Asclepiumm Taiwan

INNOVATIVE BIO-DRUGS DELIVERY & PEPTIDE DRUGS

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Introduction

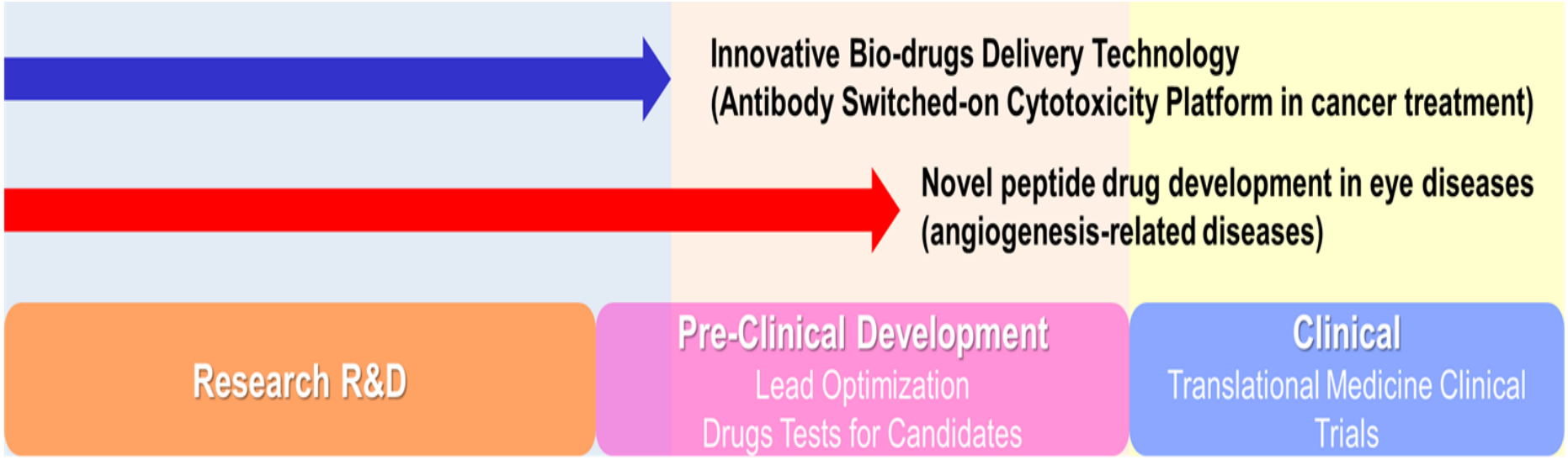
Asclepiumm Taiwan Co., Ltd is a new drug development bio-tech company. The Company is focused on the discovery and development of first-in-class antibody drugs and peptide drugs for cancer and eye diseases.

The Company's program is based on its innovative bio-drugs delivery technology, Antibody Switched-on Cytotoxicity (ASC) platform, which utilizes antibody targeted therapy and special linkers which activate in the tumor microenvironment and then deliver the payloads into cells.

The Company is developing ASC-S9, the ASC platform designed oncology product candidate, which is an antibody with alternative scaffold for cancer therapies, including lung cancer, breast cancer, prostate cancer, liver cancer, esophageal cancer, and pancreatic cancer.

The Company is also conducting a serial of Dsg2 peptide drugs for eye diseases. Dsg2 peptide drugs are novel pathway blockers of angiogenesis for developing new treatments of eye diseases, including retinopathy of prematurity (ROP), diabetic macular edema (DME), and wet age-related macular degeneration (AMD).

