

Targeting Pro-MMP-7 and Syndecan-2 Interaction to Control Inflammatory Diseases

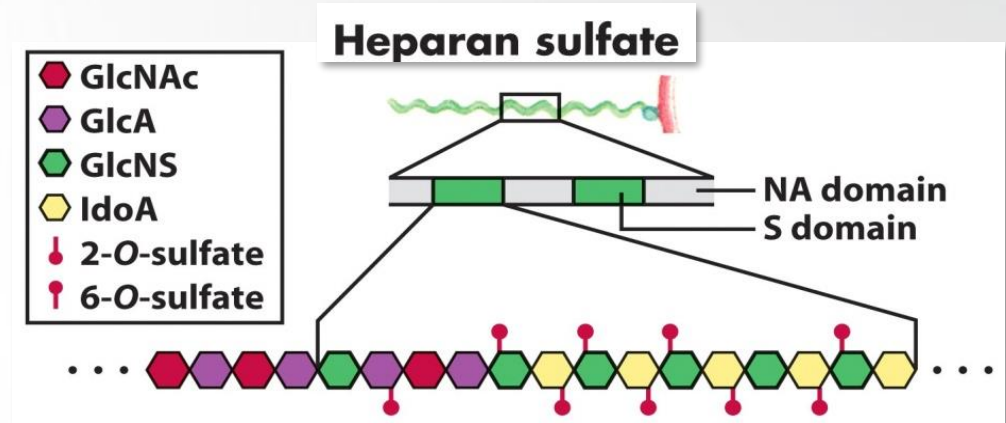
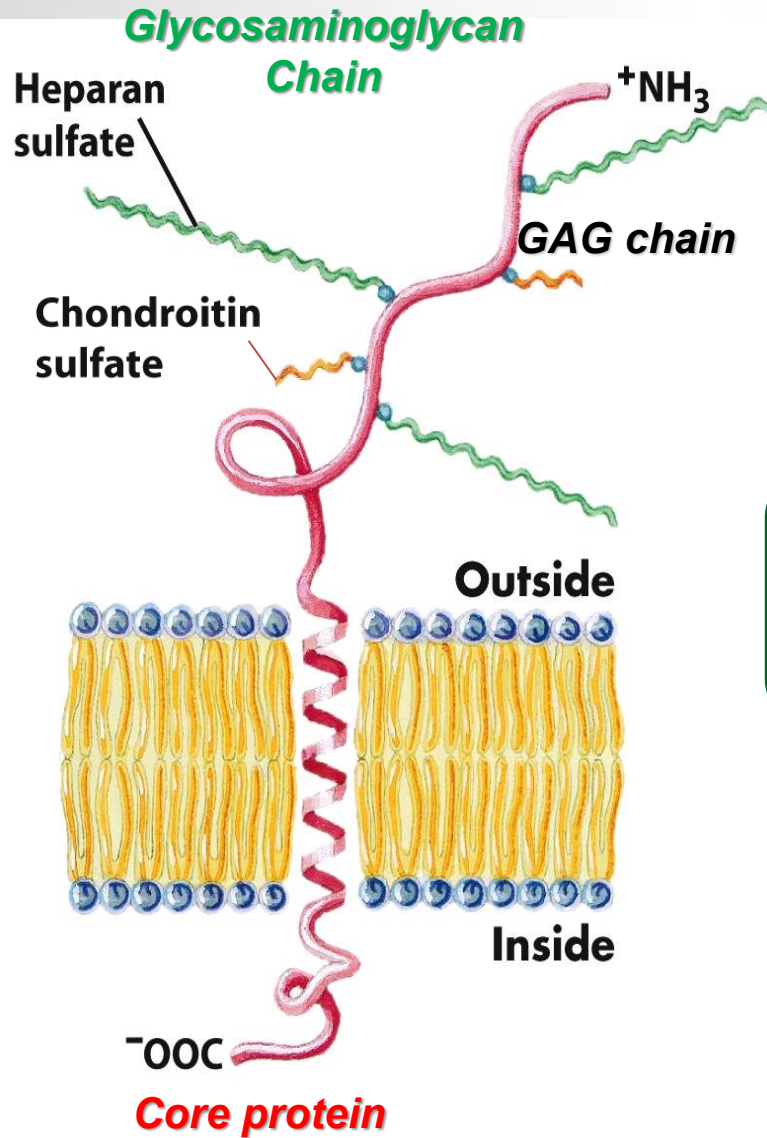
Eok-Soo Oh, Ph.D.

**Department of Life Science
Ewha Womans University**

Ewha,
Where Change Begins

SYNDECANS

Cell surface Heparan Sulfate Proteoglycans



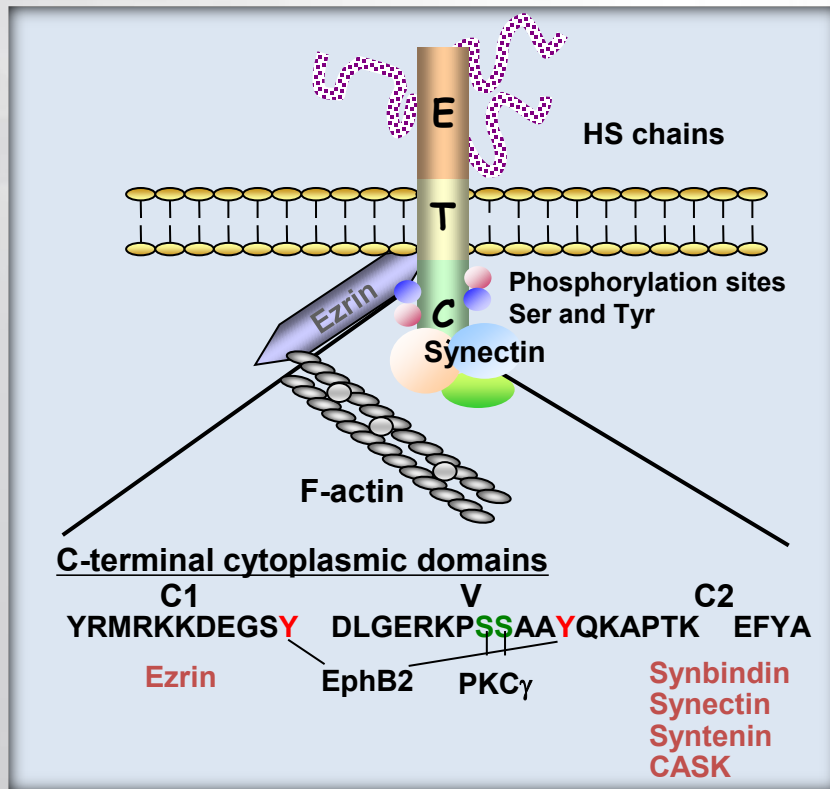
ECM Organizer

- Space filling (Organization)
- Reservoir of bioactive molecules
- Home for connective tissue cells

