SSD-004 (Systemic sclerosis treatment drug): Summary

SSD-004 could be a novel strategy for the treatment of SSc.

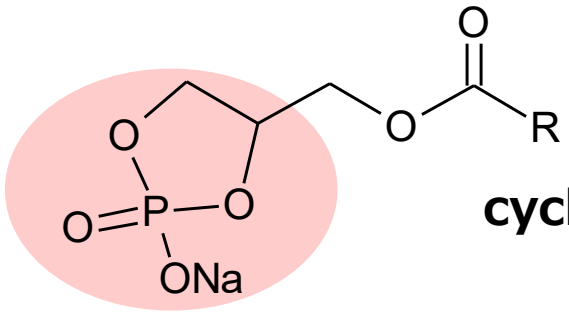
SSD-004 (API: 2ccPA) abrogates ECM production and promotes antifibrotic molecules from SSc skin fibroblasts. SSD-004 also at tenuates the progression of fibrosis in bleomycin-induced skin fibrosis. These findings suggest that SSD-004 may be a promising antifibrotic agent for the treatment of SSc.

SANSHO Development Pipeline

	Non-clinical to Pre-clinical	Phase I	Phase II
Orthopedics		SSO-001 (OA*)	
Respiratory Medicine	SSI-002 (IPF**)		
Ophthalmology	SSG-003 (Glaucoma)		
Dermatology	SSD-004 (Scleroderma) SSH-005 (Hypotrichosis)		

*Osteoarthritis
**Idiopathic pulmonary fibrosis

Conversion of cPA to chemically stable derivatives

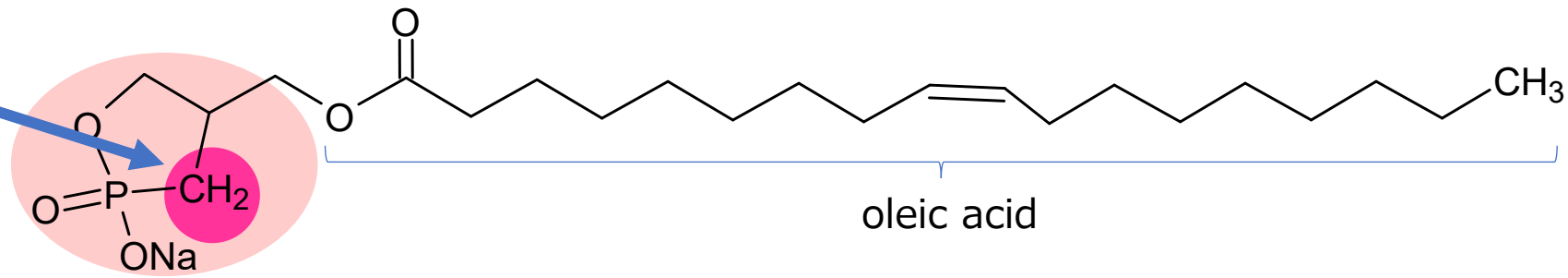


Various fatty acids such as linoleic acid, palmitic acid, and oleic acid

cyclic Phosphatidic **Acid** (cPA, R=C:16~22)

Improved in vivo stability by converting oxygen (O) to methylene (CH_2)