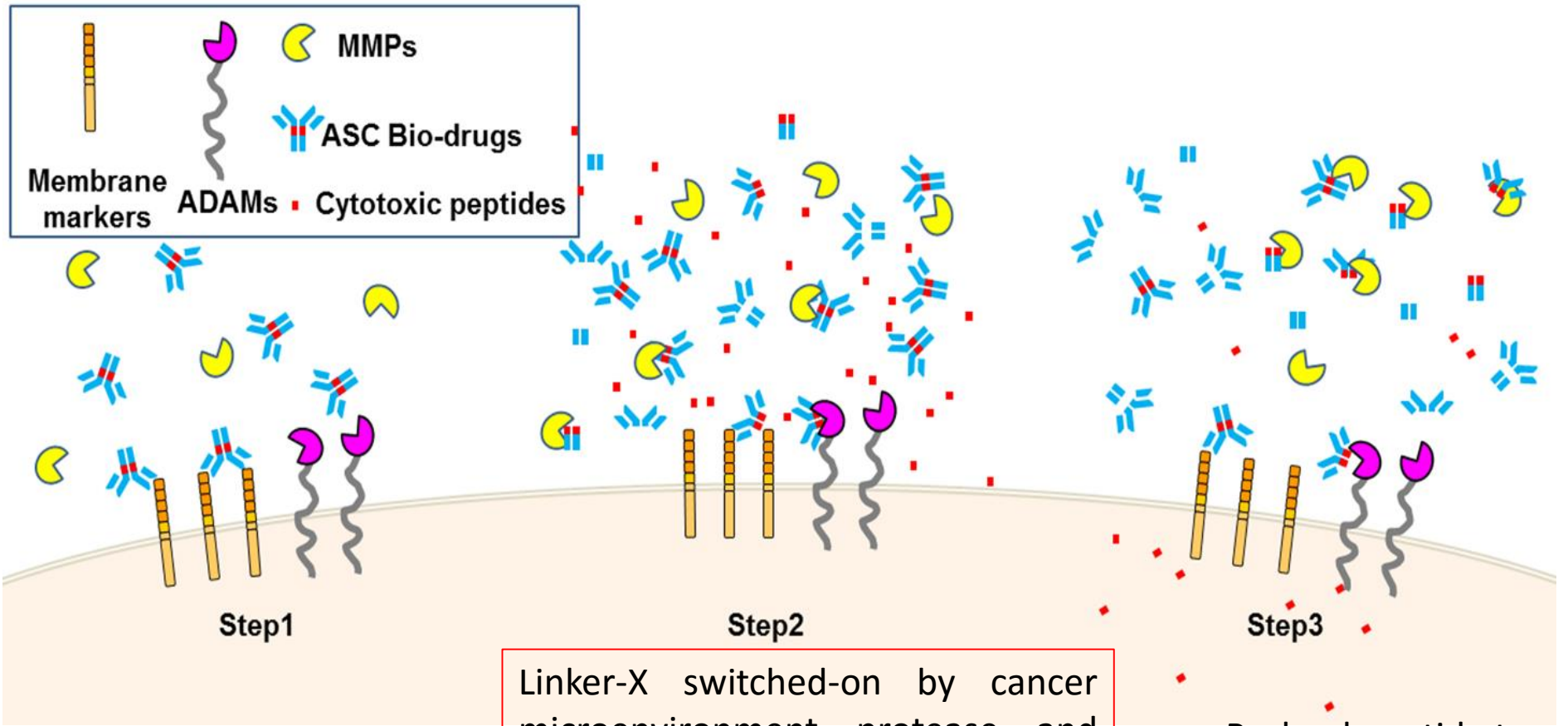
Innovation



(1) Innovative Bio-drugs Delivery Technology

(2) Novel Peptide Drug Development

Antibody Switched-on Cytotoxicity (ASC) Platform

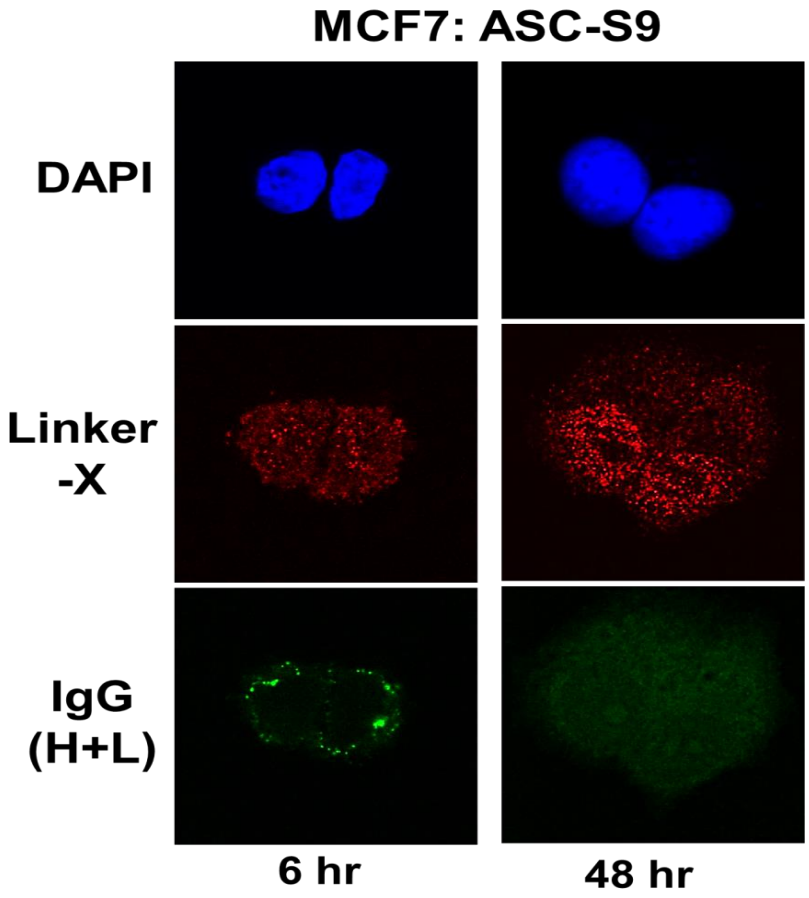


Abs to recognize cell surface markers

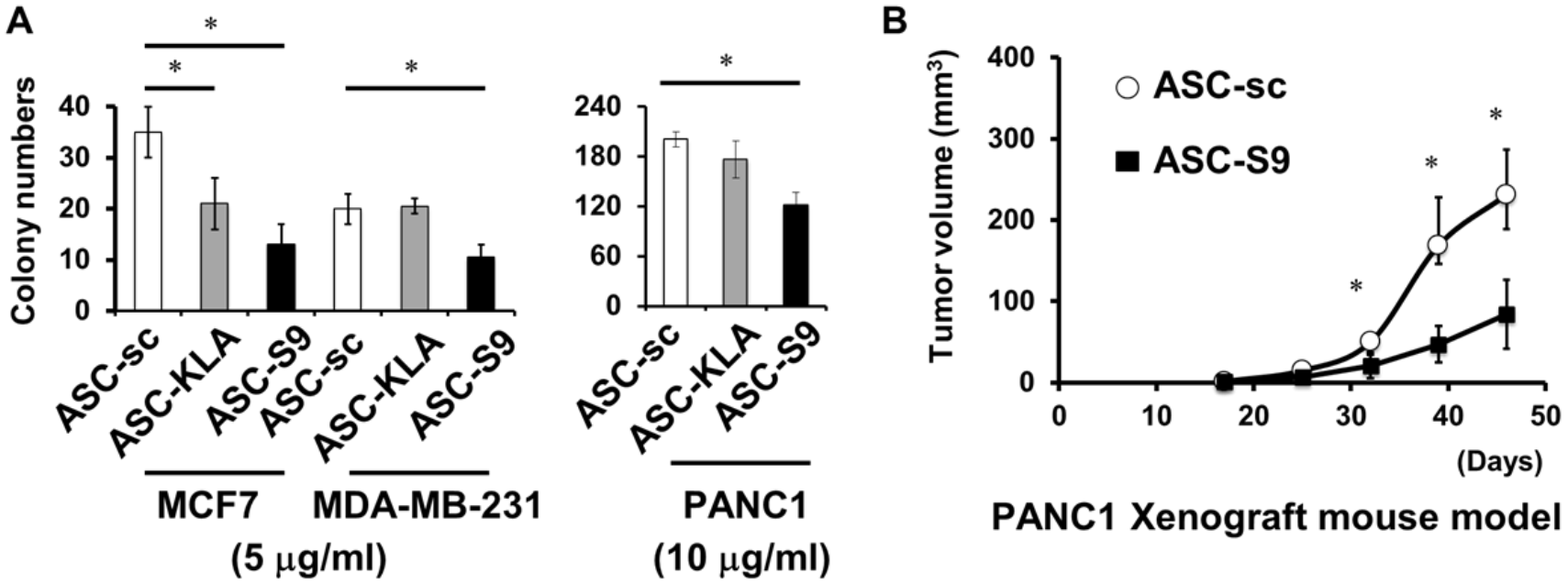
Linker-X switched-on by cancer microenvironment protease and then deliver the payloads into cells

Payload peptide to kill the cancer cells

Intra-cellular and Intra-nucleus payload peptide delivery



In vitro and *In vivo* functions



* **Proof of concept in xenograft model**

ASC platform vs. ADC

	Heterogeneous	Drug delivery	Production
ADC	Mixtures of 0-8 drug species per antibody	Endocytosis (degraded inside tumor)	Antibodies and drugs conjugation
Site-specific ADC	Near homogeneous: Drug-to-Antibody ratio (DAR): 2 or 4	Endocytosis (degraded inside tumor)	Antibodies and drugs conjugation (chemical or enzymatic)
ASC Bio	Homogeneous	Cell Penetration	No conjugation (Fusion protein)

