浩峰生技
ALPS BIOTECH CO., LTD

牛樟芝萃取物與冠狀病毒的研究

陳水田博士

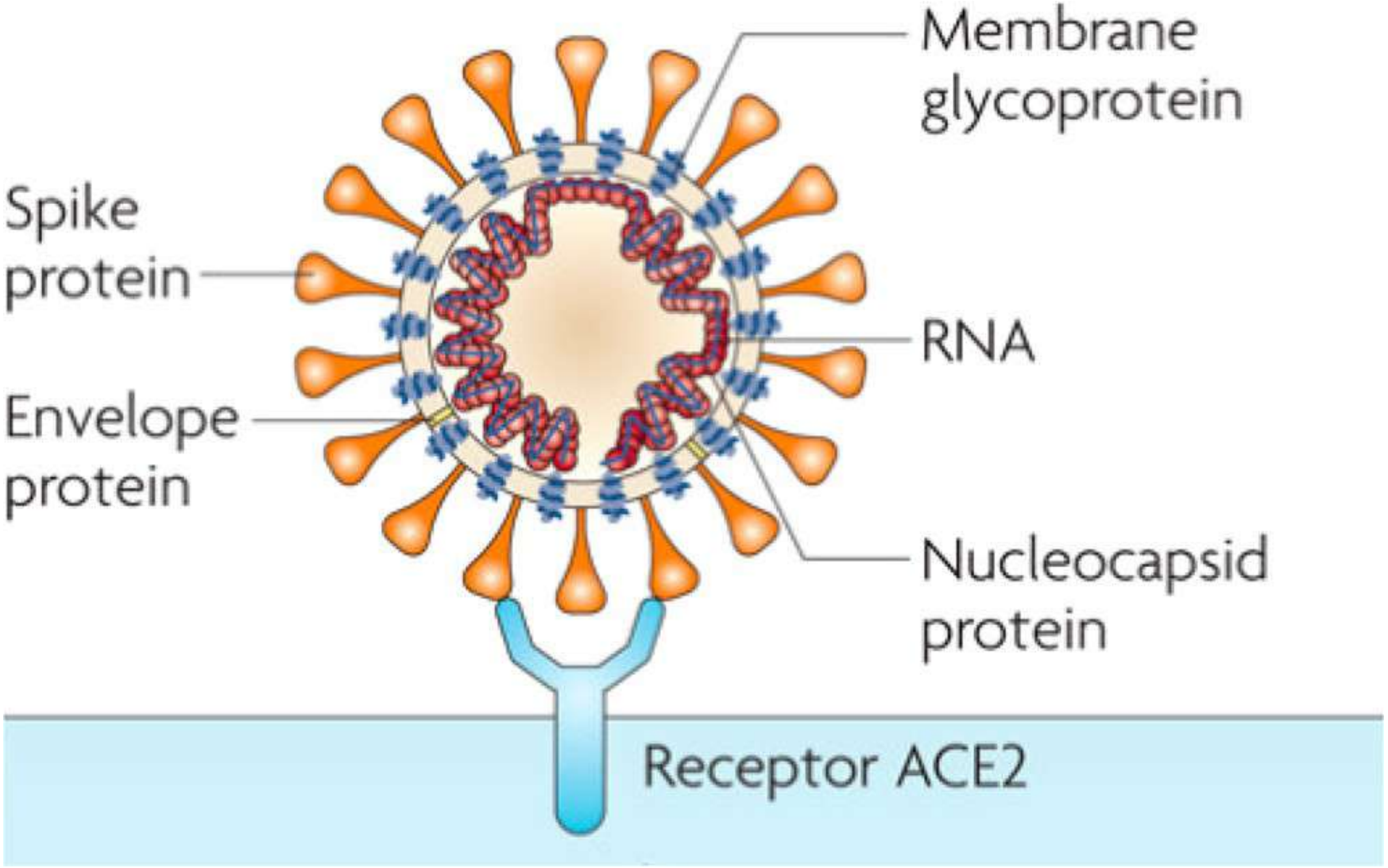
台灣國寶牛樟芝協會
浩峰生物科技股份有限公司

浩峰生技
ALPS BIOTECH CO., LTD

簡報內容

1. 簡介冠狀病毒及 ACE2
2. 細胞膜上 ACE2 是冠狀病毒感染的門戶
3. 牛樟芝萃取物降低 ACEII 的生成量
   (Gene & Protein)
4. ACE 酵素 (ACE1&2) 及 高血壓 / 腎臟病
5. 牛樟芝萃取物抑制 ACE2 酵素活性
6. 牛樟芝精油促進免疫細胞活性
7. 結 論

Coronavirus structure and viral receptor ACE2 on the host cell surface



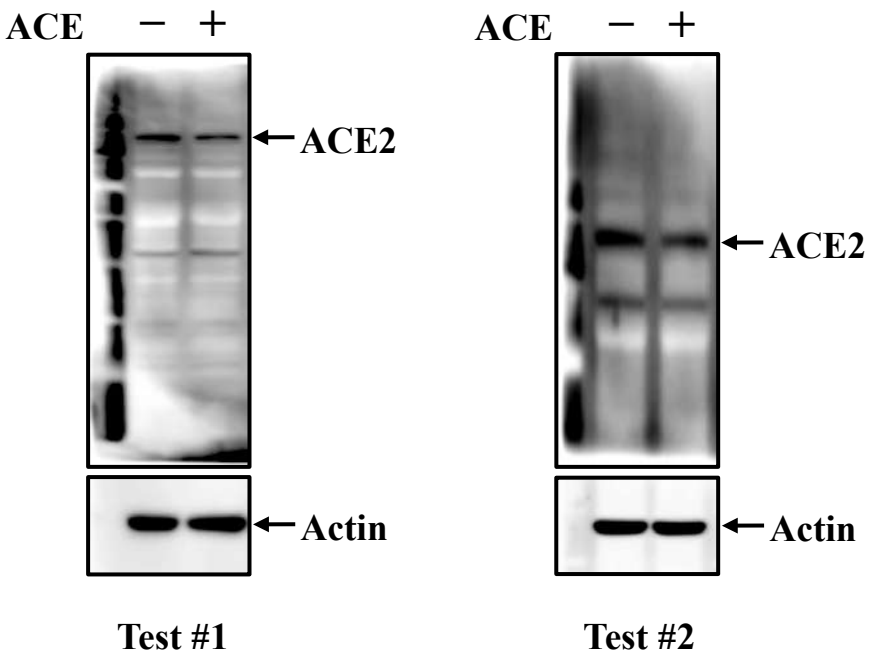
浩峰生技
ALPS BIOTECH CO., LTD

Link between ACE2 and COVID-19

- **ACE2 is essential to COVID-19 infection**
- **Increased expression of ACE2 facilitate infection with COVID-19.**
- **COVID-19 S (spike) protein use ACE2 as receptor for host cell entry, similar to SARS-CoV.**
- **S protein binds the catalytic domain of ACE2 with high affinity.**
- **Patients with cardiac diseases, hypertension, or diabetes- treated with ACE2-increasing drugs, are at higher risk for severe COVID-19 infection.**

