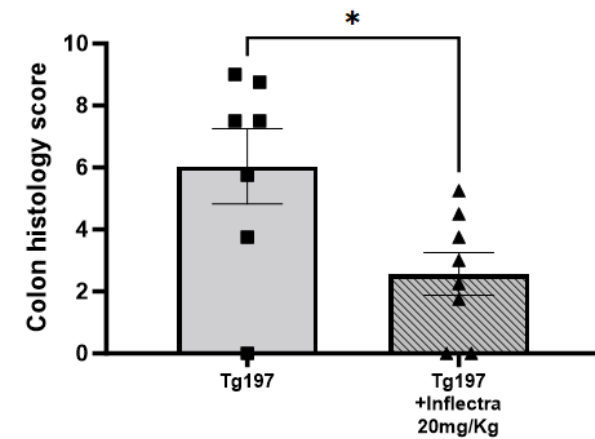
Thick Organ Culture Analysis



Histopathological Analysis

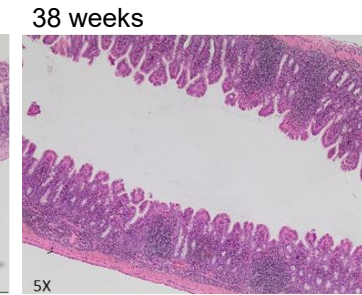
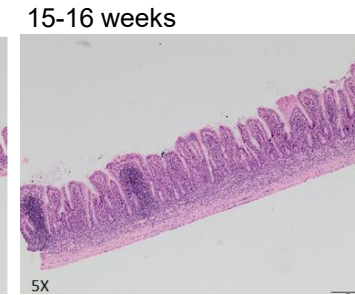
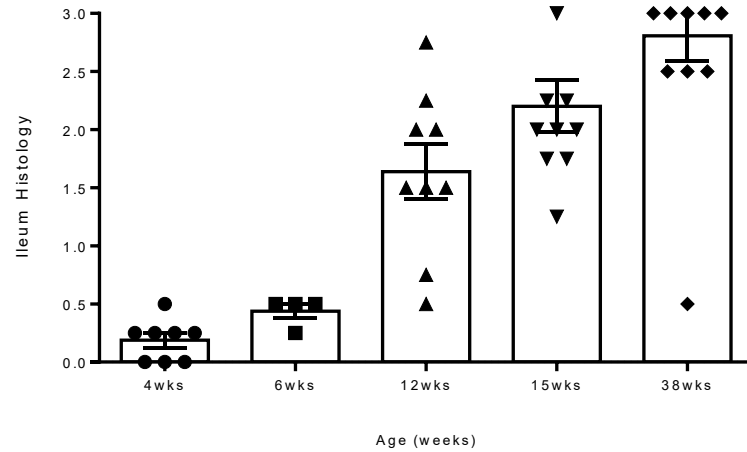


DSS-induced Colitis Model

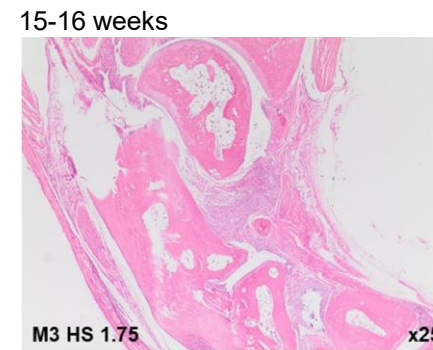
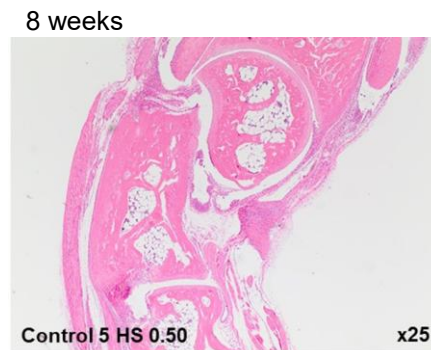


mTNF/hTNFR1 dependent mouse model of Arthritis and IBD

TNFDARE/hTNFR1KI develop a Crohn's like pathology that progressively worsens with age

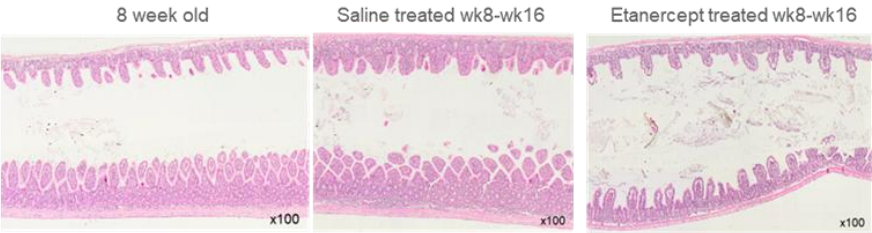
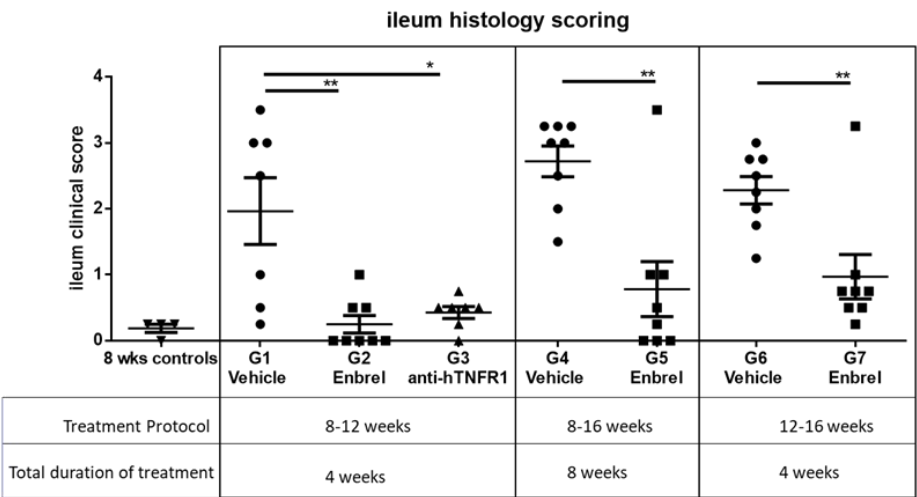