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ASC platform Application

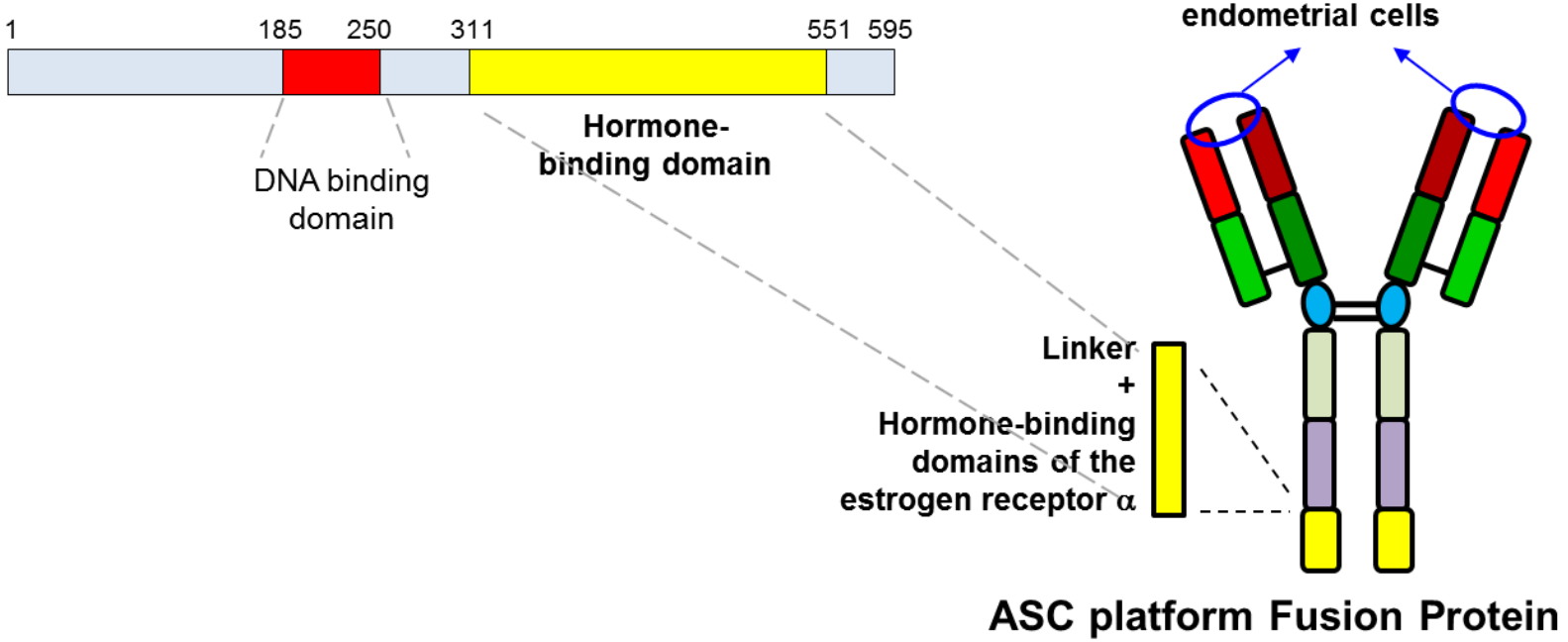
Diversities	MOA Designed	Benefits
Cancer Treatment	Cytotoxic payloads	Different types of cancer
Enzyme replacement therapy	Intra-cellular payload delivery (Lysosome-independent)	Enzyme deficiency diseases Metabolic disorder
Tissue-specific hormone inhibitor	Intra-nucleus payload delivery	Transcriptional regulation of hormone in specific tissues
Bio-better drugs	mAbs fusing with cytotoxic payload peptides	From bio-similar to bio-better
Personalized medicine	Target cell type specific, Micro-environment specific, Payload mechanism specific	Safer and Effective Bio-innovation Drugs

Tissue-specific hormone inhibitor

Estrogen Receptor α (ESR1 gene)

a ligand-activated transcription factor composed of several domains important for hormone binding, DNA binding, and activation of transcription

UniProtKB - P03372 (ESR1_HUMAN)



Application:

Adenomyosis and Endometriosis

Summary: ASC Platform

- **No chemical conjugation of ADC-like Bio-Drugs**
- **Intra-cellular and intra-nucleus delivery**

Application in Different Indications:

1. Cancer
2. Hormone therapy
3. Immunotherapy
4. Cell therapy: TCR and CAR T cell
5. Gene therapy
6. Rejuvenation (regulation of senescence pathway)
7. Weight loss (turn white fat to brown fat)