浩峰生技
ALPS BIOTECH CO., LTD

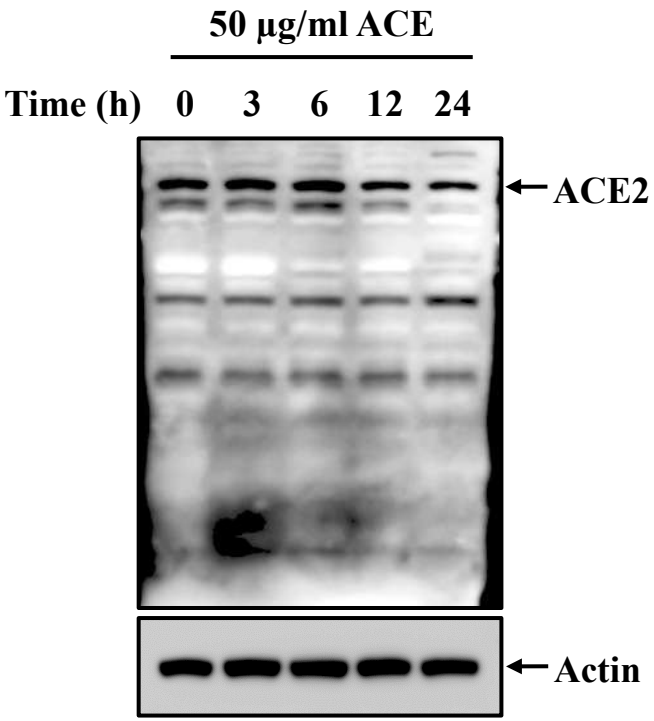
Antrodia cinnamomea extract (ACE) reduces angiotensin converting enzyme 2 (ACE2) protein expression



Human lung cancer CL1-1 cells were incubated with 50 μg/ml ACE for 24 h, ACE protein expression levels were analyzed by Western blot. ACE2 antibody was purchased from Proteintech (catalog number: 21115-1-AP).

浩峰生技
ALPS BIOTECH CO., LTD

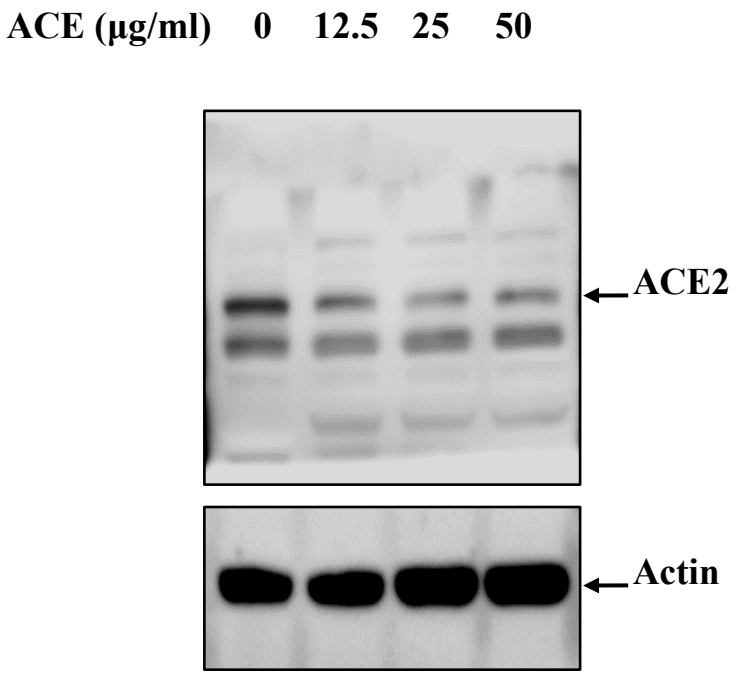
Antrodia cinnamomea extract (ACE) reduces angiotensin converting enzyme 2 (ACE2) protein expression



Human lung cancer CL1-1 cells were incubated with 50 μg/ml ACE for 0-24 h, ACE2 protein expression levels were analyzed by Western blot. ACE2 antibody was purchased from Proteintech (catalog number: 21115-1-AP).

浩峰生技
ALPS BIOTECH CO., LTD

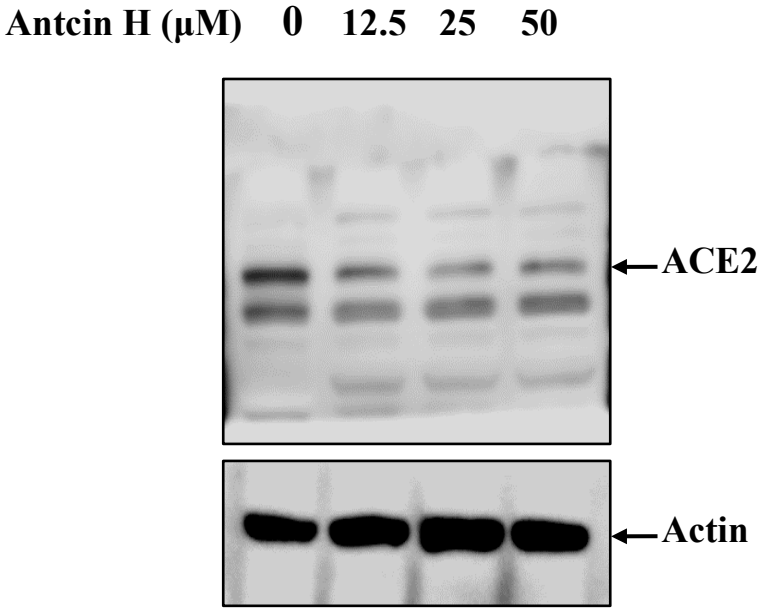
Antrodia cinnamomea extract (ACE) reduces angiotensin converting enzyme 2 (ACE2) protein expression



Human lung cancer CL1-1 cells were incubated with 12.5-50 μg/ml ACE for 24 h, ACE2 protein expression levels were analyzed by Western blot. ACE2 antibody was purchased from Proteintech (catalog number: 21115-1-AP).

浩峰生技
ALPS BIOTECH CO., LTD

Antcin H reduces angiotensin converting enzyme 2 (ACE2) protein expression



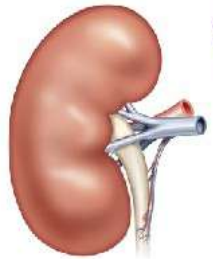
Human lung cancer CL1-1 cells were incubated with 12.5-50 μM Antcin H for 24 h, ACE2 protein expression levels were analyzed by Western blot. ACE2 antibody was purchased from Proteintech (catalog number: 21115-1-AP).

浩峰生技
ALPS BIOTECH CO., LTD

m-RNA study

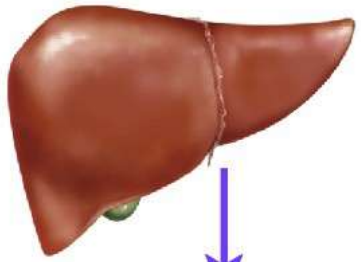
Renin-angiotensin system

Drop in blood pressure
Drop in fluid volume



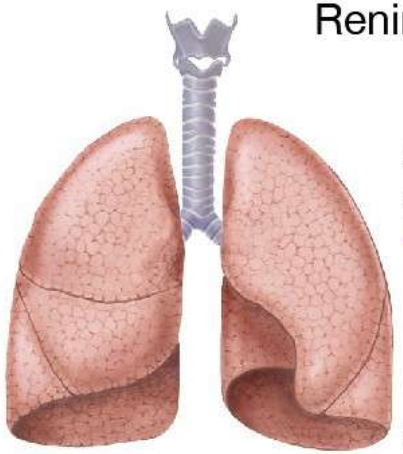
Renin release from kidney

liver



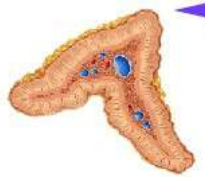
angiotensinogen

Renin acts on angiotensinogen to form **angiotensin I.**

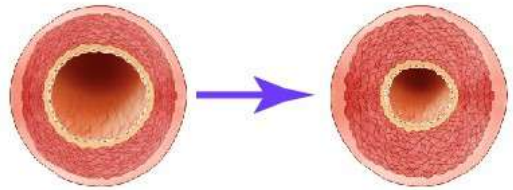


ACE (angiotensin-converting enzyme) release from lungs

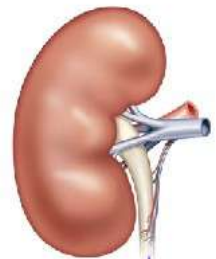
ACE acts on angiotensin I to form **angiotensin II.**