TNFDARE/hTNFR1KI develop arthritis that progressively worsens with age

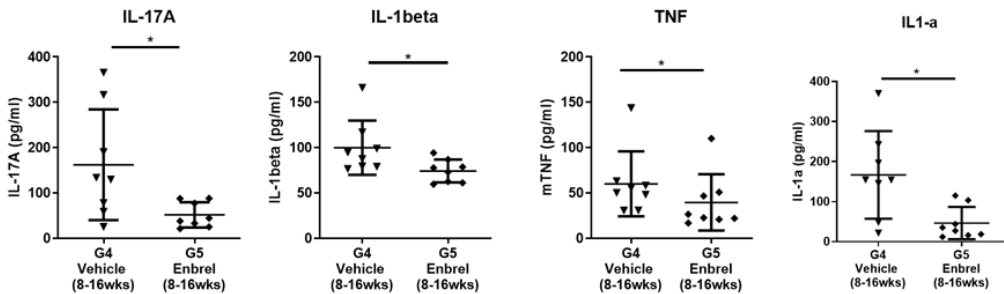


mTNF/hTNFR1 dependent mouse model of Arthritis and IBD

TNF^{ΔARE}hTNFR1KI: mouse TNF overexpression in the context of hTNFR1. These mice develop spontaneously arthritis, IBD and heart valve pathology

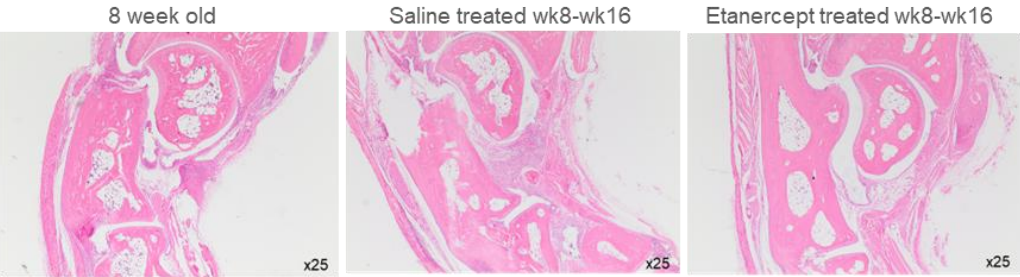
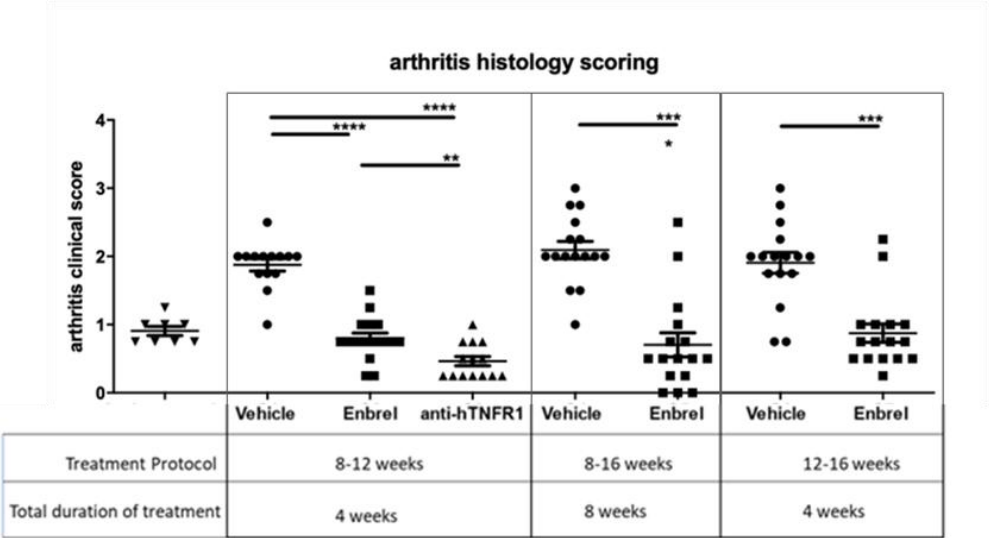


Cytokine
legendplex analysis
of ilea Thick Organ
Cultures



mTNF/hTNFR1 dependent mouse model of Arthritis and IBD

TNF^{ΔARE}hTNFR1KI: mouse TNF overexpression in the context of hTNFR1. These mice develop spontaneously arthritis, IBD and heart valve pathology



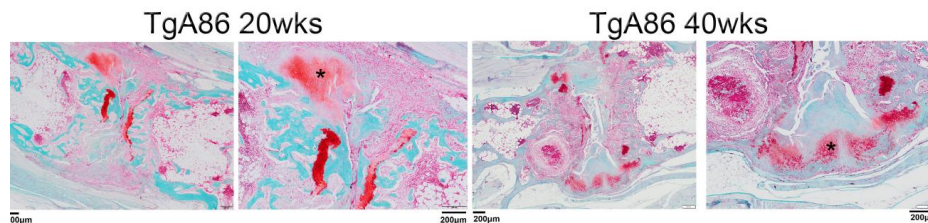
mTNF dependent mouse model of Spondyloarthritis (Spontaneous Model)

TgA86:

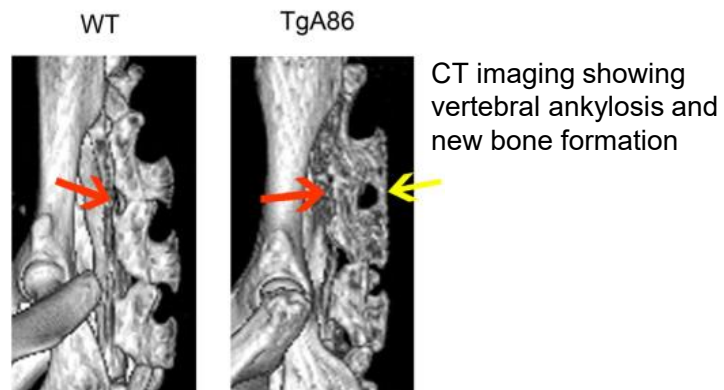
Transmembrane mouse TNF overexpression
Spontaneous development of SpA pathology signs

tmTNF-Dependent SpA Model

- Development of peripheral arthritis pathology
- Development of axial spondylitis pathology
- Ectopic new bone formation
- Systemic bone loss
- Comorbid heart valve pathology