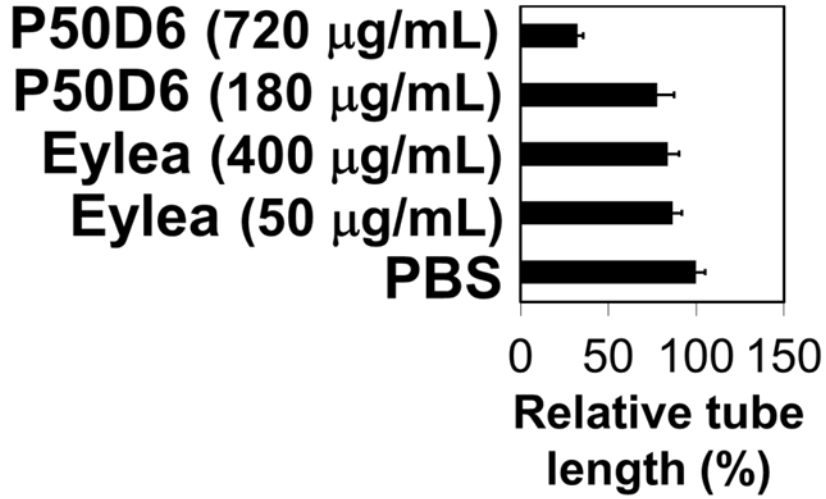
DSG2 peptide drugs

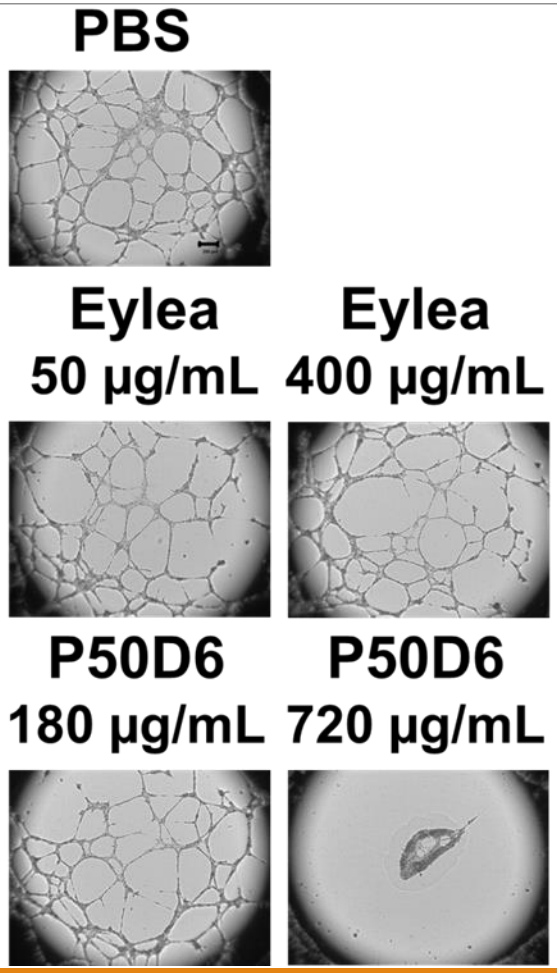
Sequence-based designed

&

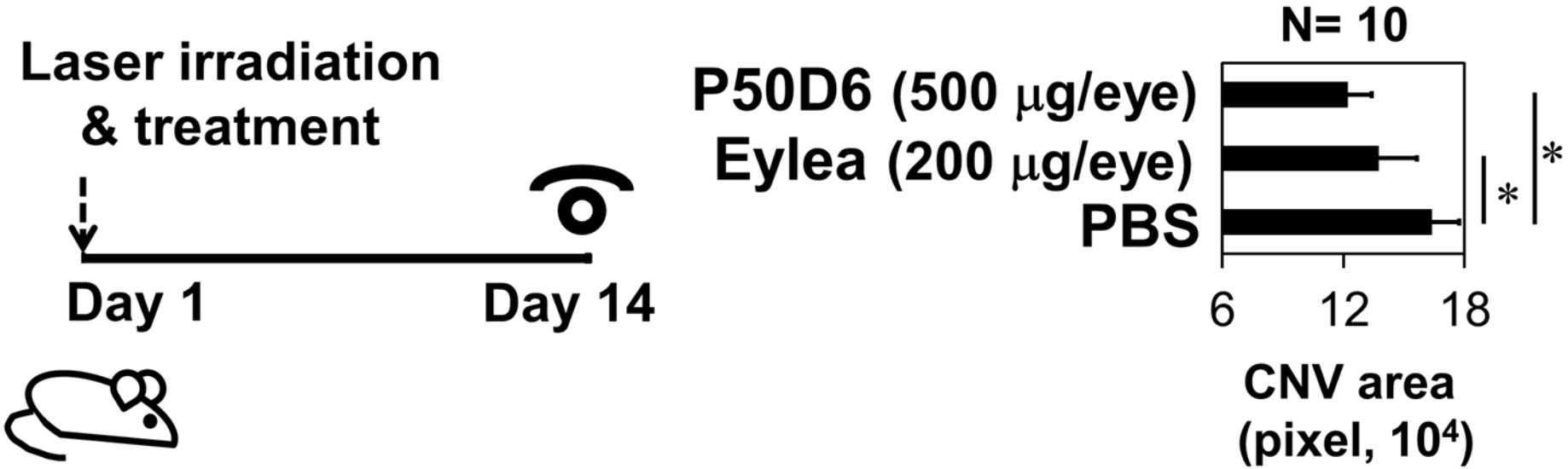
Structure-based designed

P50D6 peptide inhibits HUVEC angiogenesis





P50D6 peptide inhibits rat laser-induced CNV model



Laser-induced CNV model: Laser-induced Choroidal Neovascularization model