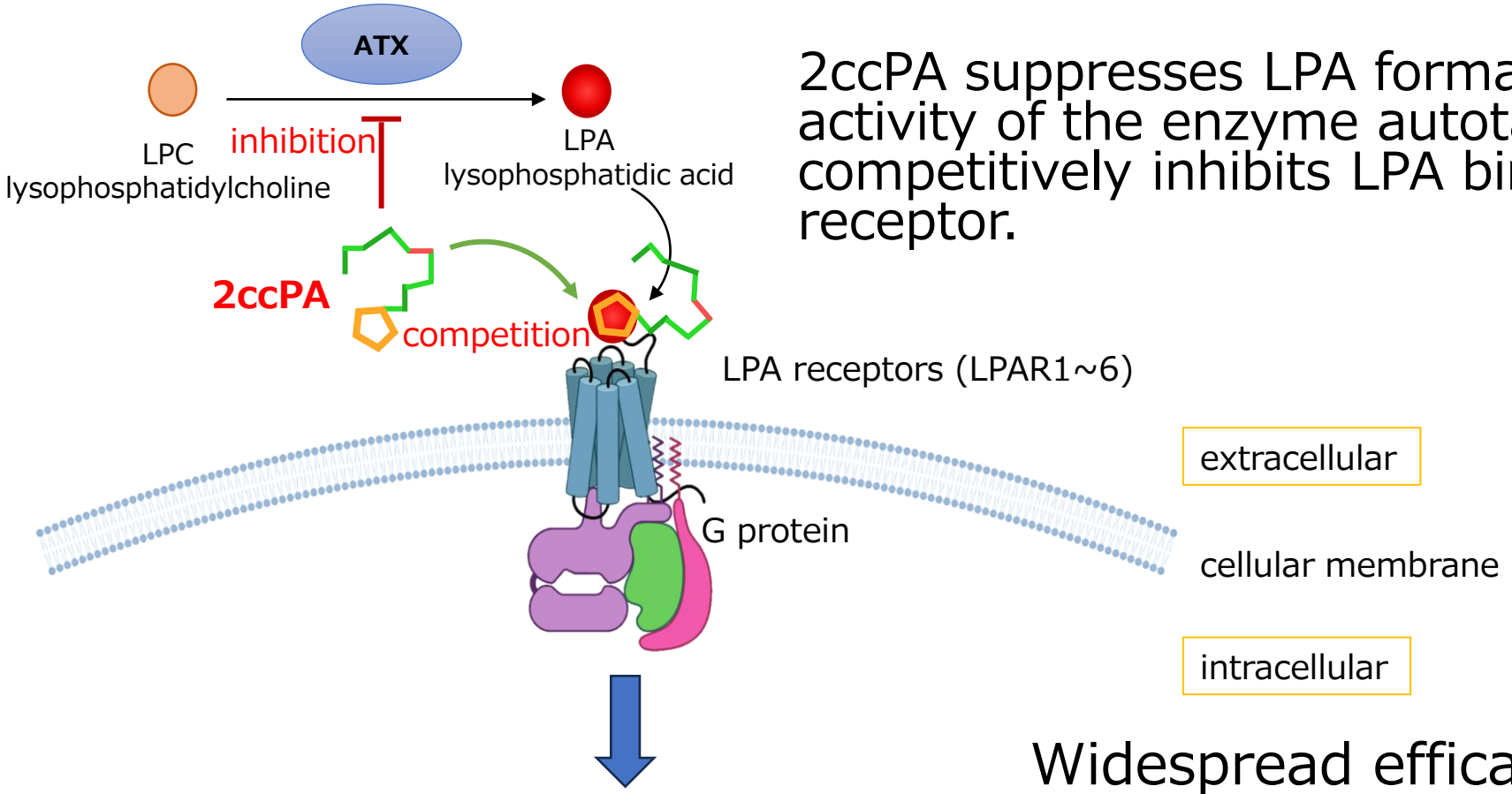
Conversion to chemically stable derivative



2-carba-cyclic phosphatidic acid (2ccPA)

Oleic acid is selected as the fatty acid

Unique mechanism of action of 2ccPA



2ccPA suppresses LPA formation by inhibiting the activity of the enzyme autotaxin (ATX) and competitively inhibits LPA binding to the LPA receptor.

Widespread efficacy in diseases caused by inflammation

Development of SSD-004 (a drug for treating systemic scleroderma)

What is systemic scleroderma?