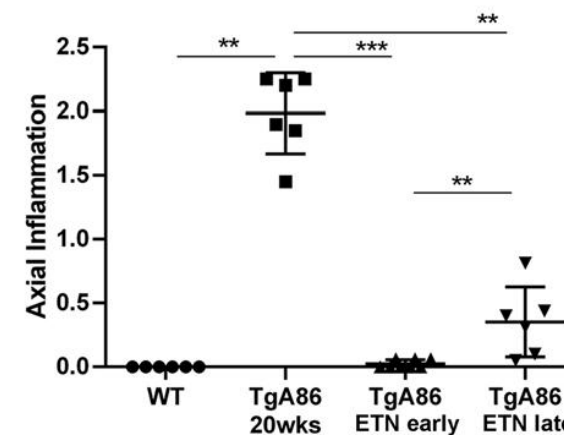
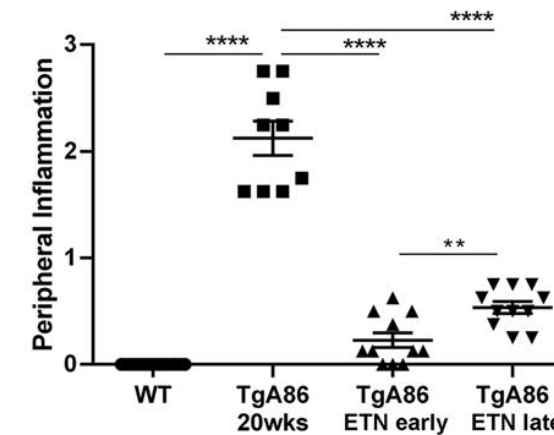
s/o staining showing new bone formation



CT imaging showing
vertebral ankylosis and
new bone formation

Model validated with:

Enbrel (Etanercept)



hIL17 dependent mouse models

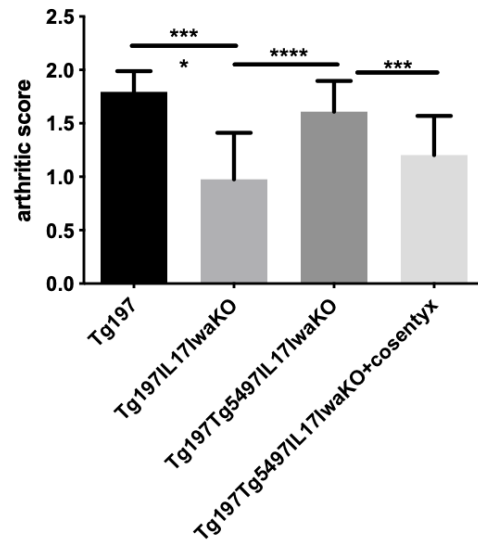
Combined with spontaneous and induced disease models

TghIL17mIL17KO: express normally regulated hIL17 in the absence of mIL17

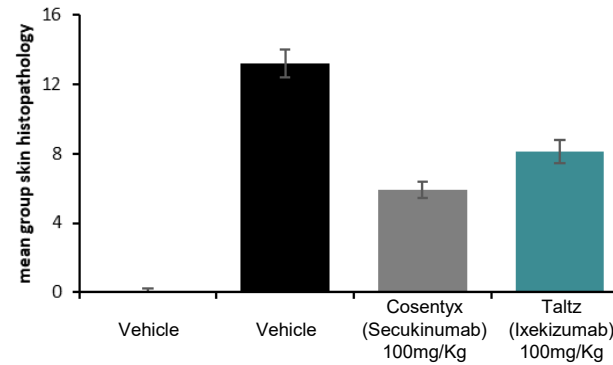
Models validated with:

- Cosentyx (Secukinumab)
- Taltz (Ixekizumab)