Dsg2 peptide vs. VEGF antagonist

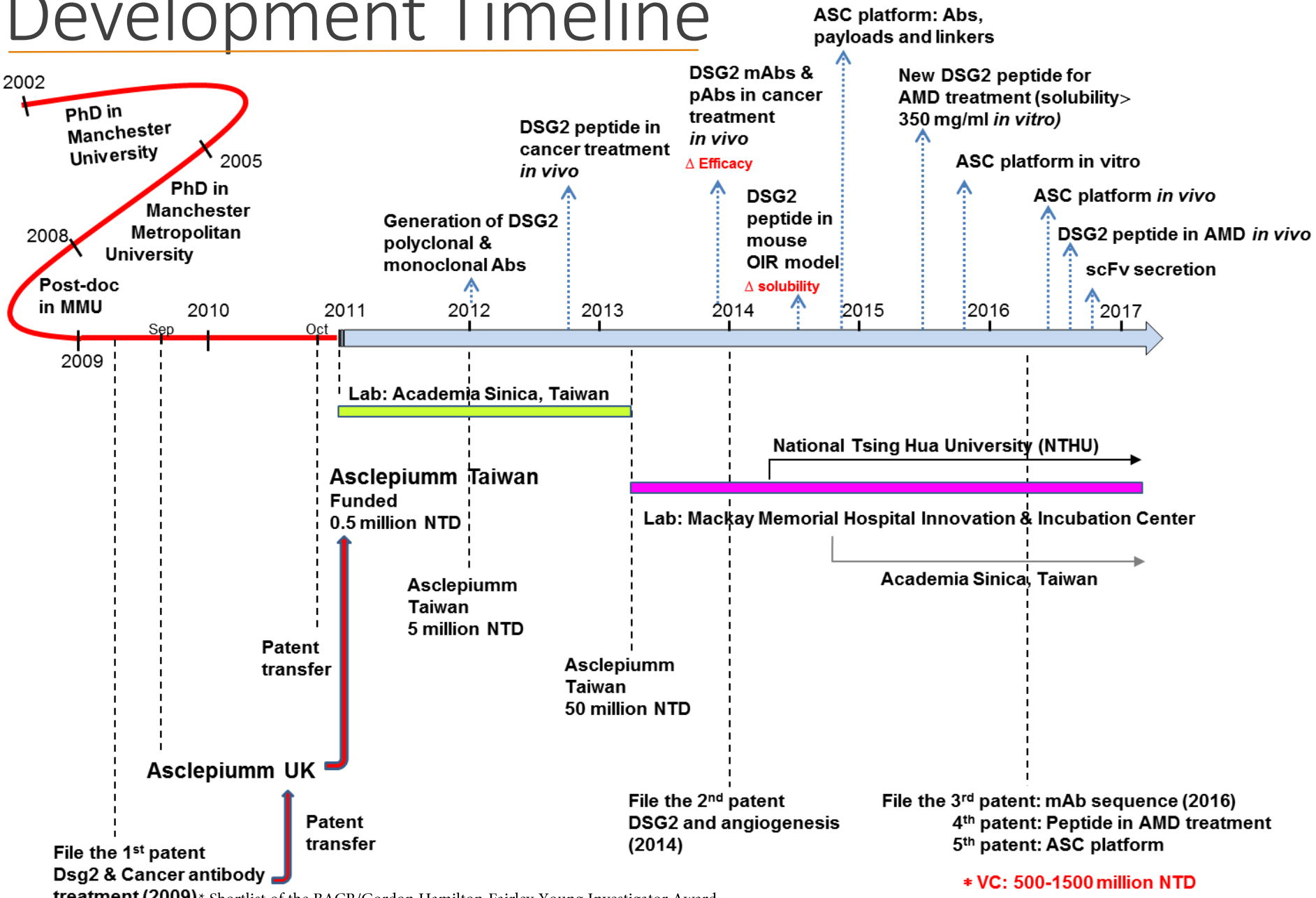
	MOA	Endothelial cell response	Production	Clinical Wet-AMD
Eylea	Anti-VEGF	(O) HUVEC (O) HAEC (X) EPC	MW (97 kDa) Fusion-protein CHO cells expression	Intra-vitreal injection 40 mg/ml
P50D6	Dsg2 peptide MMP ↓ SDF1 ↓	(O) HUVEC (O) HAEC (O) EPC *	MW (1.8 kDa) Synthetic peptide	Intra-vitreal injection 200 mg/ml Topical use