Angiotensin II acts on the adrenal gland to stimulate release of **aldosterone.**



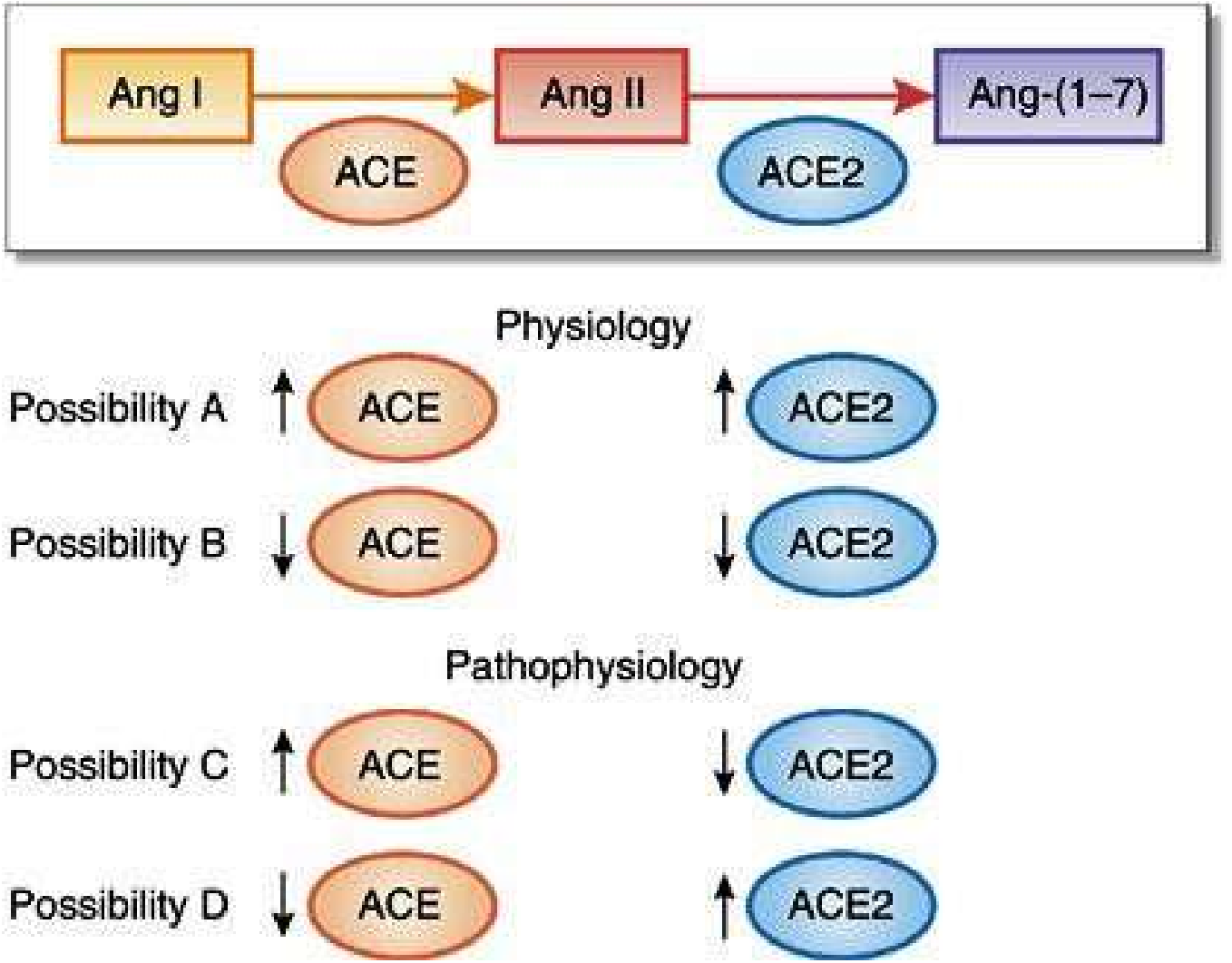
Angiotensin II also acts directly on blood vessels, stimulating vasoconstriction (narrowing).



NaCl
H_2O

Aldosterone acts on the kidneys to stimulate reabsorption of salt (NaCl) and water (H_2O).

Angiotensin II (Ang II) regulation by angiotensin-converting enzyme (ACE) and ACE2. In normal physiology- tightly regulate Ang II, if ACE activity increases, there must be a concomitant increase in ACE2 so that the rates of formation and degradation remain equal. In pathophysiological conditions, such as diabetic kidney disease, discordance in the activity of these two enzymes has been shown. For instance, the combination of high ACE and low ACE2 would result in an increase in Ang II, which would be detrimental (C) with regard to disease progression. Another situation, where ACE decreases and ACE2 increases, may prevent Ang II accumulation and therefore be renoprotective (D).



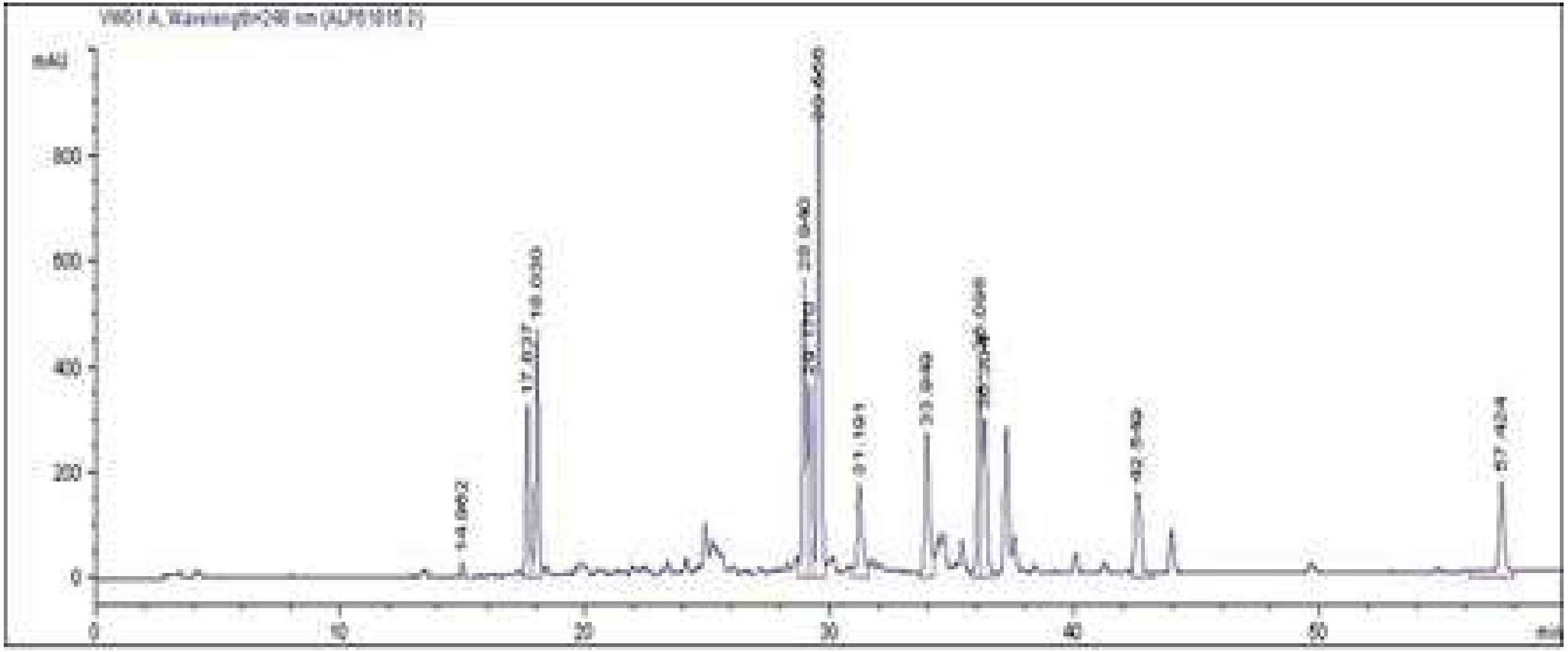
Kidney International 81(6), 520-8 (2012)