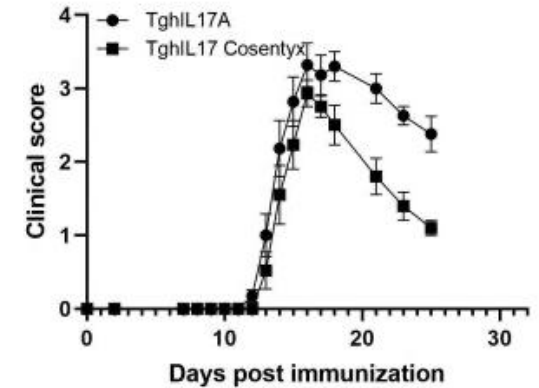
Tg197/TghIL17a Arthritis



TghIL17a IMQ-induced Psoriasis

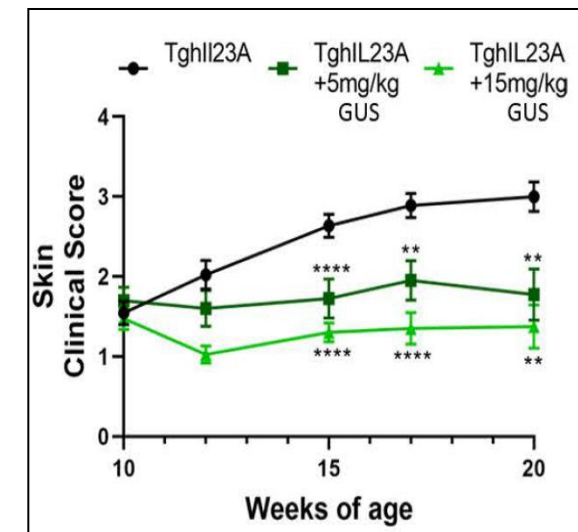
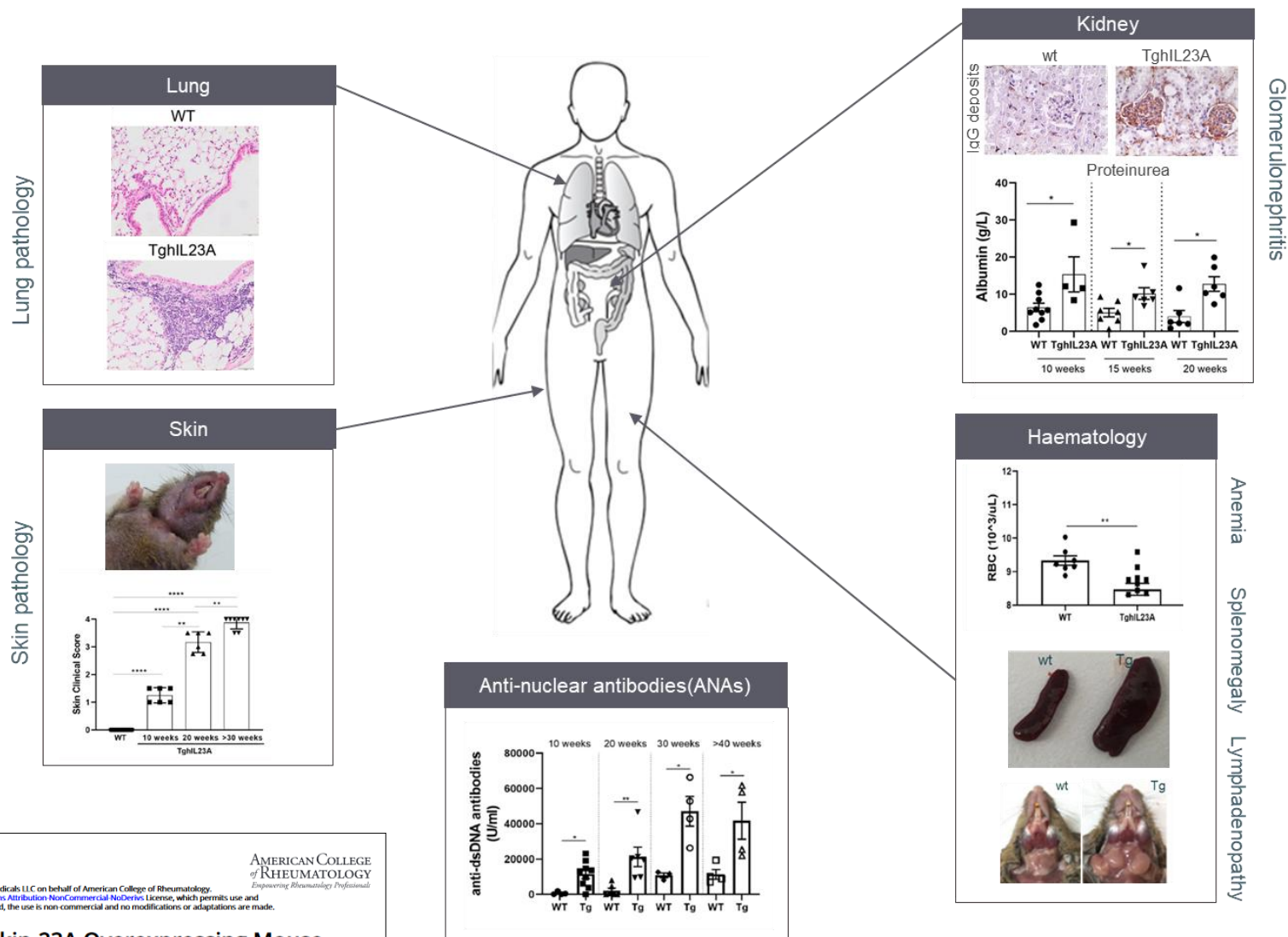


TghIL17a MOG-Induced EAE

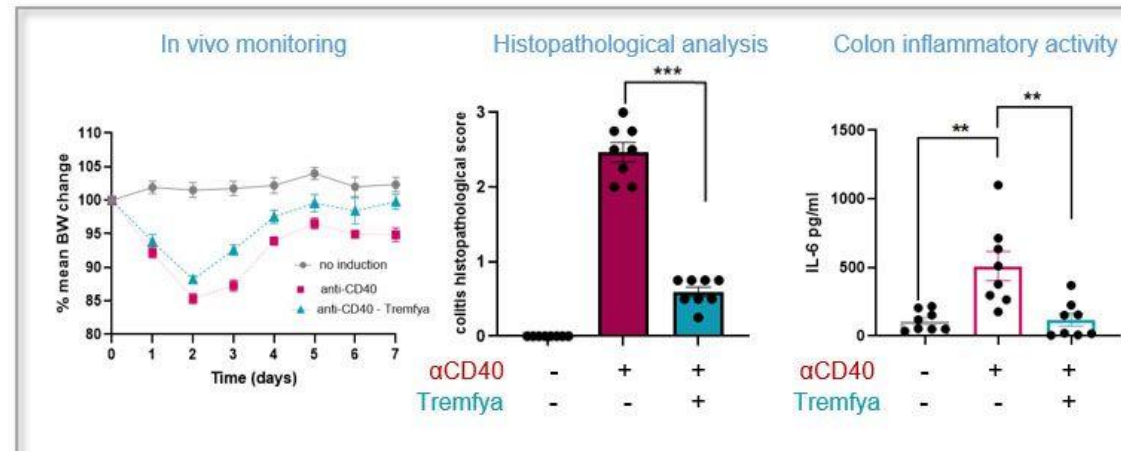
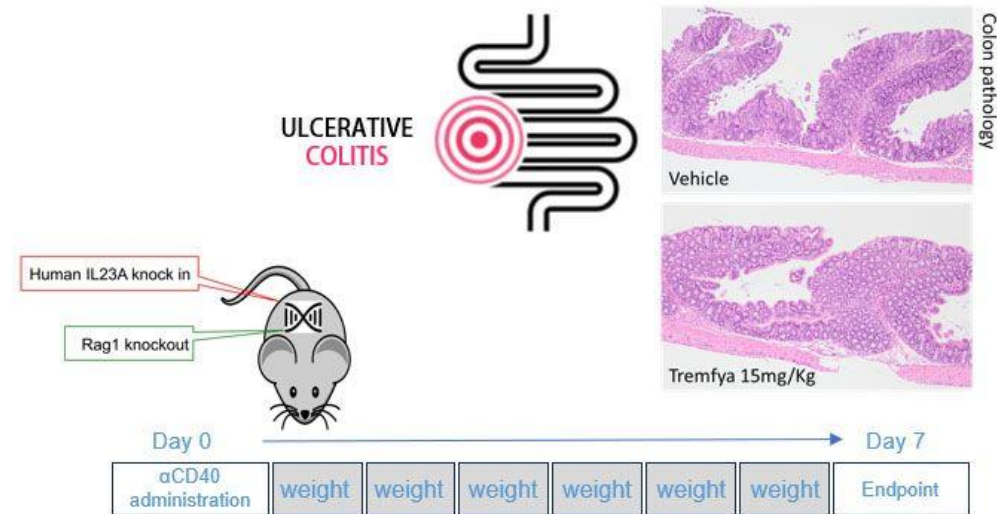