*EPC: Endothelial progenitor cell

Summary: Dsg2 peptide

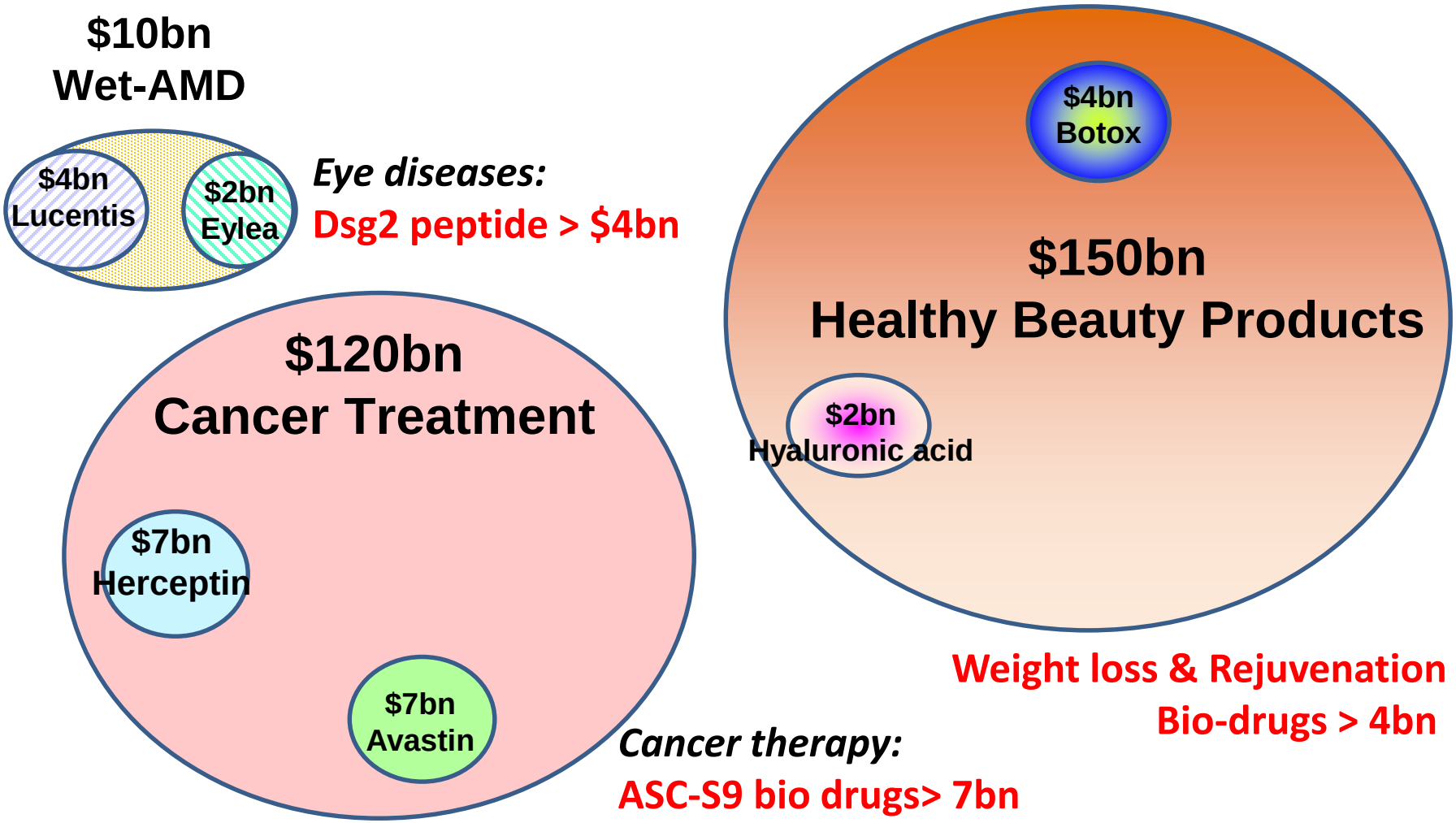
- **Block VEGF and other angiogenesis pathway**
- **Response in different types of endothelial cells**
- **Synthetic peptides are low-cost (compare to protein drugs)**
- **With MW (1.8KDa) and great solubility, suitable for intravitreal injection and topical use**

Development Timeline



* Shortlist of the BACR/Gordon Hamilton-Fairley Young Investigator Award

Market Potential



Intellectual Property

2009
Dsg2 antagonist for
Cancer treatment
(First invention)
Using antibodies and
Dsg2 peptides

2014
DSG2 peptide: KC21
in angiogenesis-related
diseases

2016
mAb: 3D4, 13D3,
CDR regions sequences and medical
applications for cancer treatment

2016
Peptide: P50D6
Excellent solubility, Blocking
Angiogenesis and Vasculogenic mimicry

2016
ASC platform (Ab Fusion Protein)
Linker and Payload: unique aspects of
normal cell protection, and targeted cell
micro-environment-switched on toxicity.

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Intellectual Property (developing)

A. scFv: secretion protein production	D. Bio-panning of the Peptide library
B. X-linkers development	E. Antibody mimetic
C. Peptide payloads development	F. Indications: Eye diseases; Cancer; Hormone therapy

Team Background

Dr. Min-Che Chen **(Funder and CEO)**	Taipei Municipal Jianguo High School National Tsing Hua University, Taiwan (BSc. Life Sciences) National Taiwan University (MSc.) Manchester University, UK Manchester Metropolitan University, UK (PhD)	Discovered the **novel Dsg2 function** in 2004 Develop the **Dsg2 antagonists** in 2009 **Inventor of Dsg2 patents**
Dr. Ya-Chuan Liu	National Tsing Hua University (PhD)	Protein Biochemistry
Dr. Po-Hao Chang	National Taiwan University (PhD)	Oncology
Dr. Ya-Ping Tsai	National Yang Ming University (PhD)	Molecular Cell Biology
Chun-Wei Chen	National Cheng Kung University (MSc.)	Immunology
Pei-Yi Lee	National Tsing Hua University (MSc.)	Protein expression