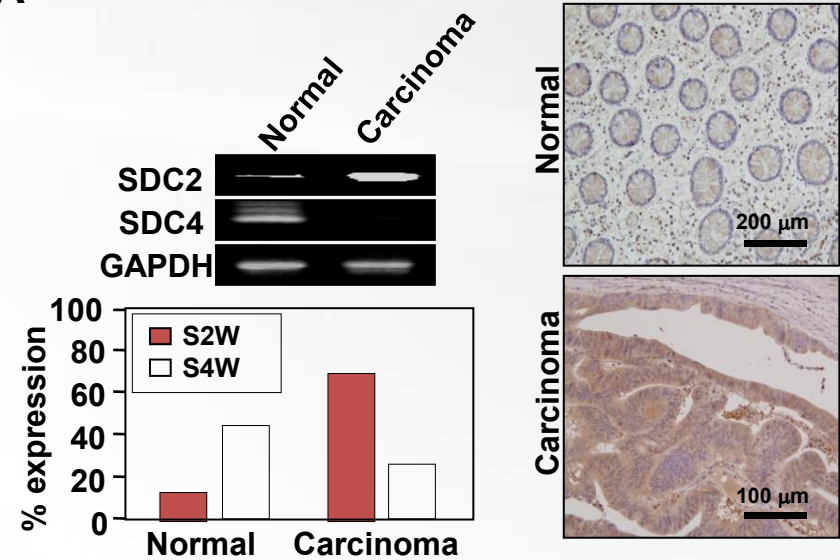
Signal Transducer

- Ligands**
- (i) ECM proteins (FN, LN, Col etc..)
 - (ii) GFs (*FGF*, *VEGF*, *PDGF*, *EGF* etc..)
 - (iii) Bioactive molecules (*Antithrombin III* etc)
 - (iv) Enzymes (*Acetylcholinesterase*, *MMPs*..)
 - (v) CAMs (*L-selectin*, *N-CAM*, *PECAM*..)
 - (vi) Pathogens (*Virus*, *Diphtheria toxin*, *Prion*.)

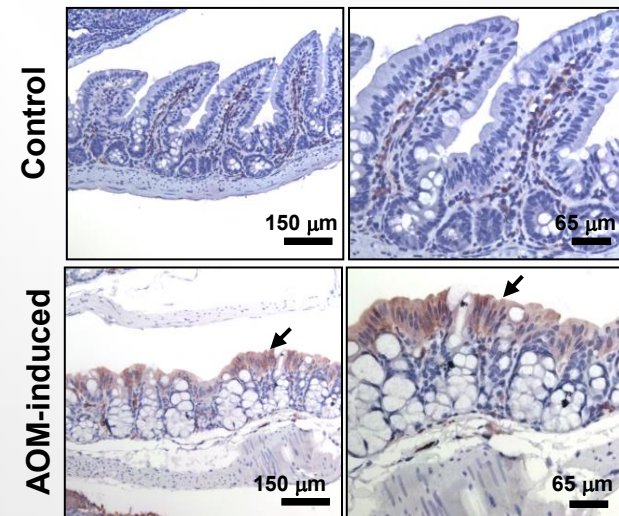
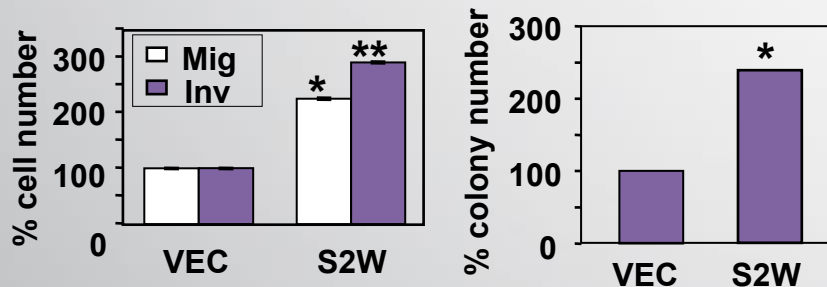
Syndecan-2 Expression is Increased During Colon Cancer Formation



A



B



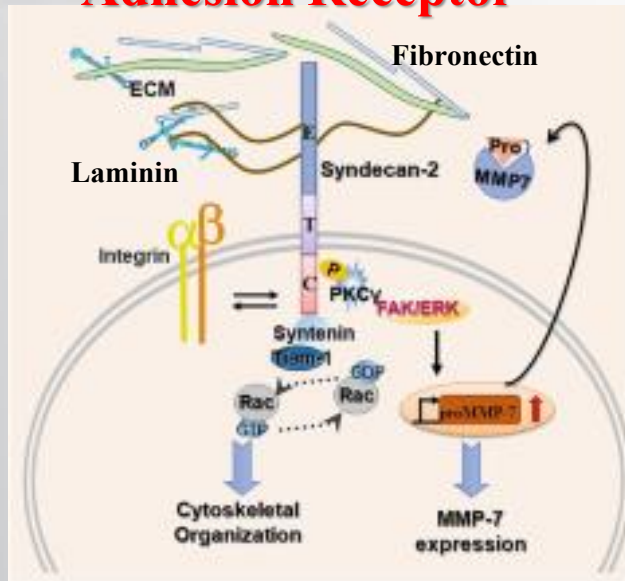
Multi-functional Role of Syndecan-2 During Colon Carcinogenesis

Abnormal
Epithelial cell

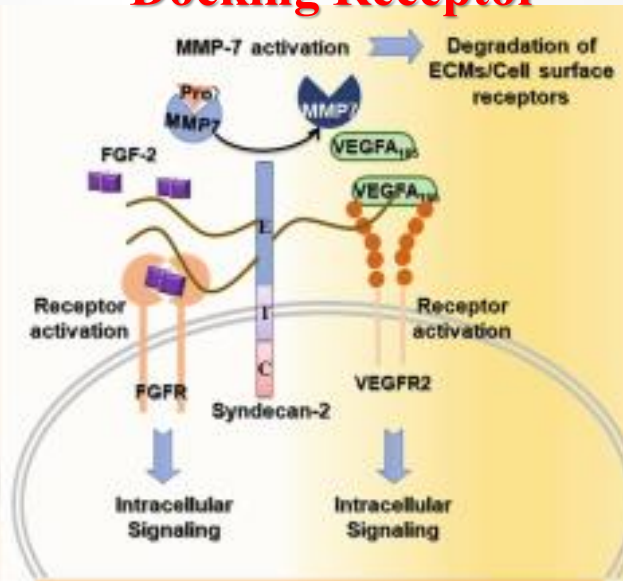
Regulatory Functions

Carcinoma

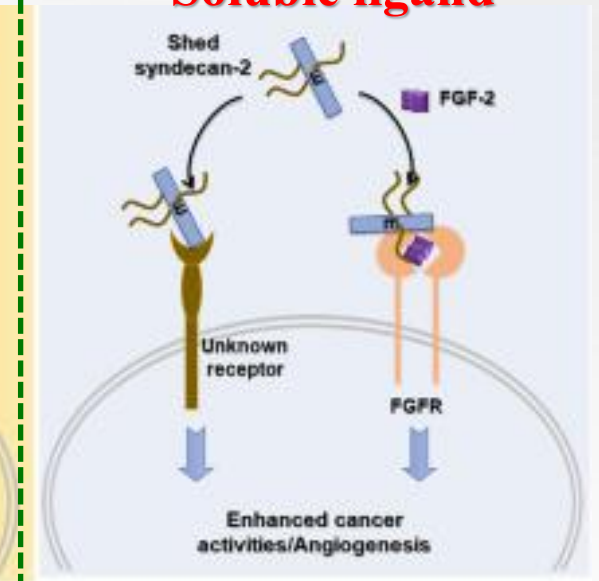
Adhesion Receptor



Docking Receptor



Soluble ligand



Syndecan-2 Mediates Adhesion and Proliferation of Colon Carcinoma Cells*

Oncogene

Decreased syndecan-2 expression correlates with trichostatin-A induced-morphological changes and reduced tumorigenic activity in colon carcinoma cells

