

Evaluation based on **Alternative Method to Animal Testing**

Safety evaluation contract service

Bringing innovation to safety evaluation with **accurate blood cells** and **new test methods** of measuring command substances.

In Alternative Methods to Animal Testing, there are many challenges based on the differences between the cells used* and normal human cells. MiCAN has solved this problem by using a brand-new approach based on regenerative medicine technologies and drastically increased the reliability of evaluation

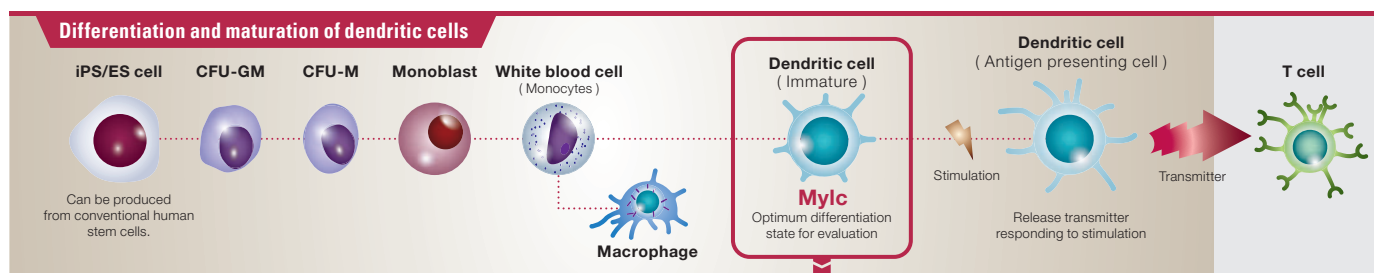
results and choice of evaluation designs. We are offering essential evaluations for the development of pharmaceutical products and cosmetics at low cost in an efficient and speedy manner. Our cutting-edge technology will drastically change the future development of pharmaceutical products and cosmetics.

* Cell lines represented by THP-1, Mono-Mac-6, etc.



Highly accurate examination is now available with **Mylc**, new blood cells for tests.

Mylc blood cells are produced from healthy human cells using regenerative medicine technologies. Mylc blood cells, which are controlled at a pre-stimulated (immature) state before receiving external stimuli and are genetically homogeneous, show pure and clear responses to stimulations in examinations and assure highly reliable test results. Mylc blood cells show very similar biological responses to those of humans and have no problems in reproducibility of results.



Characteristics of Mylc

Homogeneous blood cells with identical genetic information

The same genetic information and conditions can be always reproduced because they are produced in our laboratory. This feature contributes to a drastic improvement in the accuracy and applicability of pharmaceutical evaluation.

We can control the differentiation stage to the optimum conditions

Differentiation stage (maturity) can be minutely controlled with our high level of regenerative medicine technologies and product control. Research and evaluation of high accuracy are available.

Stable mass-production and supply are possible

You can obtain blood cells in the sufficient quantities in ideal condition any time. You can conduct research and development and efficacy evaluation with no delay and accelerate your development.

Three types of blood cells based on the origins.

Different genetic background can be selected depending on the purpose.

We provide three types of (immature) dendritic cells based on the original cell types. For example, tests examining individual characteristics such as sensitive skin and allergic predisposition can be conducted, allowing a wide variety of evaluation designs.

aMylc

Human peripheral blood mononuclear cells

Blood cells that show in vivo-like characteristics and reactions.

iMylc

iPS cell-derived blood cells

Blood cells with standardized genetic background. Standard reactions can be elicited.

uMylc

Customization using provided blood

Blood cell materials with characteristics of the donor can be prepared.

Wide variety of evaluation designs are available

- Want to compare the degrees of responses to drugs in humans with sensitive skin.
- Want to accurately determine response patterns in people who have idiosyncrasies.
- Want to advance development of drugs quickly by measuring drug effect in each evaluation.
- Want to accurately evaluate and compare the effect of drugs under identical conditions.

Test method

Our new test methods can greatly reduce the time and cost.

Major alternative methods to animal testing such as the h-CLAT, a skin sensitization assay, or a pyrogen test using cell lines have various problems such as high cost, long evaluation time, reproducibility, and sensitivity (in particular, false positives). On the other hand, in MiCAN's new method, which uses only iMylc-2 (iPS cell-derived non-stimulated dendritic cells), the relationship between stimulation with substances and the released transmitter (IL-8, a cytokine) is clear.

Our method using a simple ELISA method can drastically reduce the time and cost, helping speedy product development. Moreover, the quantitative measurement of cytokines enables numerical comparisons in response intensities and time course of the changes in addition to the determination of presence/absence of response to stimulation, realizing unconventionally efficient examinations.