浩峰生技
ALPS BIOTECH CO., LTD

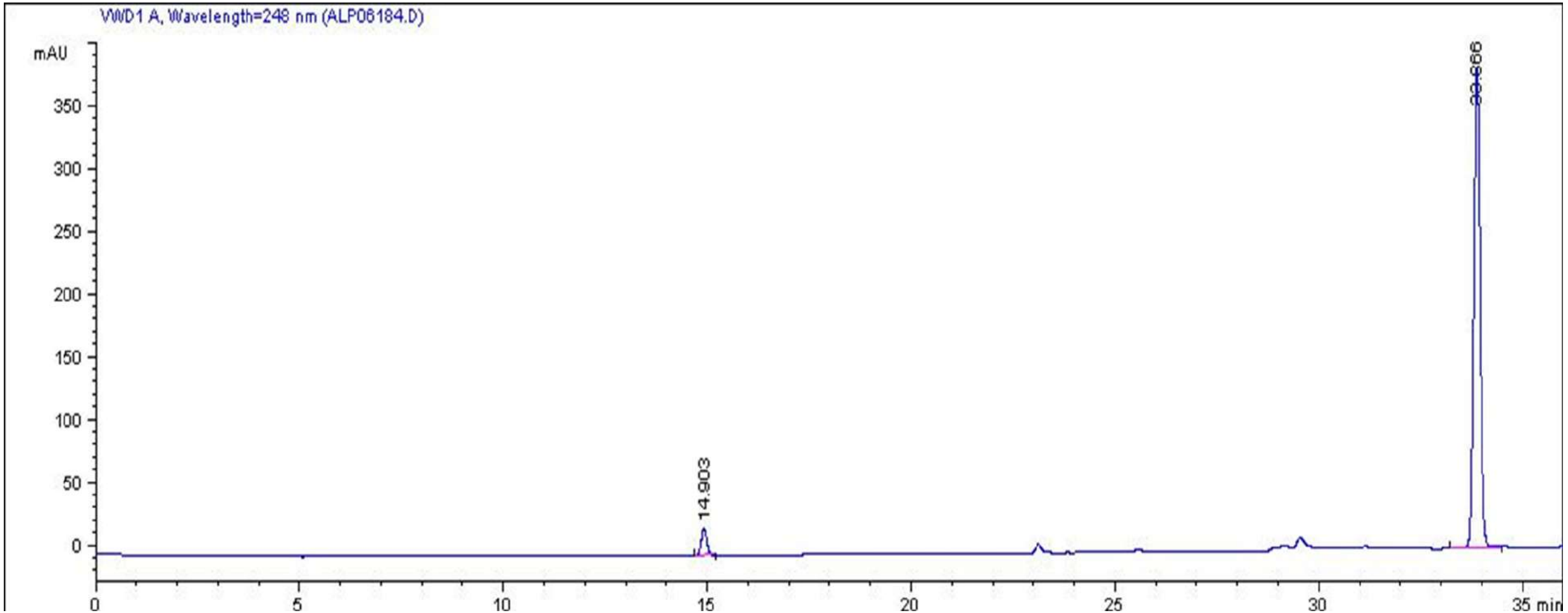
DSA (dehydrosulphuric acid) from *Antrodia cinnamomea* , can inhibit the enzymatic activity of ACE-2