Focal Adhesion Kinase Regulates Syndecan-2-Mediated Tumorigenic Activity of HT1080 Fibrosarcoma Cells

Syndecan-2 cytoplasmic domain up-regulates matrix metalloproteinase-7 expression via the protein kinase C γ -mediated FAK/ERK signaling pathway in colon cancer

Syndecan Transmembrane Domain Specifically Regulates Downstream Signaling Events of the Transmembrane Receptor Cytoplasmic Domain

Syndecan-2 Functions as a Docking Receptor for Pro-matrix Metalloproteinase-7 in Human Colon Cancer Cells*

scientific reports

Tyrosine 51 residue of the syndecan-2 extracellular domain is involved in the interaction with and activation of pro-matrix metalloproteinase-7

Journal of Inflammation Research

Open Access Full Text Article

Dovepress
ORIGINAL RESEARCH

Colocalization with MMP-7 in the Distal Colon is Crucial for Syndecan-2 Shedding in Dextran Sulfate Sodium-Induced Colitis Mice

Am J Physiol Cell Physiol 322: C960–C966, 2022.
First published April 6, 2022; doi:10.1152/ajpcell.00048.2022

Emerging role of syndecans in maintaining homeostasis of colon epithelium during inflammation

AMERICAN PHYSIOLOGICAL SOCIETY
CELL PHYSIOLOGY

Shed syndecan-2 enhances tumorigenic activities of colon cancer cells

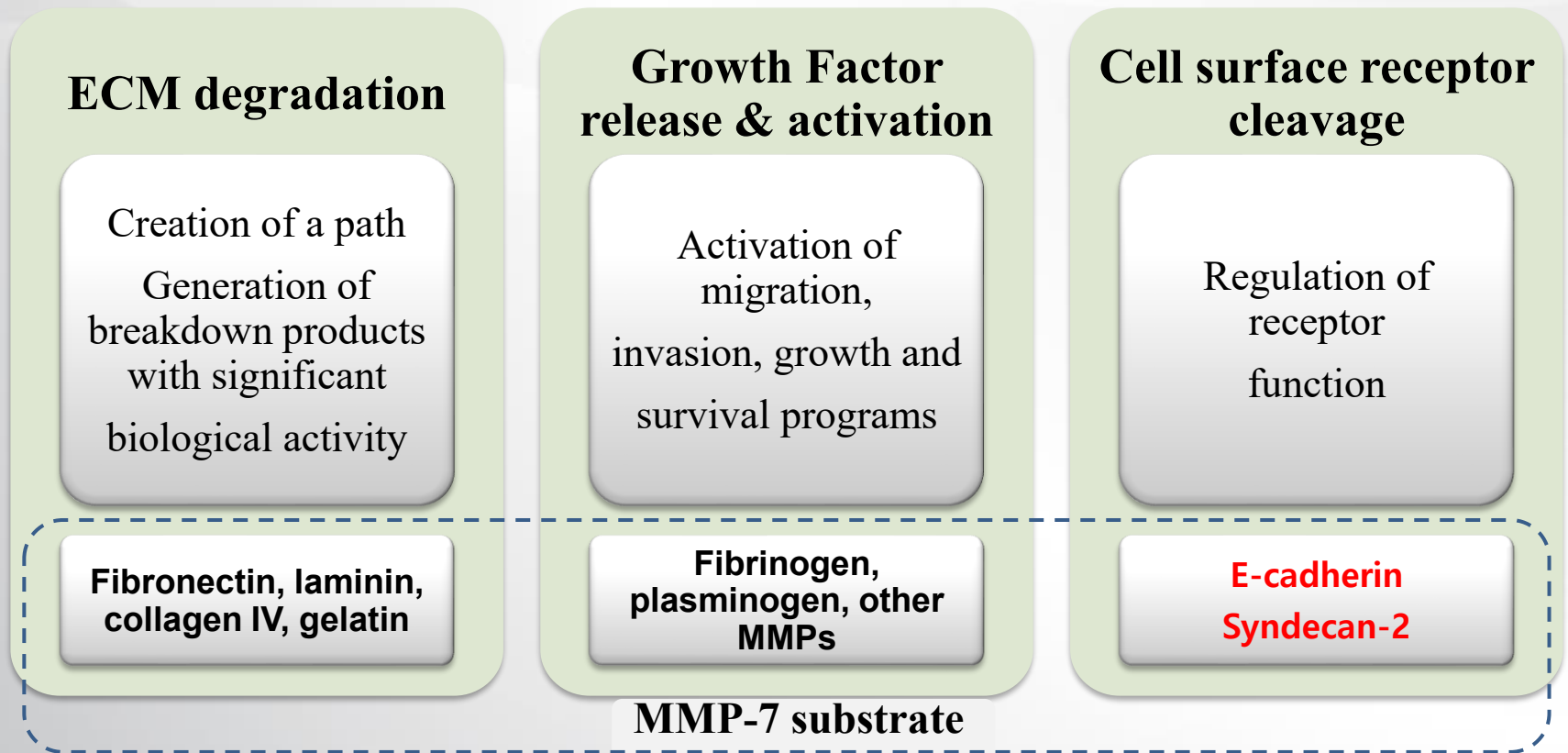
Oncotarget

Syndecan-2 enhances E-cadherin shedding and fibroblast-like morphological changes by inducing MMP-7 expression in colon cancer cells

Shed syndecan-2 enhances colon cancer progression by increasing cooperative angiogenesis in the tumor microenvironment

MMP-7-Mediated Proteolysis in Cancer Progression

Proteolysis in Cancer Progression



- **Shedding:** Process whereby the extracellular domain of membrane protein is cleaved, separated and released from the cell surface.

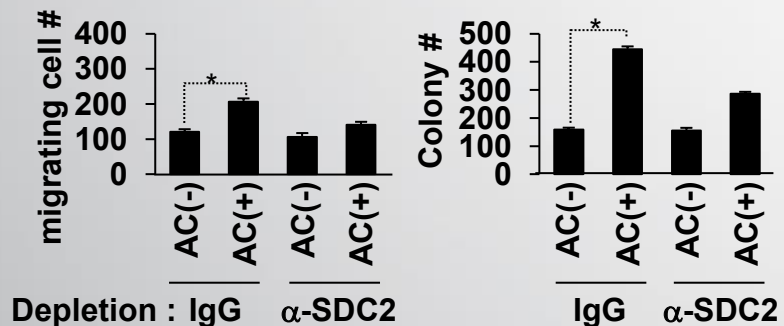
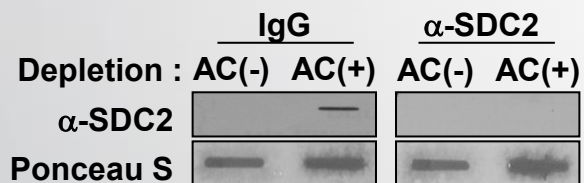
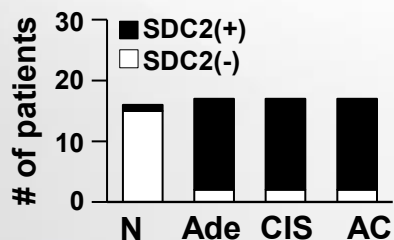
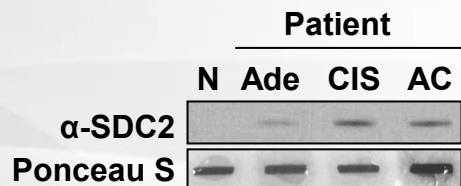
Question 1

How Does Syndecan-2 Act as a Soluble Ligand to Regulate Cancer Progression?