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Team Background (R&D)

Technic point of view

Protein expression

Biochemistry

National Tsing Hua University (NTHU)

Ab engineering

Mechanism

Animal Model

Academia Sinica, Taiwan

Contract Manufacture Organization (CMO)

Contract Research Organization (CRO)

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Institute of Nuclear Energy Research (INER)

National Health Research Institutes (NHRI)

MacKay Memorial Hospital

Department of ophthalmology
Dr. Chen

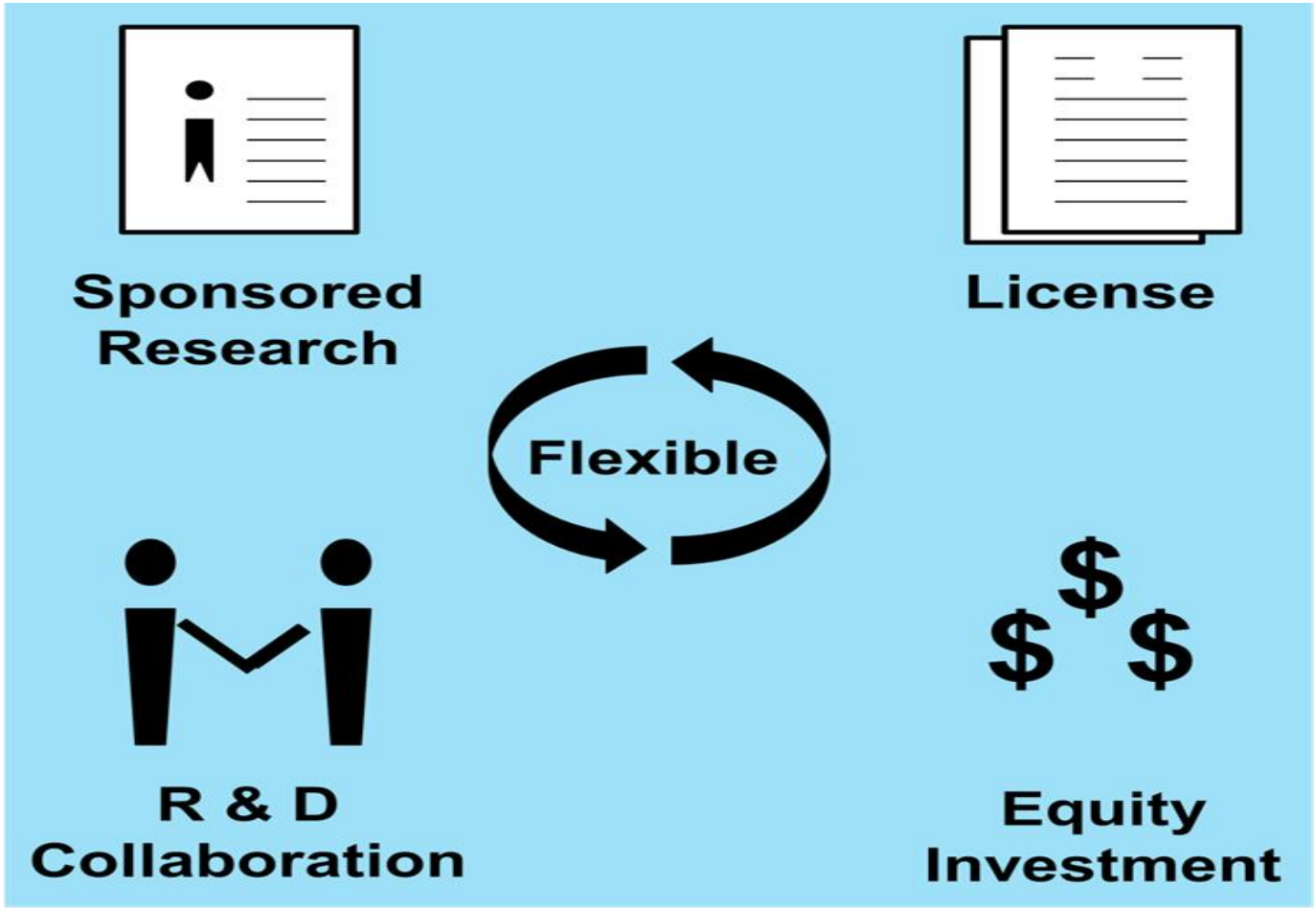
Department of oncology
Dr. Chen

Department of cardiovascular disease
Dr. Yeh

Department of pathology
Dr. Chen

CLINICAL OPINION

Future Plans



The Team
(from invention to idea drugs)