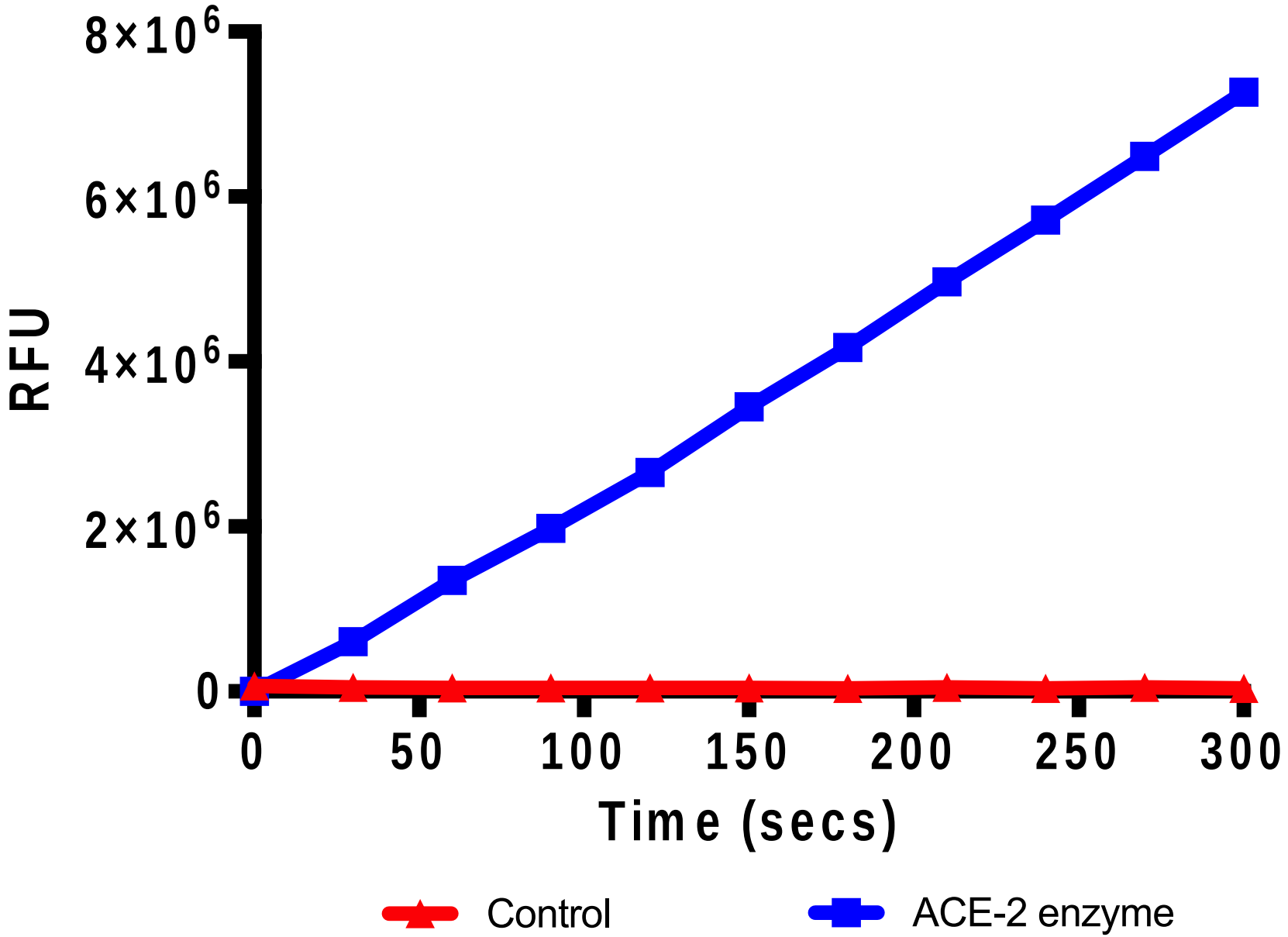
浩峰生技
ALPS BIOTECH CO., LTD

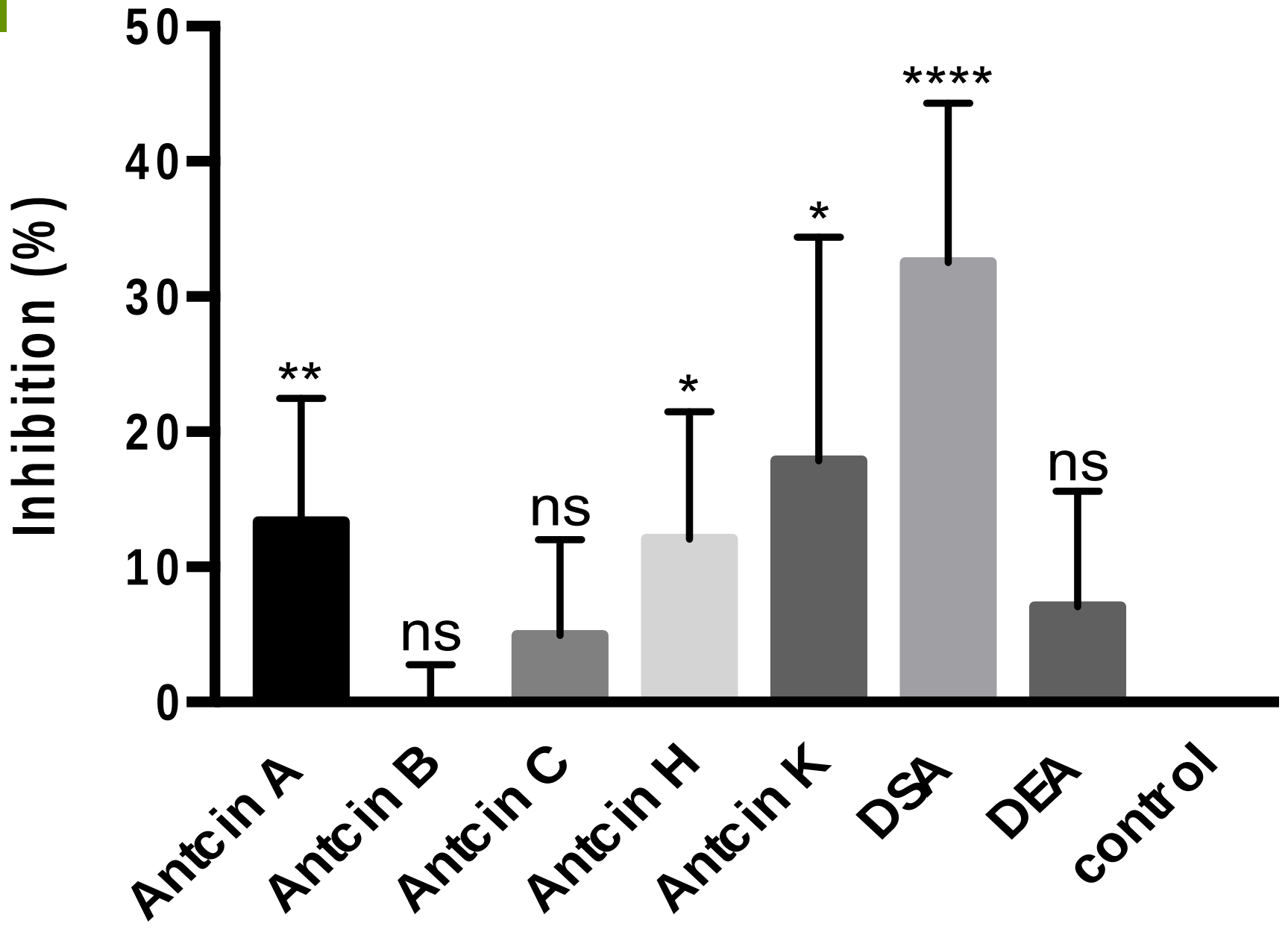
浩峰生技
ALPS BIOTECH CO., LTD

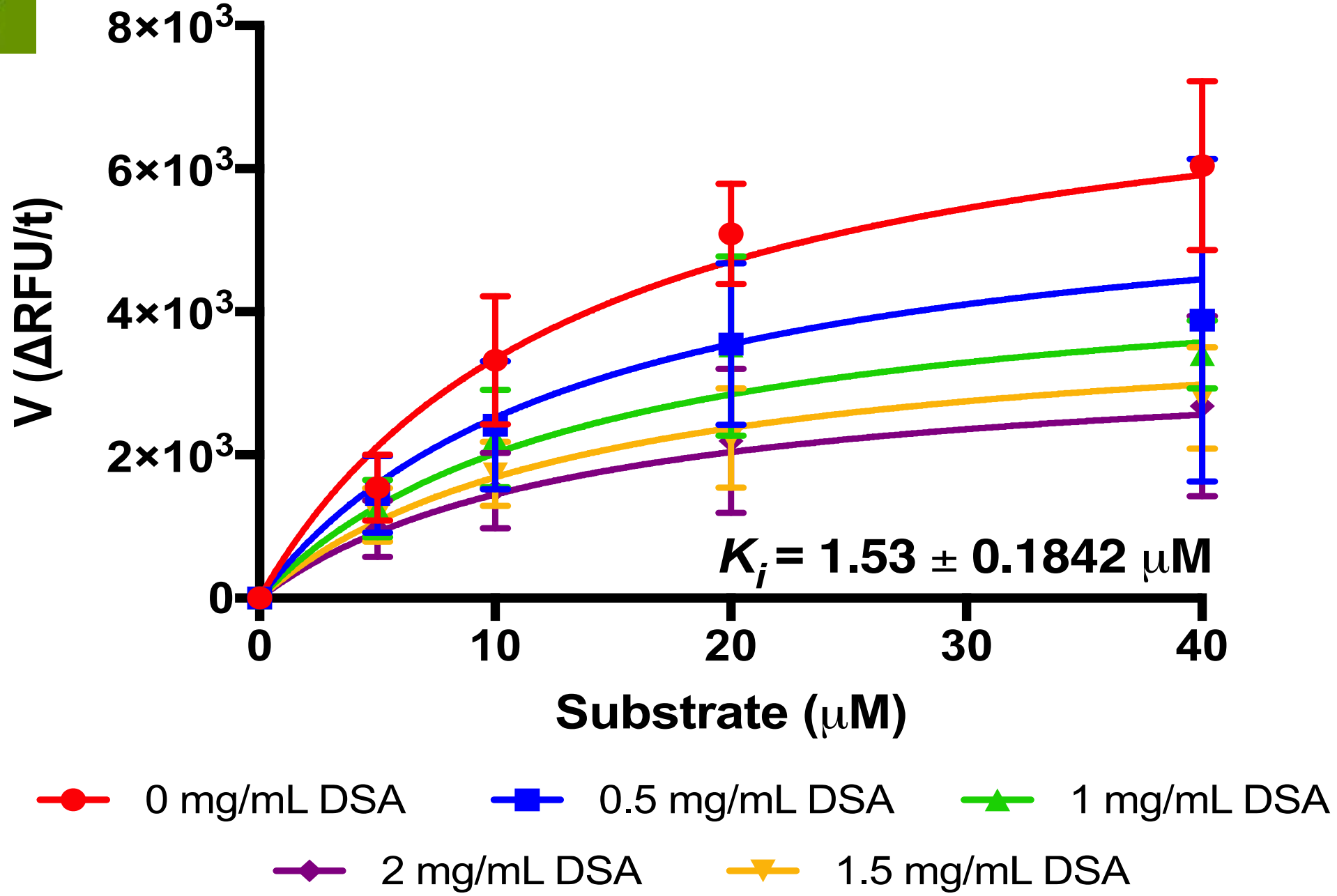


浩峰生技
ALPS BIOTECH CO., LTD





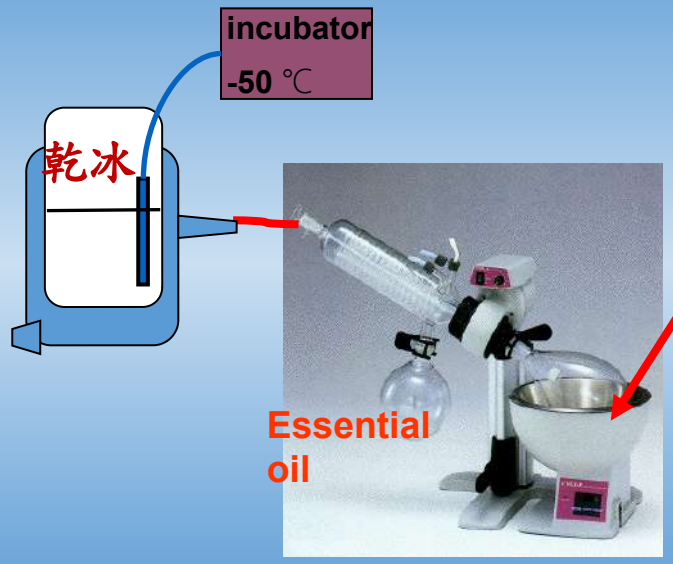




浩峰生技
ALPS BIOTECH CO., LTD

Preparation of essential oil from fermented culture of *A. cinnamonia*

Isolate essential oil of *A. camphorata*



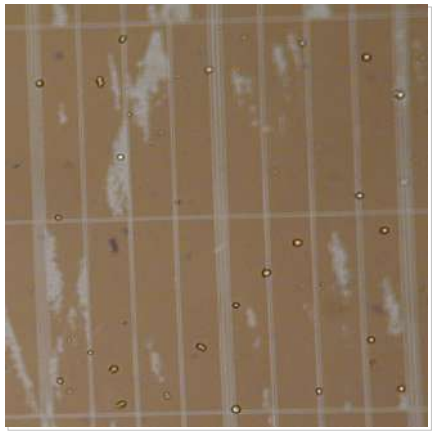
By 伯珠

浩峰生技
ALPS BIOTECH

human umbilical cord blood

centrifugation

isolation of UCB mononuclear Cells



cell count

treat with γ-DDL

flow cytometric analysis

浩峰生技
ALPS BIOTECH CO., LTD

Immuno-phenotypic changes of hUCB-MNC and hPBMCs

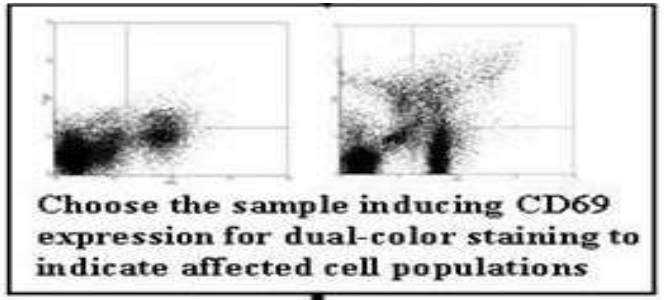
The CD markers used in the characterization of cell surface antigens for immuno-phenotyping

Cell Types	CD marker
T Lymphocyte	CD3
Monocyte/Macrophage	CD14
B Lymphocyte	CD19
Hematopoietic Stem Cell	CD34
Leukocyte	CD45
NK Cell	CD56
Dendritic Cell	CD83, CD1a