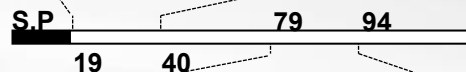
Shed Syndecan-2 in Patient Serum Positively Regulates Cancer Activity

A

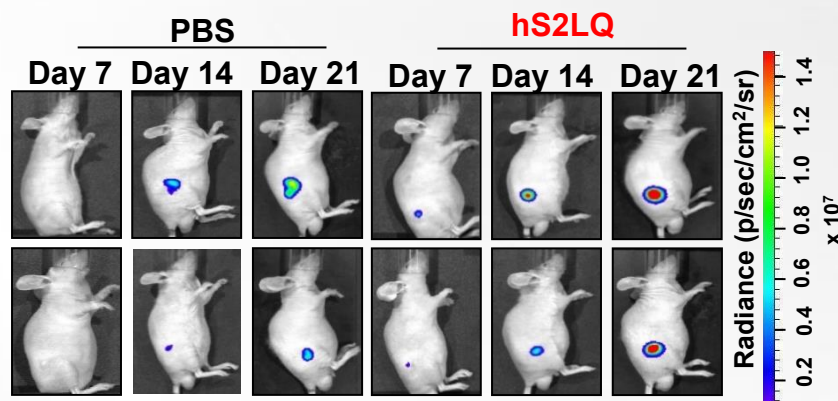


B

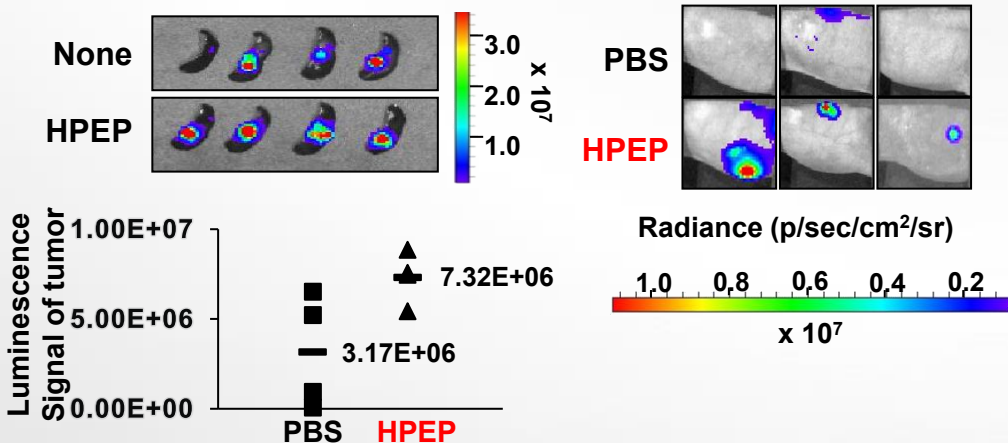
hS2EA : E¹⁹SRAELTSDKDMYLDNSSIEEA⁴⁰



hS2LQ : L⁷⁹TSAAPKVETTTLNIQ⁹⁴



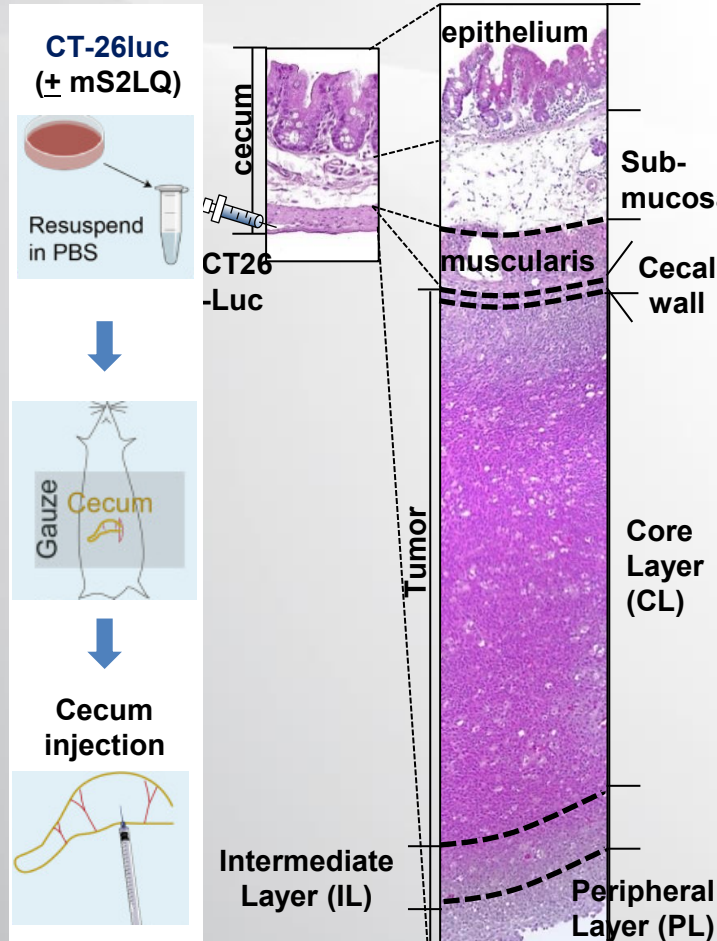
C



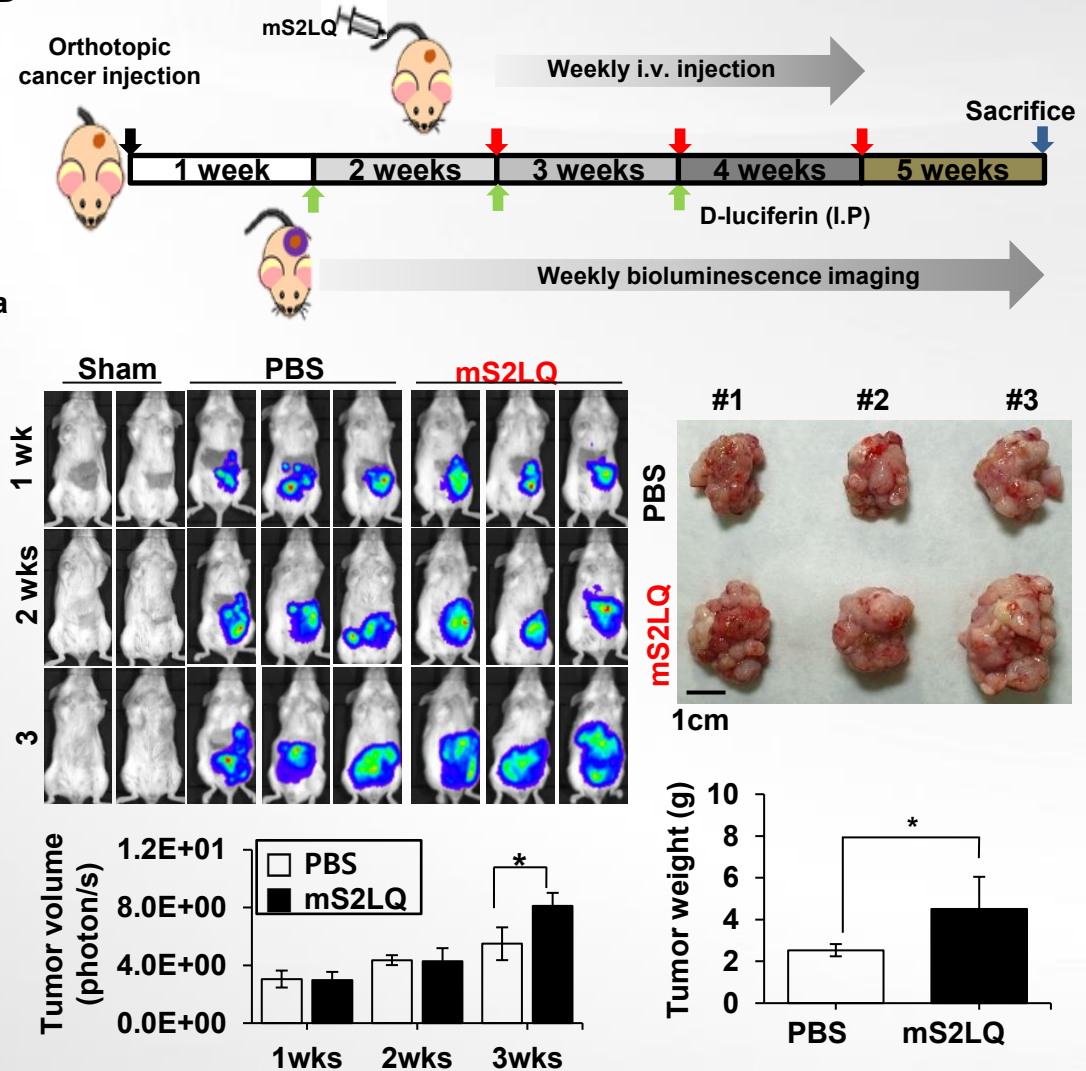
Shed Syndecan-2 Enhances the Survival of CT26 Cells Implanted Into the Cecum