hIL23A dependent mouse model of lupus (Spontaneous Model)-Transgenic hIL23p19

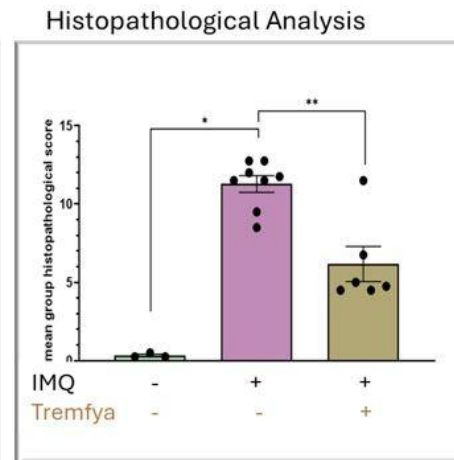
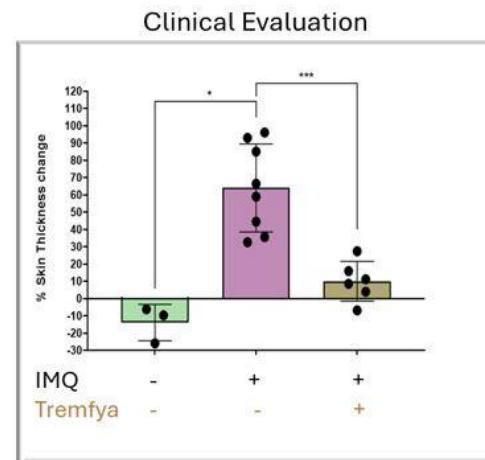
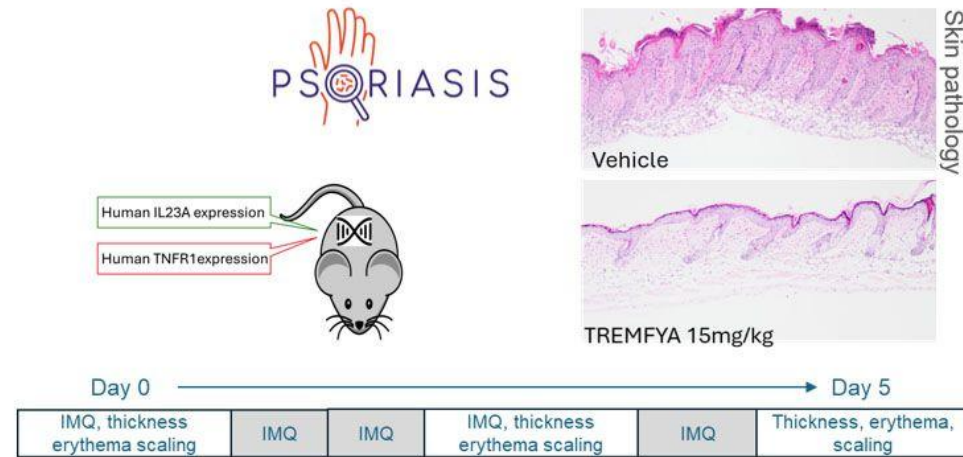
Lupus



hIL23A dependent mouse model of colitis (Induced Model)-hIL23p19 Knock In mouse



hIL23A dependent mouse model of psoriasis (Induced Model)- hIL23p19 Knock In mouse



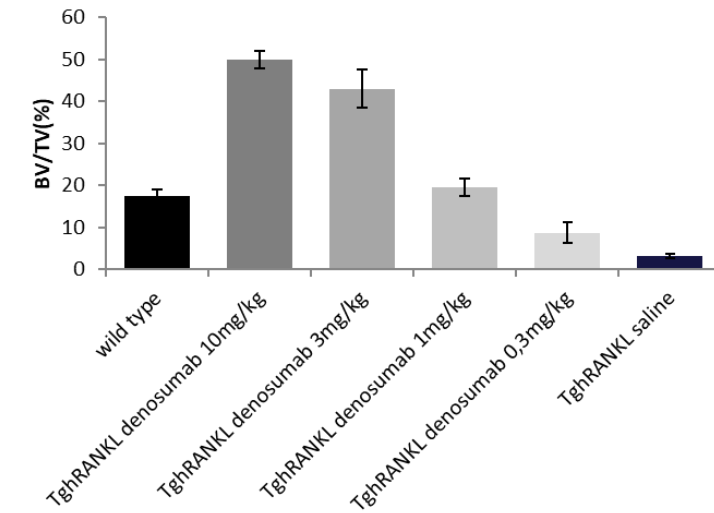
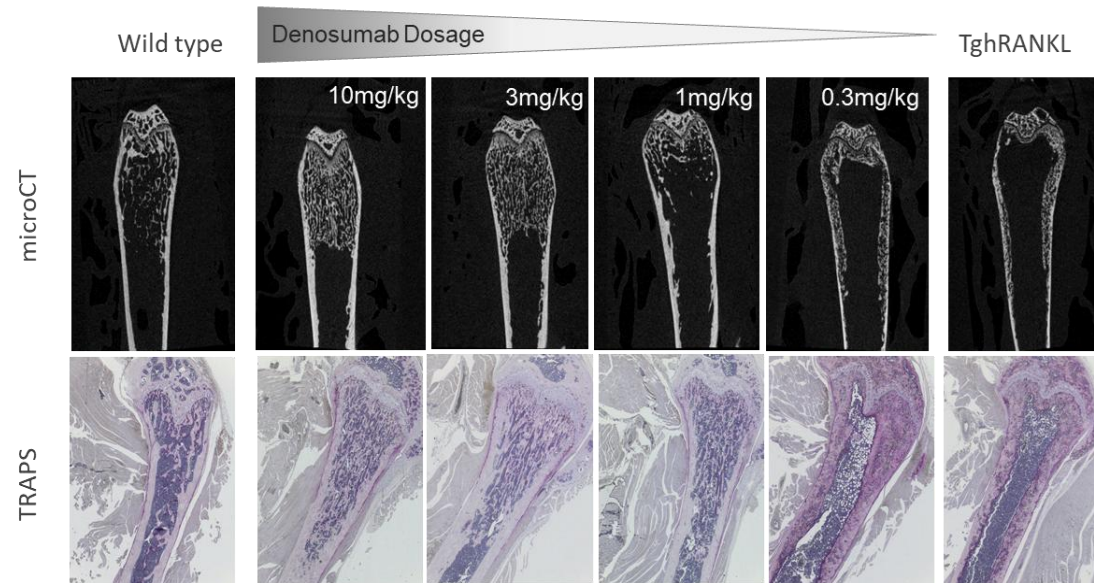
hRANKL dependent mouse model of Osteoporosis (Spontaneous Model)