Immune cell activation markers

CD69

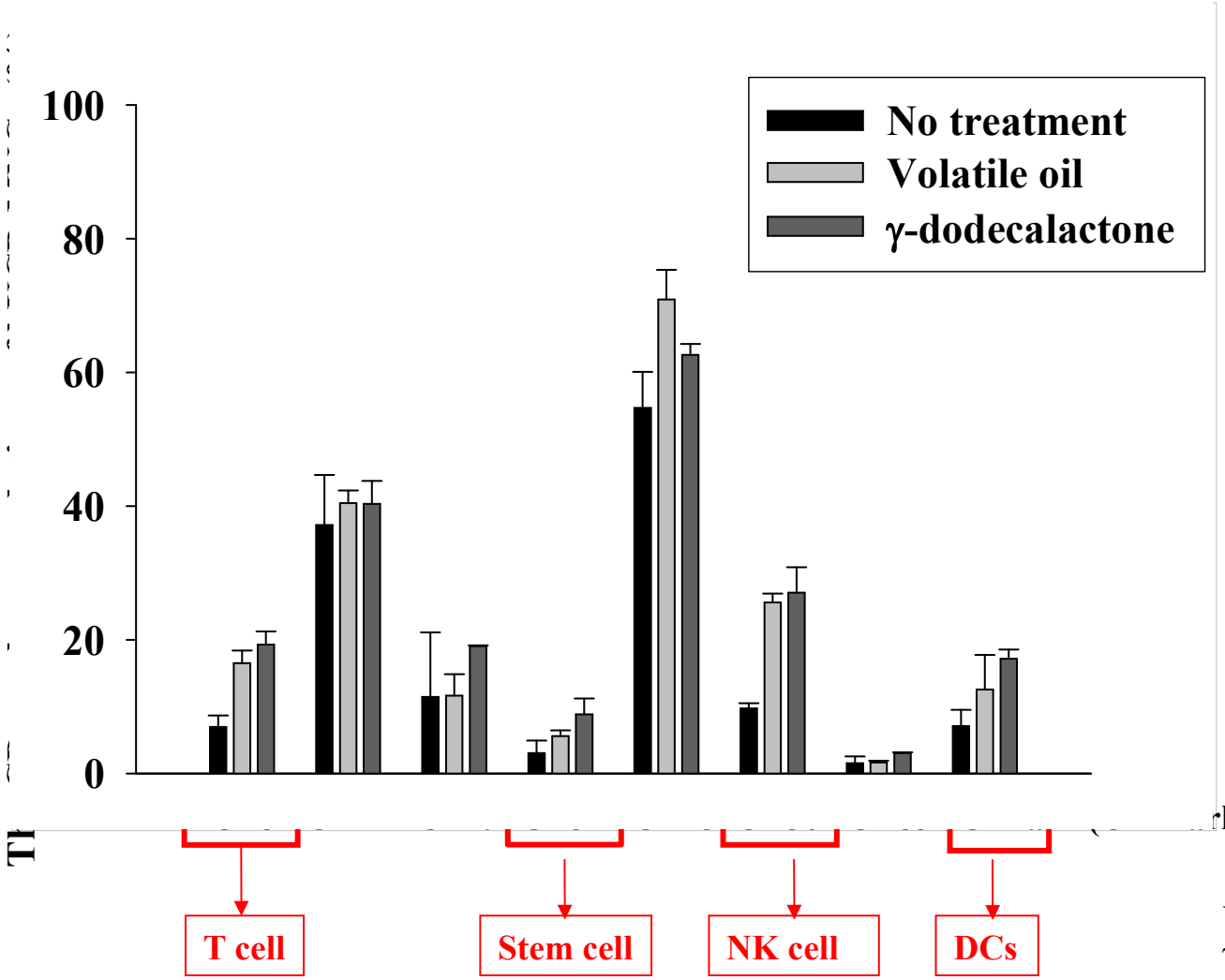
CD80, 86



Choose the sample inducing CD69 expression for dual-color staining to indicate affected cell populations

浩峰生技
ALPS BIOTECH CO., LTD

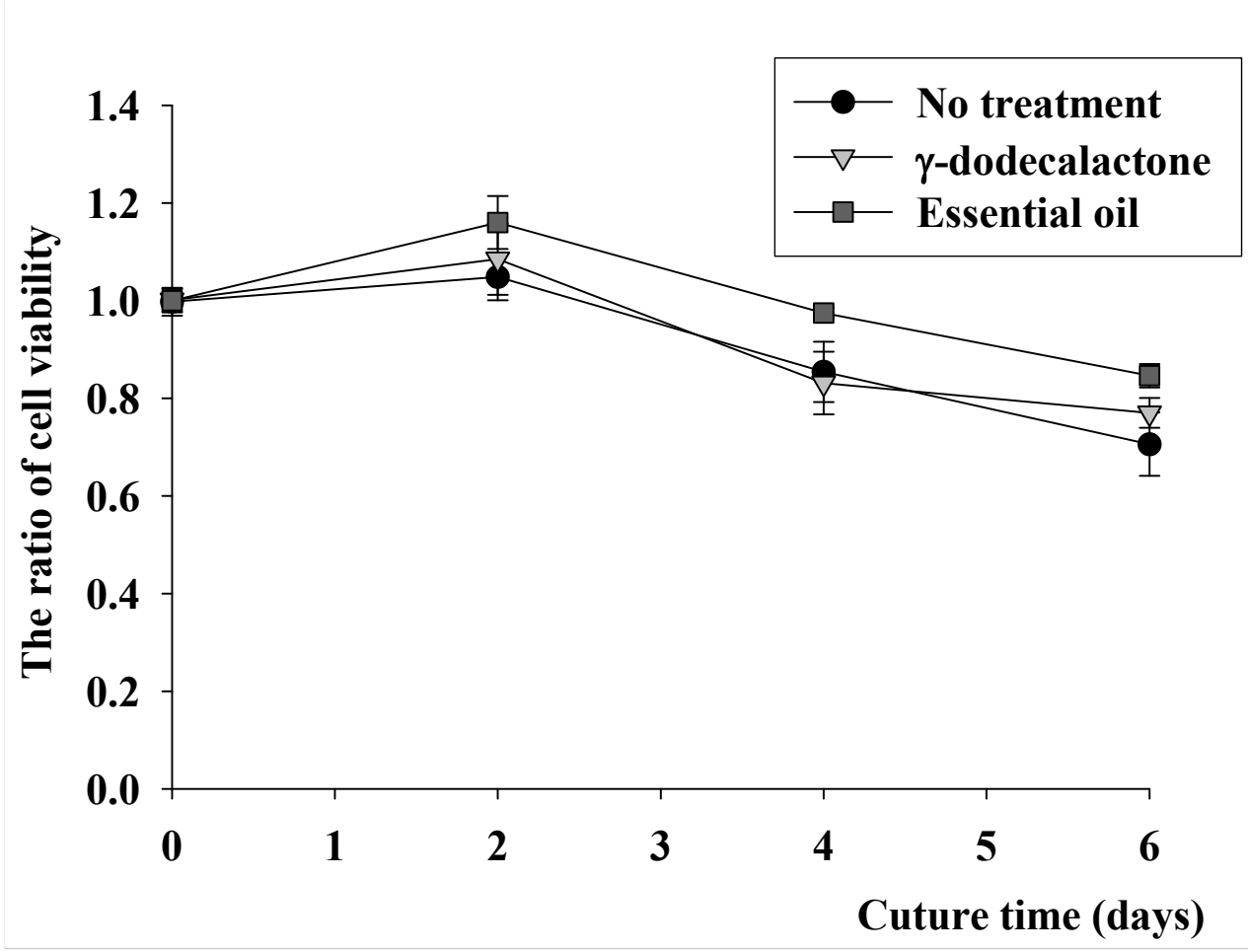
Flow cytometry analysis of hUCB phenotypic changes after γ-DDL and essential oil treatment