A

Orthotopic tumor



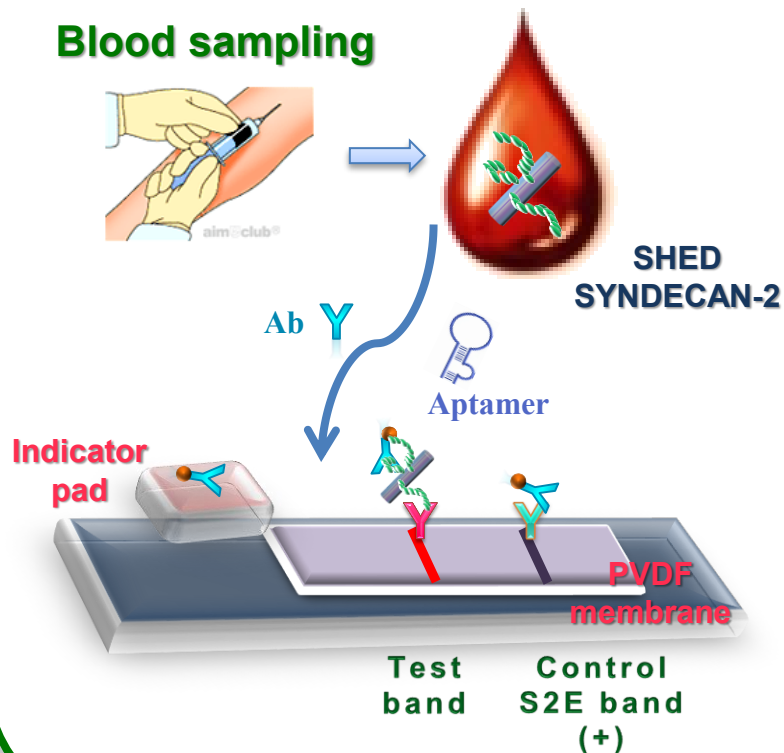
B



Cancer Theragnosis

Colon Cancer Diagnostic Kit

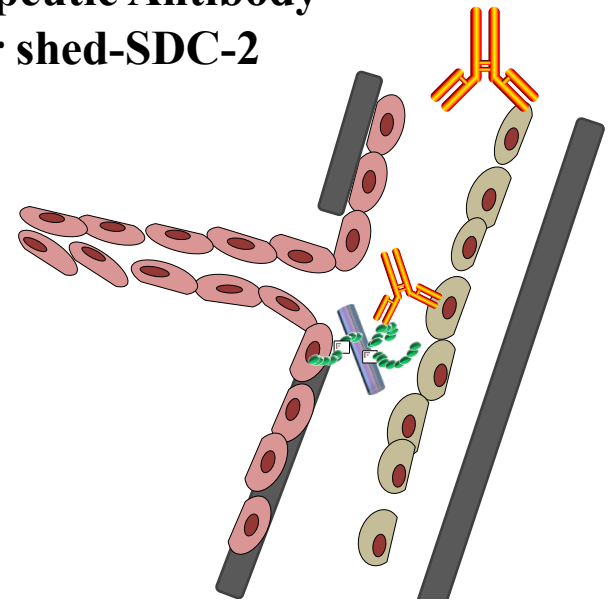
(Molecular Target: Shed-SDC-2)



Cancer Therapeutics

(Molecular Target 1: Shed-SDC-2)

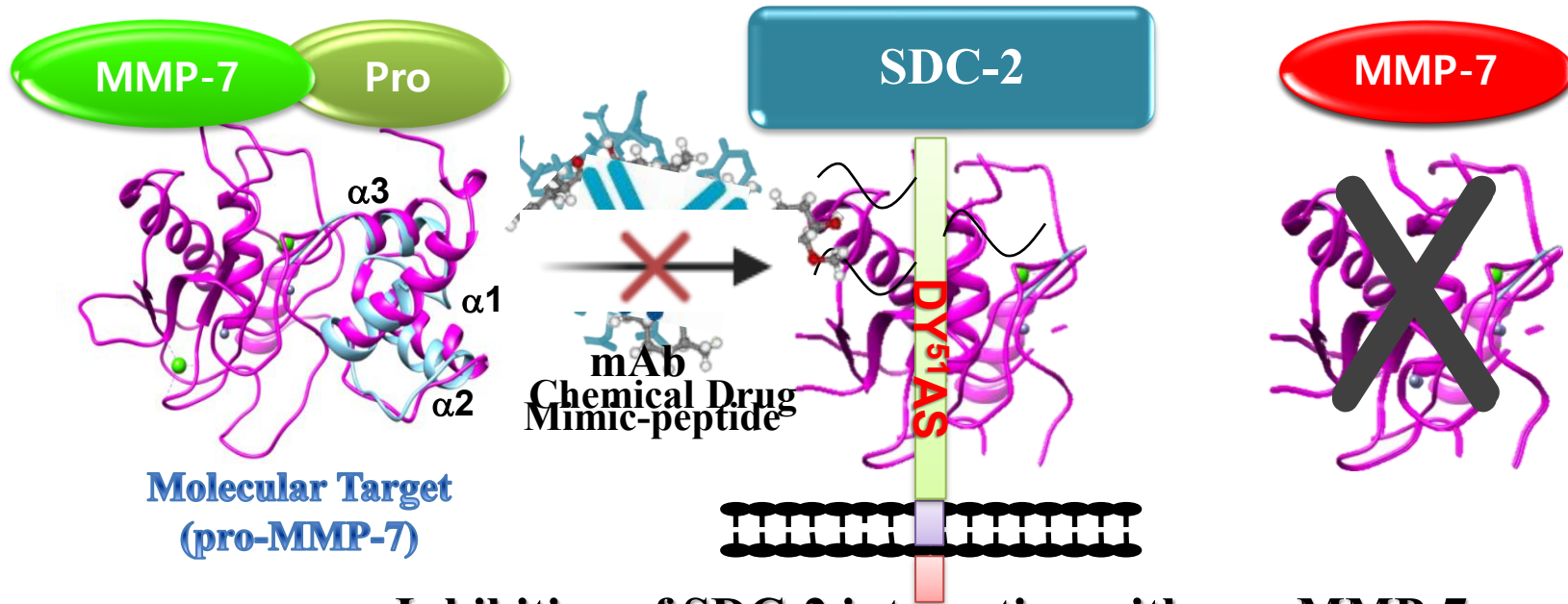
Therapeutic Antibody
for shed-SDC-2



DEPLETION OF **SHED SDC2** IN BLOOD

(Molecular Target 2: pro-MMP-7)