TghRANKL:
hRANKL overexpression
Spontaneous development of osteoporosis

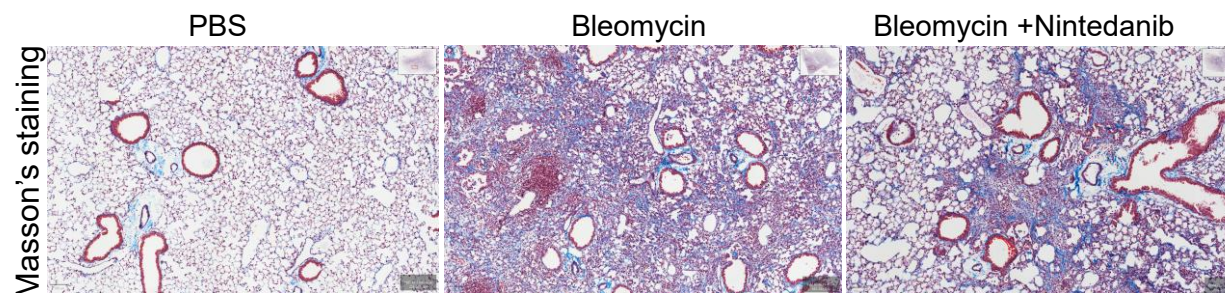
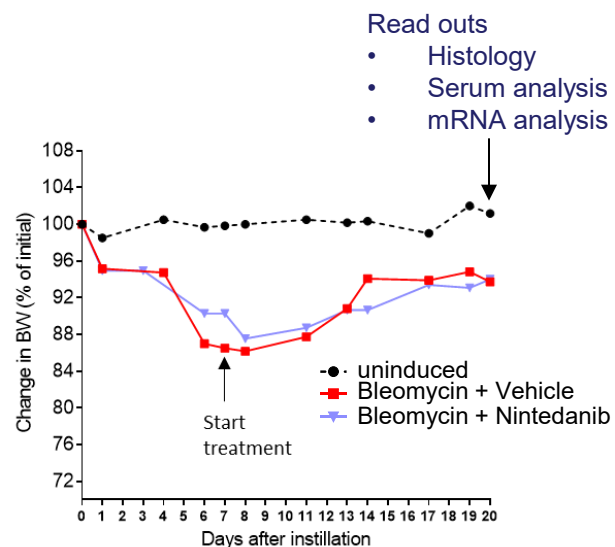
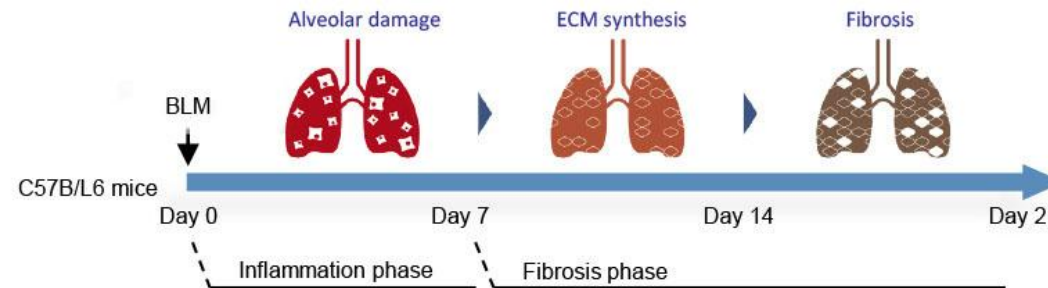
Model validated with:
Prolia (Denosumab)

TghRANKL Osteoporosis Model

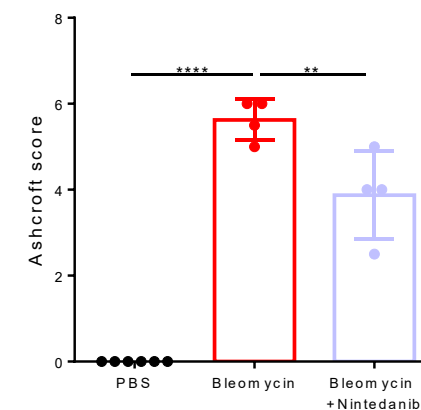
- Osteoporosis development with 100% penetrance
- Loss of trabecular bone
- Increased cortical porosity



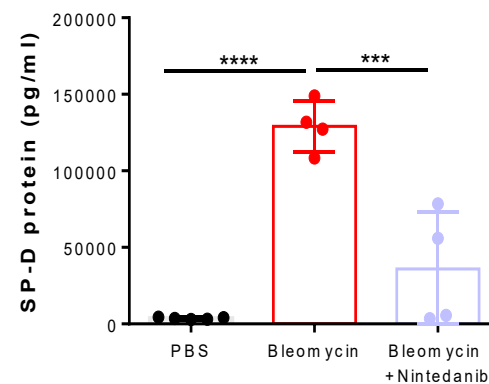
Bleomycin-induced interstitial lung disease (IPF) (Induced Model)