Volatile oil : 10 μl/mL
γ-DDL: 100 μM

浩峰生技
ALPS BIOTECH CO., LTD

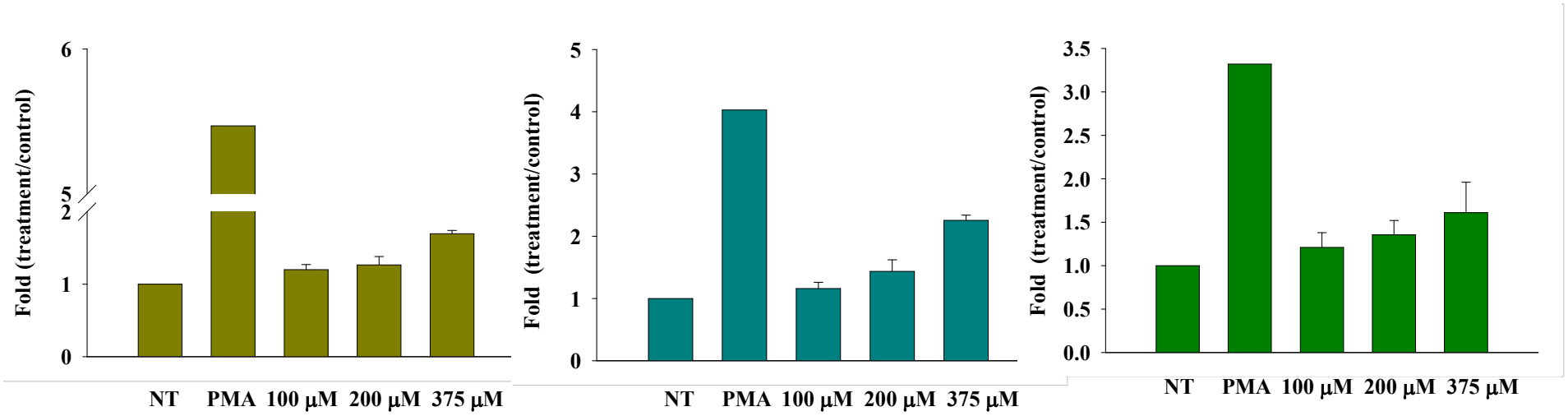
hUCB-MNCs viability test by WST assay

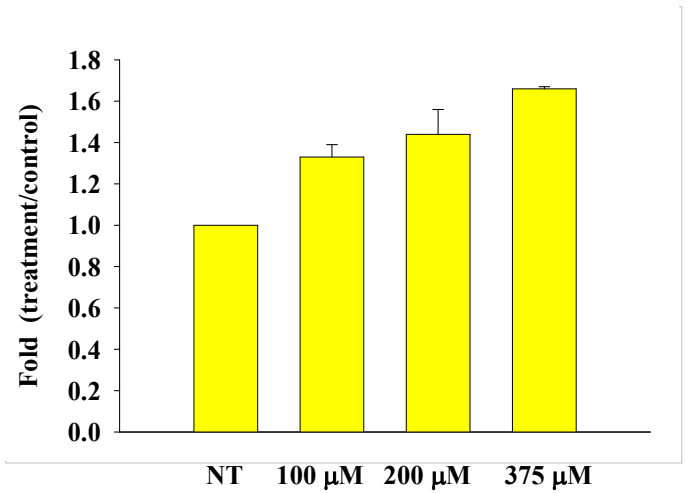


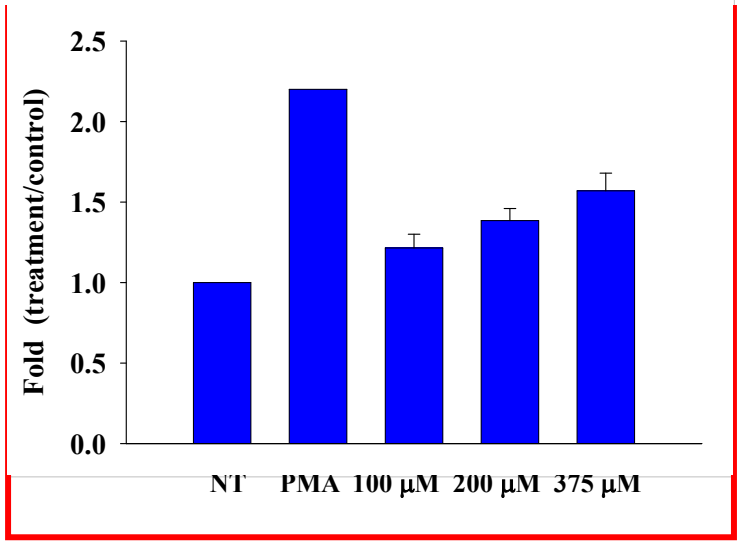
Essential oi : 10 μl/mL
γ-DDL: 100 μM

浩峰生技
ALPS BIOTECH CO., LTD

Induction of CD69 or CD80 expression by γ-DDL in different cell populations of hPBMCs



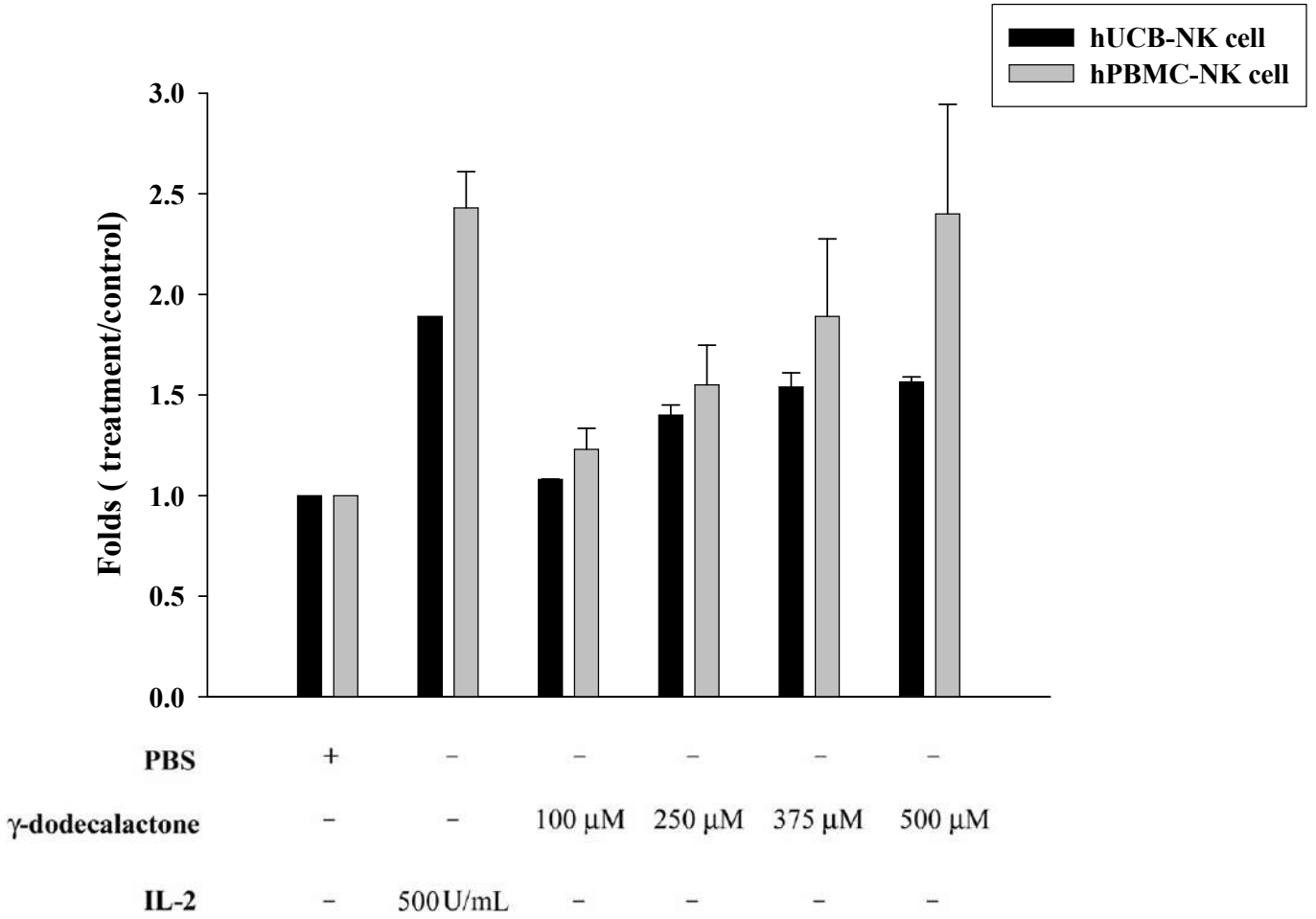




浩峰生技
ALPS BIOTECH CO., LTD

Activation of specific cell population

Comparison of the CD69 marker activation between hUCB-NK and hPB-NK cells after treatment with γ-DDL



浩峰生技
ALPS BIOTECH CO., LTD

結　　論

1. 牛樟芝萃取物降低細胞膜上 ACEII 1/3 的 Gene & Protein,
   降低冠狀病毒感染細胞的機會

2. 牛樟芝分離出 3-5 種三帖類化合物可有效抑制 ACE 酵素活性
   可調控血壓及血液電解質濃度

3. 牛樟芝精油促進免疫細胞活性
   增加身體免疫力對抗外來細菌或病毒

浩峰生技
ALPS BIOTECH CO., LTD

感　　謝

國立宜蘭大學花國峰特聘教授
研究團隊的合作

浩峰身生物科技股份有限公司
研究部同仁的努力