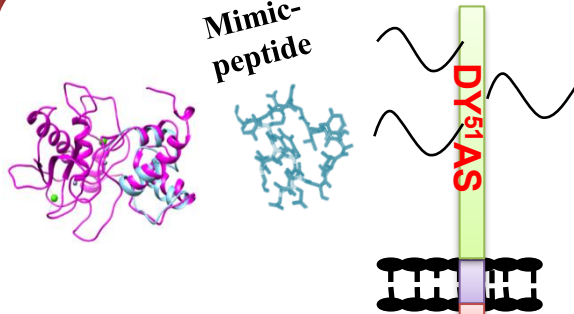
Cancer Therapeutics



Inhibition of SDC-2 interaction with pro-MMP-7

Peptide-Drug

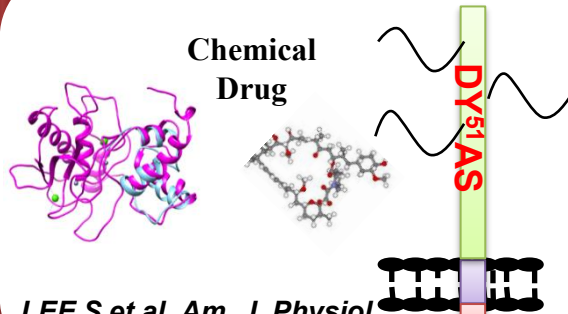
Mimic-peptide



Jang B et al. *Int. J. Mol. Sci.* 2022

FDA-Drugs

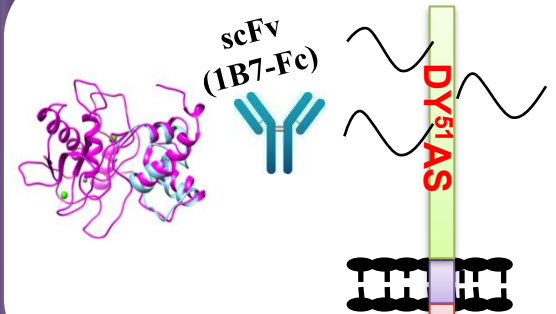
Chemical Drug



LEE S et al. *Am. J. Physiol. Cell Physiol.* 2024

Therapeutic Ab

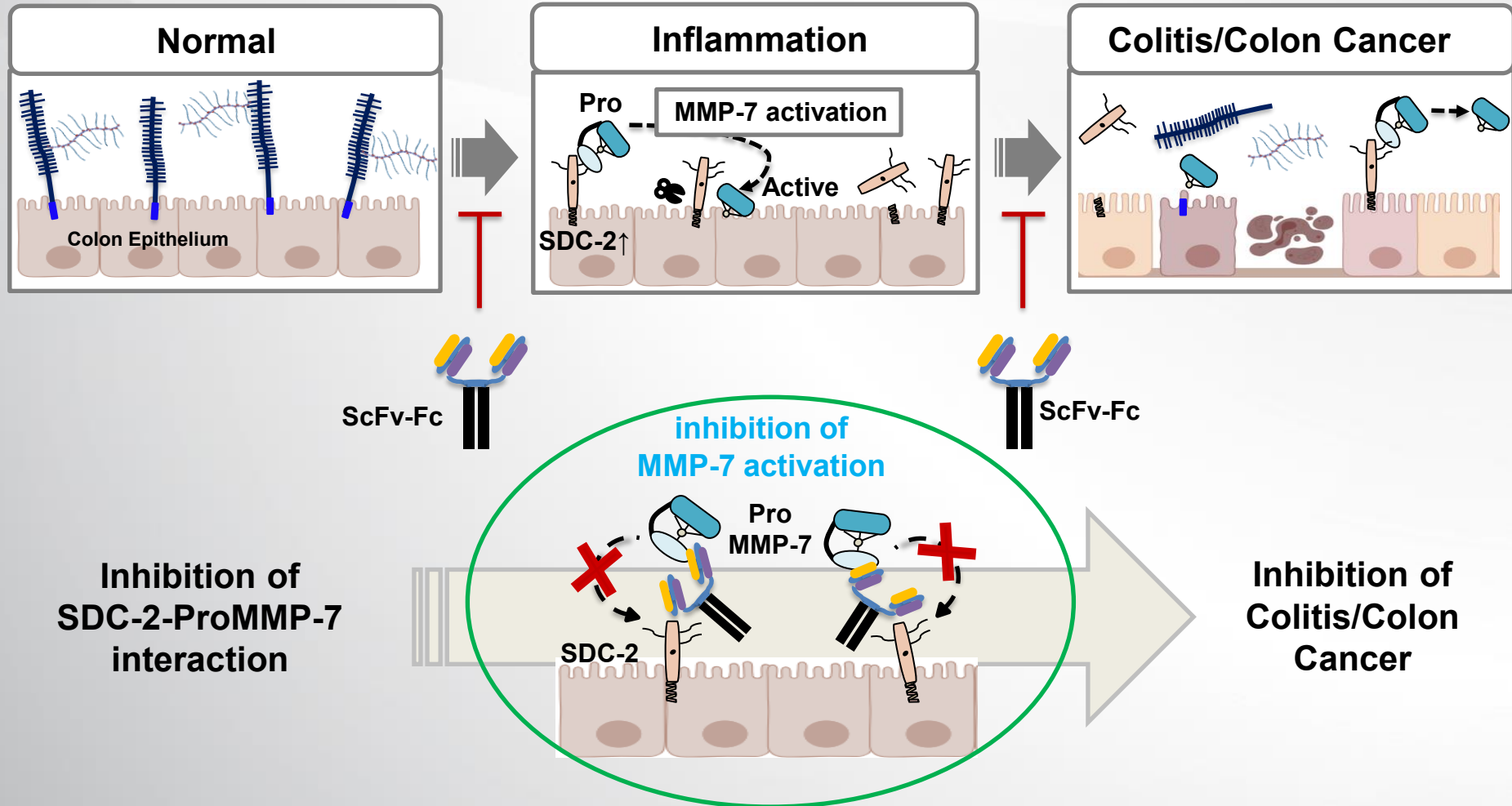
scFv (1B7-Fc)



Min S et al. *Matrix Biol.* 2025

Strategies to Suppress Inflammatory Diseases

Strategies to suppress colitis and inflammatory colon cancer by ScFv



Question II

Could this strategy be applied to other diseases?



Glycocalyx

- The **glycocalyx** (the pericellular matrix, cell coat) is a glycoprotein and glycolipid covering which surrounds the cell membranes of bacteria, **epithelial cells**, **vascular endothelial cells** and other cells.