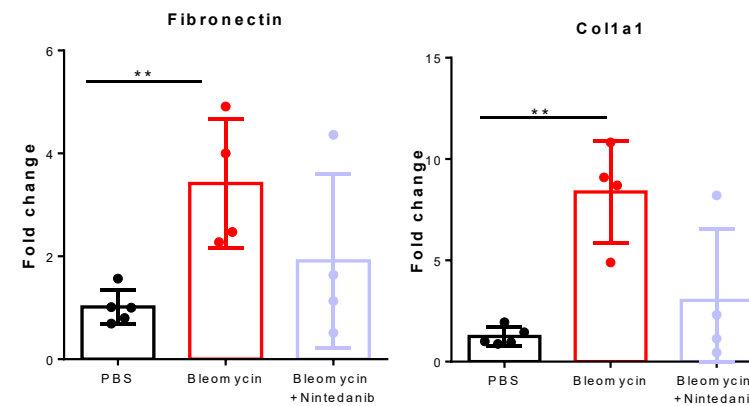
Histopathological Analysis



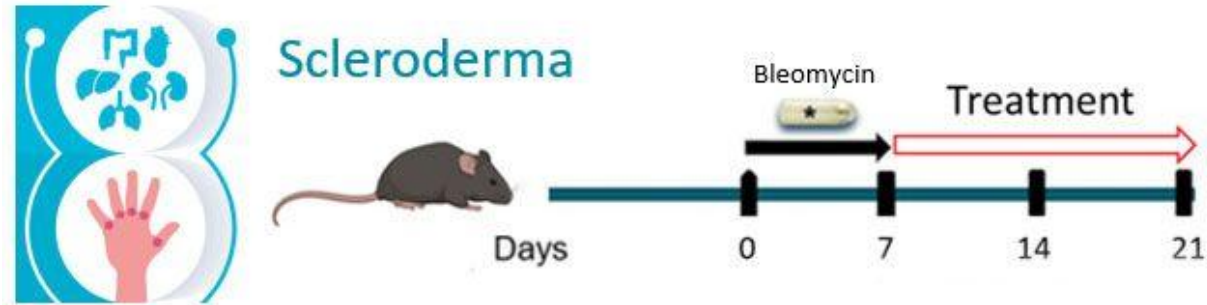
Serum Analysis



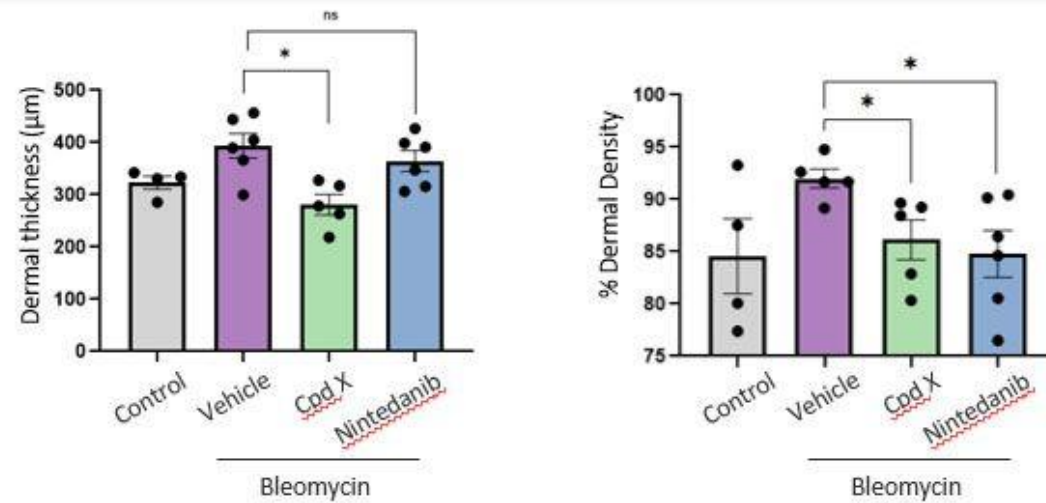
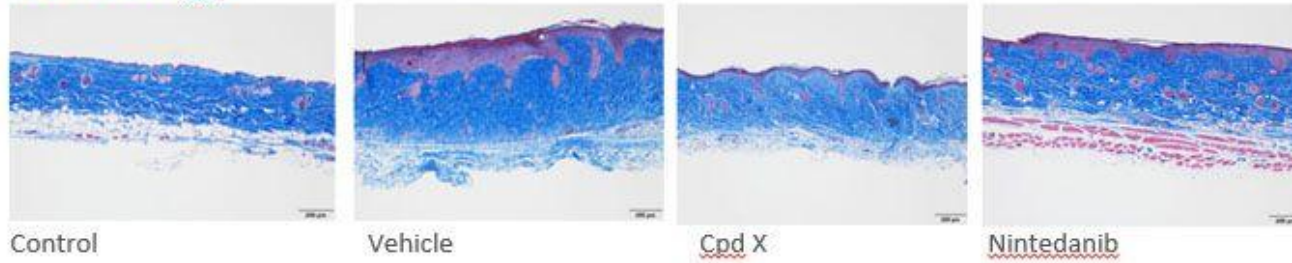
qPCR mRNA analysis of lung tissue



Bleomycin-induced Scleroderma Model (Induced Model)

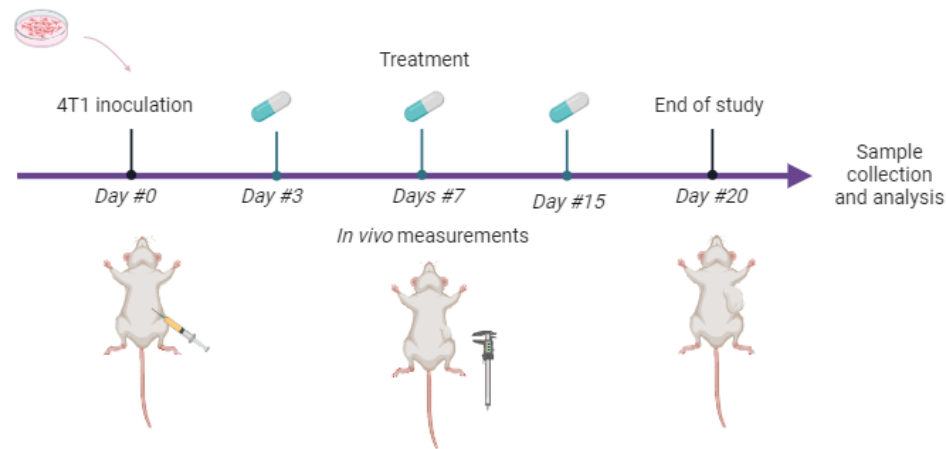


Skin Histology



4T1 Breast Cancer Model (Syngeneic Model)