- A disease in which the skin and internal organs harden, it is one of the collagen diseases. It has three main characteristics: hardening of the skin, Raynaud's phenomenon, and symptoms in the internal organs (including pulmonary fibrosis).
- According to the Japan Rheumatism Association, the estimated number of patients is about 30,000, with a male-to-female ratio of 1:10, and it is said to be more prevalent in women and more likely to develop in people in their 30s to 60s.
- Treatment is aimed at alleviating symptoms and slowing progression, and includes drug therapy (immunosuppressants, vasodilators, etc.) and rehabilitation.

Development plan

- 2ccPA was provided to the Ministry of Health, Labour and Welfare Sciences Research Grant-in-Aid for Research on Overcoming Intractable Diseases, which concluded that 2ccPA is expected to improve the skin hardening observed in systemic sclerosis by suppressing the production of extracellular matrix such as type I collagen produced by scleroderma skin fibroblasts.
- Due to the high medical need, it is planned to be developed as an orphan drug.

Suppression of fibrotic marker expression in TGF-β1-stimulated normal skin fibroblasts

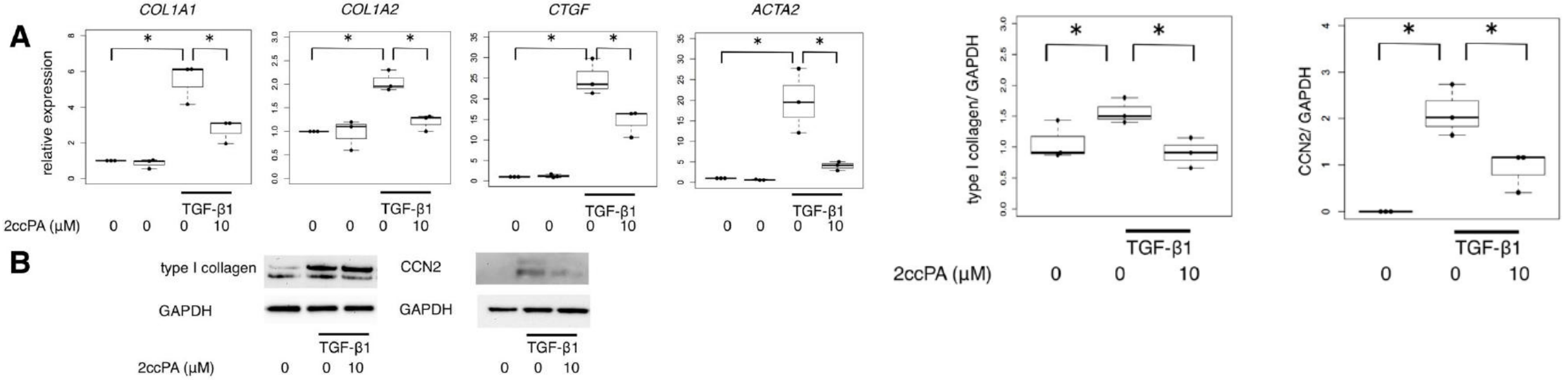


Fig. 3 2ccPA inhibited the upregulation of profibrotic markers in normal skin fibroblasts stimulated with TGF-β1. Normal skin fibroblasts ($n = 3$) were incubated with or without 10 μM 2ccPA in the presence or absence of 10 ng/mL TGF-β1 for 48 h. **a** The expression of *COL1A1*, *COL1A2*, *CTGF*, and *ACTA2* mRNA were determined by qPCR. **b** Normal skin fibroblasts ($n = 3$) were incubated with 10 μM 2ccPA in the presence or absence of 10 ng/mL TGF-β1 for 72 h. The protein expression of type I collagen and CCN2 in cell lysates of normal skin fibroblasts were assessed with Western blotting. Data are the representative of three independent experiments. The bars represent as median with IQR. *$p < 0.05$

SSD-004 (2ccPA) inhibited the high expression of fibrotic markers in normal skin fibroblasts stimulated with TGF-β1