01 Skin sensitization assay

For the standard 10 compounds of the h-CLAT (P1 – N10), similar results to those in model cells (LLNA) can be obtained. Time and cost can be drastically reduced because our method is free from the time-consuming procedures and confirmation required in the h-CLAT.

Comparison study with the h-CLAT Our method showed consistent responses to compounds to which inconsistent responses were observed between CD86 and CD54 in the h-CLAT, and our results were similar to those in LLNA.

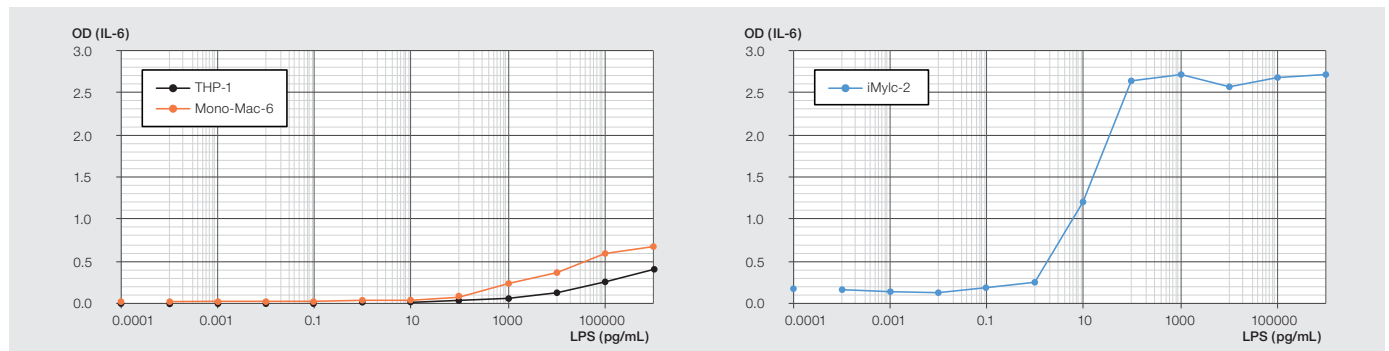
ID	Chemical name	LLNA potency	h-CLAT		iMylc-2	Solvent	CAS No.
			CD86	CD54	IL-8		
P1	2,4-Dinitrochlorobenzene	extreme	P	P	P	DMSO	97-00-7
P2	4-Phenylenediamine	strong	P	N	P	EtOH	106-50-3
P3	Nickel sulfate hexahydrate	moderate	P	P	P	PBS	10101-97-0
P4	2-mercaptobenzothiazole	moderate	N	p	P	EtOH	149-30-4
P5	R(+)-Limonene	weak	N	p	P	EtOH	5989-27-5
P6	Imidazolidinyl urea	weak	P	P	P	PBS	39236-46-9
N7	Isopropanol	Non-sensitizer	N	N	N	PBS	67-63-0
N8	Glycerol	Non-sensitizer	N	N	N	PBS	56-81-5
N9	Lactic acid	Non-sensitizer	N	N	N	DMSO	50-21-5
N10	4-Aminobenzoic acid	Non-sensitizer	N	N	N	PBS	150-13-0
11	Isoeugenol	Moderate	N	N	P		97-54-1
12	1-Bromobutane	Non-sensitizer	P	P	N		109-65-9
13	Propyl paraben	Non-sensitizer	P	P	N		94-13-3
14	Phthalic anhydride	Strong	N	N	N		85-44-9
15	Benzoyl peroxide	Strong	N	N	N		94-36-0
16	Abietic acid	Weak	N	N	N		514-10-3
17	Geraniol	Weak	P	N	N		106-24-1

At present, this assay cannot detect a compound in cases where its metabolites are the cause of sensitivity.

02 Pyrogen test

Mylc, which shows similar response to in vivo cells, is superior in sensitivity in sensitization and stability compared with model cells (Mono-Mac-6, etc.) used in alternative methods to animal testing.

Comparison study with the Mono-Mac-6 Comparison study in IL-6 production assay, in which a pyrogen (LPS) was added. (expressed in OD) In Mylc-2 (right figure), used in this study, the production was detectable at lower concentrations than in Mono-Mac-6 (left figure), indicating a higher response.



Evaluation and research in a common laboratory with Kyoto University

Our headquarters and research laboratory are located in Kyoto-University Katsura Venture Plaza, where Kyoto University nurtures the creation of new businesses utilizing new ideas/technologies and intellectual properties.



- Patent application for non-stimulated dendritic cells for research of viruses (Second product)
- Adopted for the Economic Gardening Support Grant supported by Kyoto Industrial Support Organization 21
- Certified as Management of Wisdom by the Kyoto Chamber of Commerce and Industry (2018)

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