Cancer

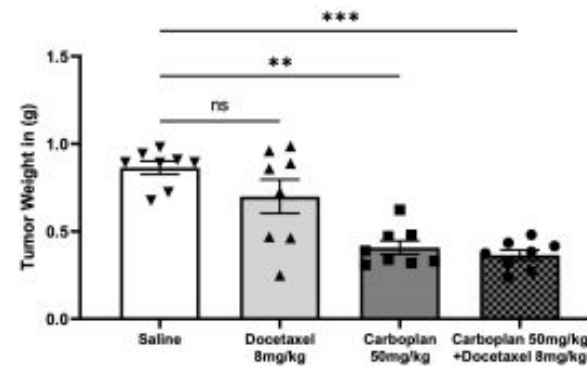
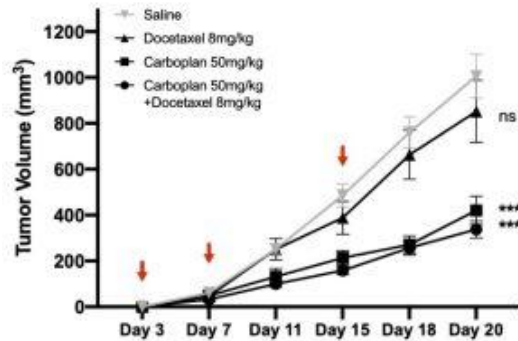


Read outs

- Tumor volume, measurements by caliper



- Tumor weight, at the end of the in vivo part
- Histology (optional)



4T1 Metastatic mouse breast cancer cells

Mice 6-8 weeks old female Balb-c

Implantation Orthotopic in the breast fat pad

Monitoring Weight and tumor measurement 3 /week

Treatment Systemic or local

Duration 3 weeks or until tumors reach 1500mm³

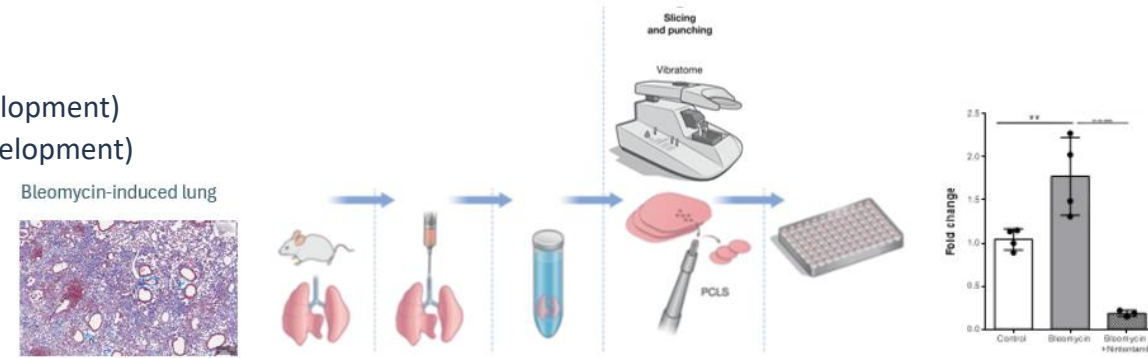
Other syngeneic cancer models available include LLC, GL261, B16F10 etc.

In vitro: 4T1 cell line is also available for in vitro cellular assays, such as cell apoptosis, proliferation, viability and wound healing

Moving towards New Approach Methodologies (NAMs)

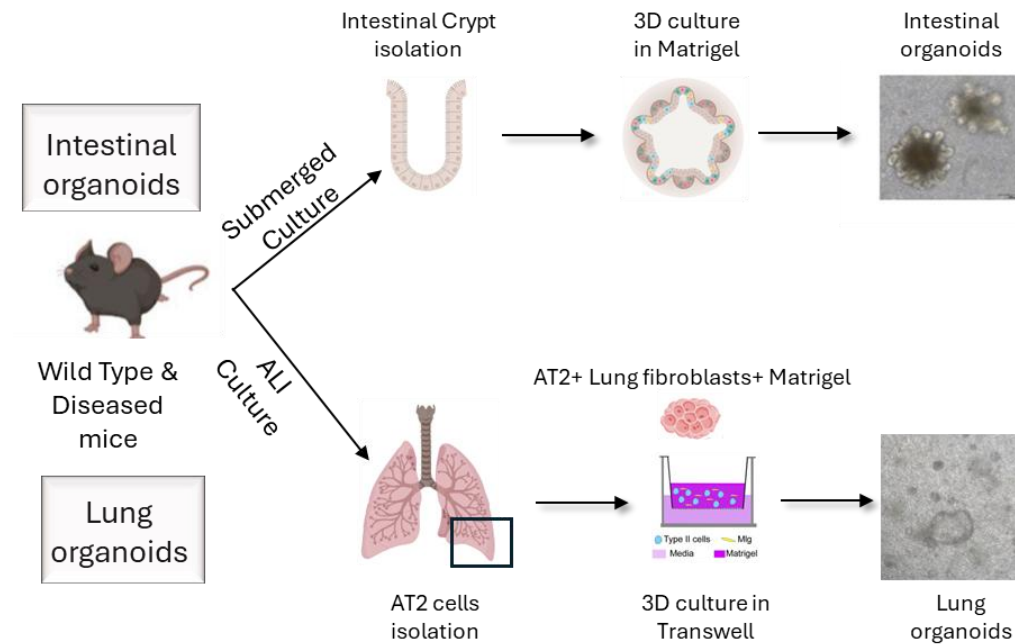
Expanded Portfolio with Organotypic Cell Cultures

- Thick organ cultures (intestine, skin)
- Precise cut lung sections (PCLS)
- Precise cut liver sections (under development)
- Precise cut heart sections (under development)



Organoids

- Air-liquid interface lung organoids
- Intestinal organoids





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Disease models

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SPONDYLOARTHRITIS	MULTIPLE SCLEROSIS
PSORIASIS	LUPUS
INFECTIOUS MODELS	PULMONARY FIBROSIS
ARTHRITIS	OSTEOPOROSIS
CANCER	SYSTEMIC SCLEROSIS

HUMANIZED MOUSE MODELS

Biomedcode offers mice humanized for the following targets:

- TNF
- TNFR1
- IL17
- RANKL
- IL23p19
- IL23p40
- hTL1a**

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