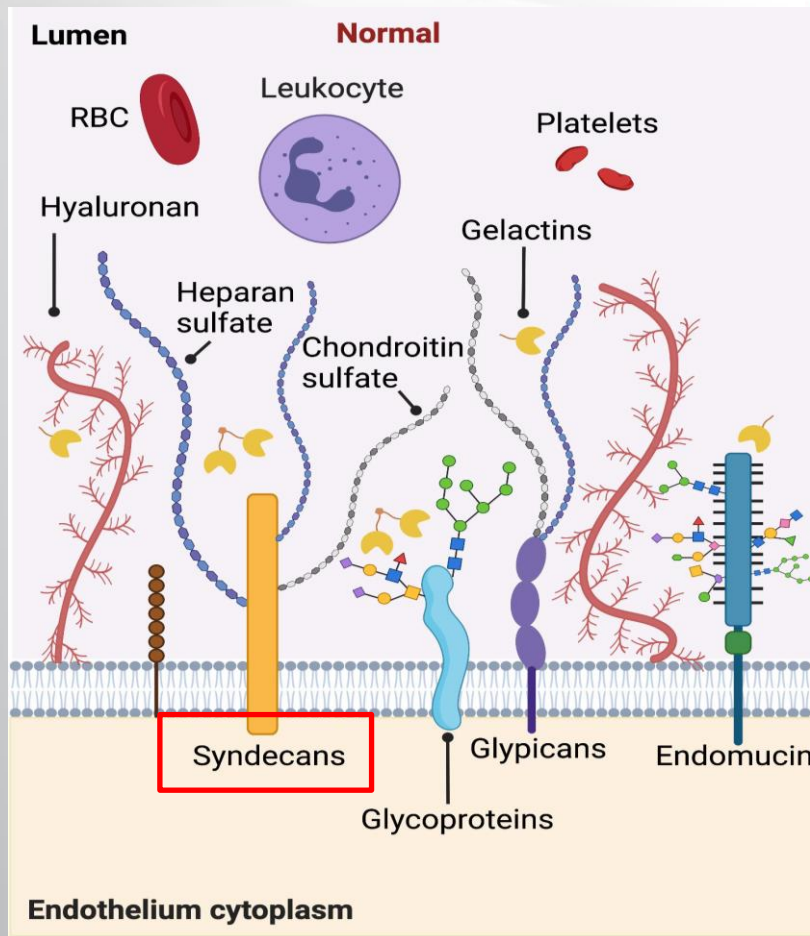


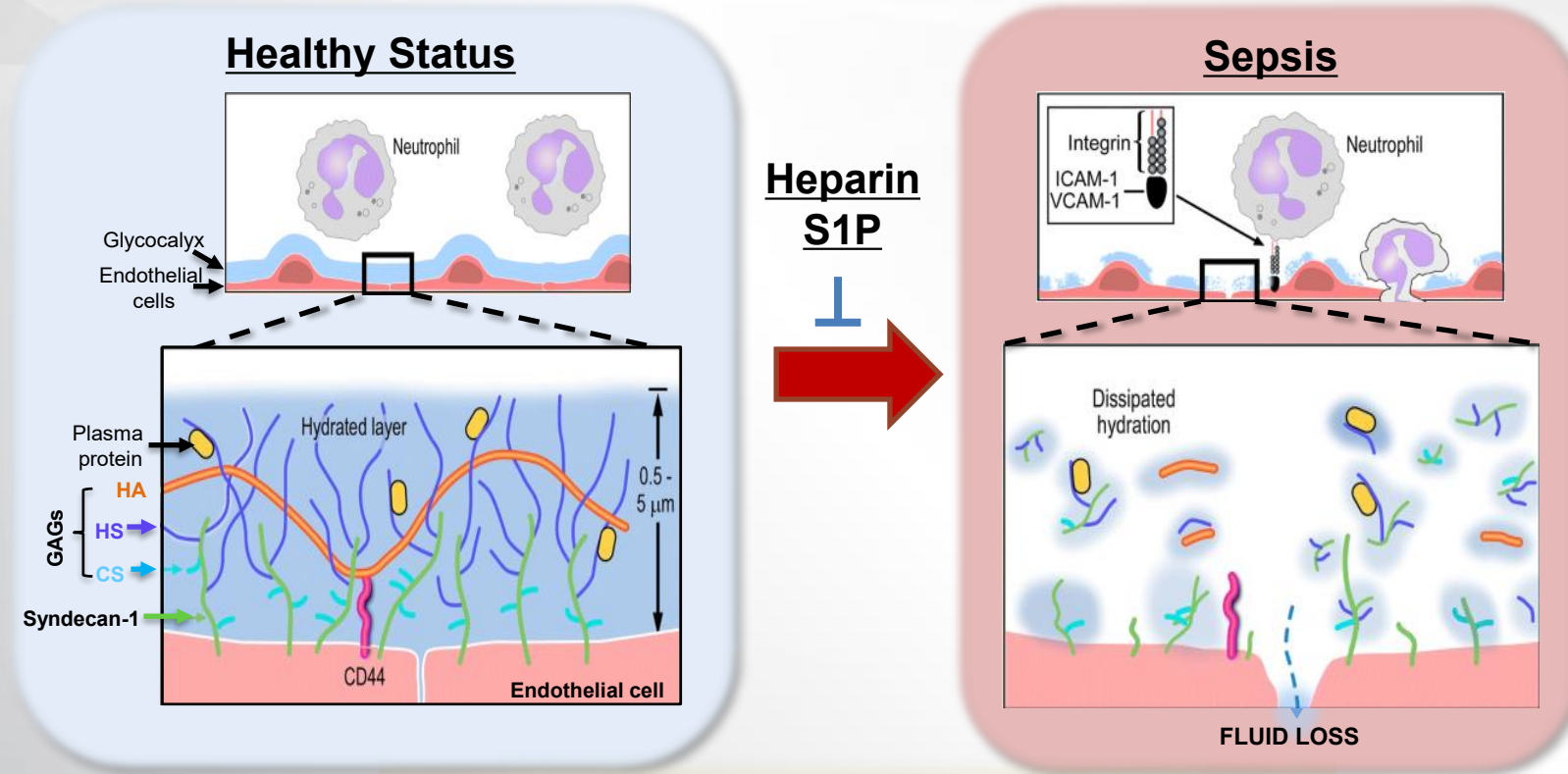
TABLE 3.2

Functions of the Glycocalyx

Protection	Cushions the plasma membrane and protects it from physical and chemical injury
Immunity to infection	Enables the immune system to recognize and selectively attack foreign organisms
Defense against cancer	Changes in the glycocalyx of cancerous cells enable the immune system to recognize and destroy them
Transplant compatibility	Forms the basis for compatibility of blood transfusions, tissue grafts, and organ transplants
Cell adhesion	Binds cells together so tissues do not fall apart
Fertilization	Enables sperm to recognize and bind to eggs
Embryonic development	Guides embryonic cells to their destinations in the body

Glycocalyx of Vascular Endothelial Cells

Endothelial glycocalyx structure during health and degradation during sepsis



Degraded glycocalyx layer (thinner and sparse)

↑
vascular permeability, tissue edema
leukocyte adhesion, platelet aggregation
dysregulated vasodilation

Releases glycocalyx components

↑
SDC-1, HS, HA, CS

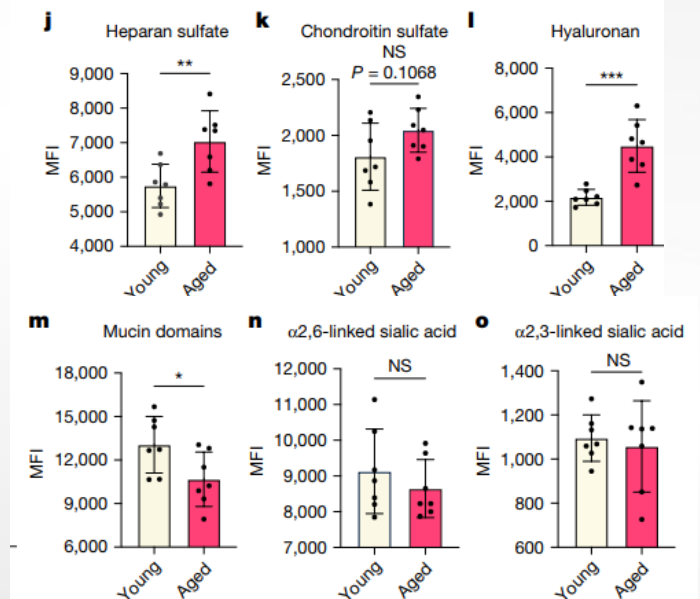
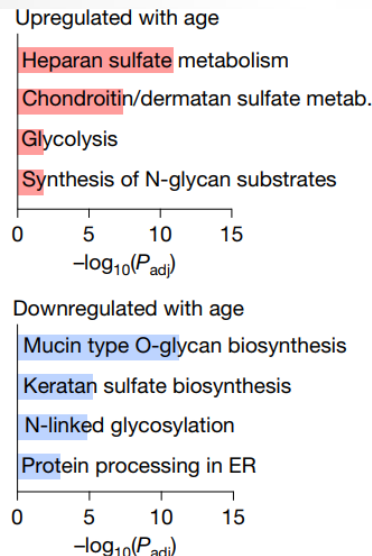
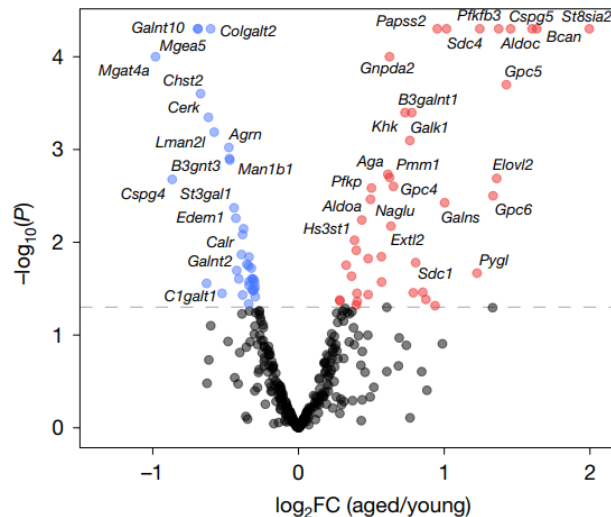
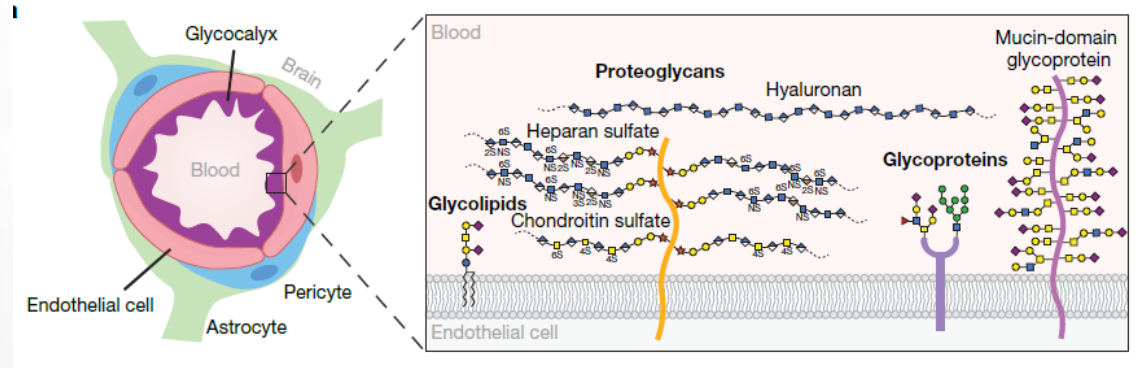
Glycocalyx of Vascular Endothelial Cells

nature

Article | [Open access](#) | Published: 26 February 2025

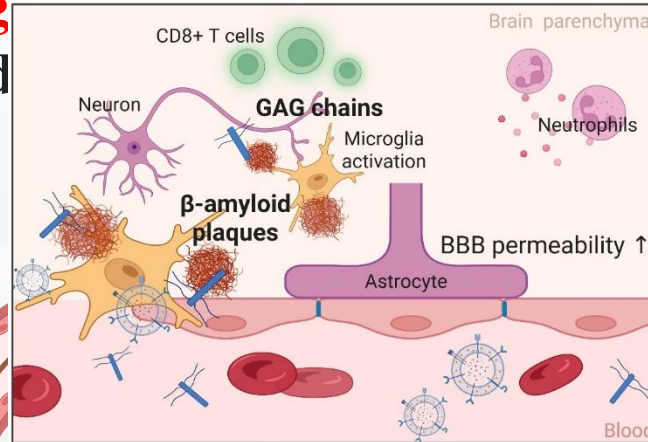
Glycocalyx dysregulation impairs blood–brain barrier in ageing and disease

- Notable upregulation of genes involved in HS metabolism (Sdc4, SDC1, Hs3st1, Extl2 and Gpc5) in aged brain endothelial cells...



Syndecan Shedding and Systemic Inflammation

- **Syndecan shedding** leads to disruption of glycocalyx and production of inflammatory mediators



Neuroinflammation

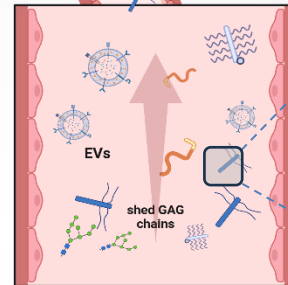
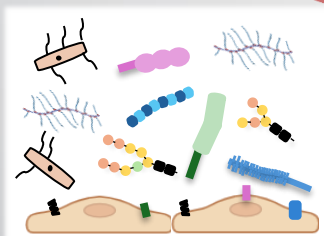
- ① BBB barrier disruption
- ② Neurodegenerative disease

Leukocyte activation
Adhesion molecules ↑
Cytokines ↑

Vascular inflammation

**Systemic Inflammation
Gut-Brain axis**

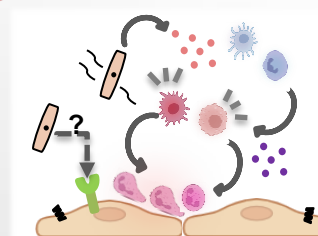
Glycocalyx disruption



Circulating inflammatory mediators

EVs
GAG chains
Shed SDC-2
·
·

Shed SDC-mediated inflammation



Colitis

Potential Korea-EU Collaboration Under Horizon Europe



Two Possible Collaborations exploring within Horizon Europe

1

Regulatory Mechanism of shed SDC-mediated inflammatory diseases

2

Inflammatory diseases in which 1B7-Fc can be applied.

A photograph of a Gothic-style church with a large arched window, surrounded by lush green trees under a clear blue sky.

Thank You

A photograph of the same church, but in winter. The trees are covered in white snow, and the sky is a pale, overcast white.