

Plant Stem Cell:

Opening a New Era for Nutrition Ingredient





Have you encountered with these problems?

I developed a series of great products with some good natural ingredient and next year's revenue can be 10 times of this year. But, my supplier came to me and told me that ...

- No enough supply of the key ingredient (Quantity)
- Cannot get those supply on time (Timing)
- Next batch of the natural ingredient was not that good as this batch (Quality & Stability)
- Some toxic components found during QC..... (Safety)

My scientist developed really good ingredeient / product, but it can never be commercialized because...

- no one can provide the key ingredient in the industrial level at reasonable price.... (Quantity, Timing, Cost)





Rong Yu Biotech's Plant Stem Cell Platform Technology provides total solution to you

- Quality & Standardization:** Get the best nutrition ingredient on earth with no compromise
- Quantity, Speed & Stability:** Enjoy the most trustworthy supply system without limitation in time or quantity
- Safety & Morality:** Say bye-bye to all types of pesticide, heavy metal, antibiotics, bacteria, GMO or pollution





Cultivation and Harvest

- Difficulties in Standardization
- Depending on Weather
- Limited by land, location, etc.
- Production cycle can be very long
- Various environment pollutants





Plant Stem Cells

Stem cell is an innately undifferentiated cell which is the precursor to all tissues and organs of a living organism. Stem cells exist within plants as well as animals, enabling plants to grow and regenerate for hundreds, or even thousands of years.

Plant stem cell is an immortal cell and the origin of plant vitality in which the growth and regeneration of plant is programmed in its entirety.

“Plant stem cells, contained in specialized structures called meristems, have amazing regenerative powers. They enable plants to grow and produce new organs throughout lifetimes that can span hundreds of years.”
- 'Nature' 415, 751-754 (2002)



The oldest living organism on earth

Bristlecone Pines in California, U.S., which have been alive for 4,772 years.



The largest living organism on earth

The Giant Sequoia in California, U.S., with 87 meters in height and 2,000 tons in weight



Adonis annua is a perennial plant which does not lose its vitality, even blooming flowers breaking through the snow



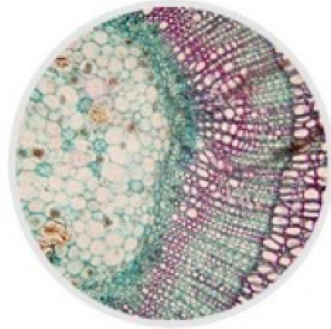
Ginkgo tree is also known as “living fossil,” as it coexisted with dinosaurs 250 million years ago and survived through Ice Age with strong vitality.





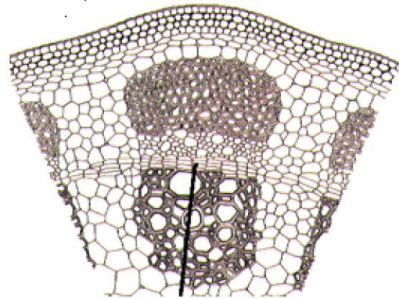
Plant Stem Cell (cont.)

However due to the distinct structural characteristic of plant vascular stem cell, none succeeded in isolation and culture of cambial meristematic cell in spite of 160 years of research and effort.



*"The cambium (plant stem cell) consists of a few layers of narrow, elongated, thin-walled cells, easily damaged during sampling."
Life Science (1999) 322:633-650*

*"Part of the reason for this dearth is the technical difficulty of dealing with cambium, which consists of narrow, axially elongated, thin-walled, highly vacuolated cells sandwiched between much thicker-walled secondary vascular tissue and which are, consequently, easily damaged during sampling."
Journal of Microscopy' (1997) 187:77-84*



Cambium is a type of meristem which is known as plant stem cell tissue. Cambium has thin cell walls which minutely exist in small populations within plant. Due to this structural characteristic, once physical force is applied, it is easily damaged in the very process of isolation, thus losing its stem cell characteristics.

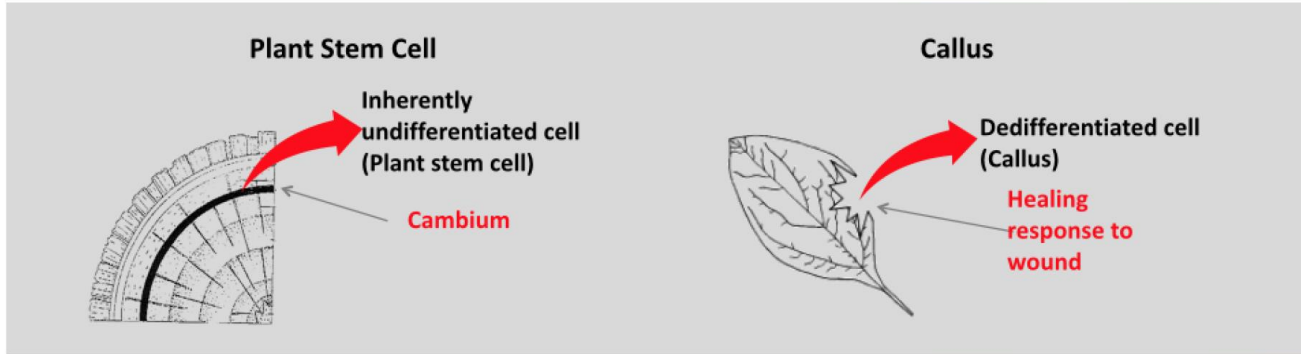




Plant Stem Cell vs. Callus

The Real Plant Stem Cell from Cambium

Plant stem cell is different from callus in its origin as **plant stem cell exists in the plant cambium** while callus is obtained as a temporary response to wound. Moreover callus experiences dedifferentiation in which genetic variation is inevitable. For this reason, continuous and stable cell division of callus is difficult. Hence plant stem cell originated from cambium is an immortal cell while callus is a cell obtained from stimulating the cell.



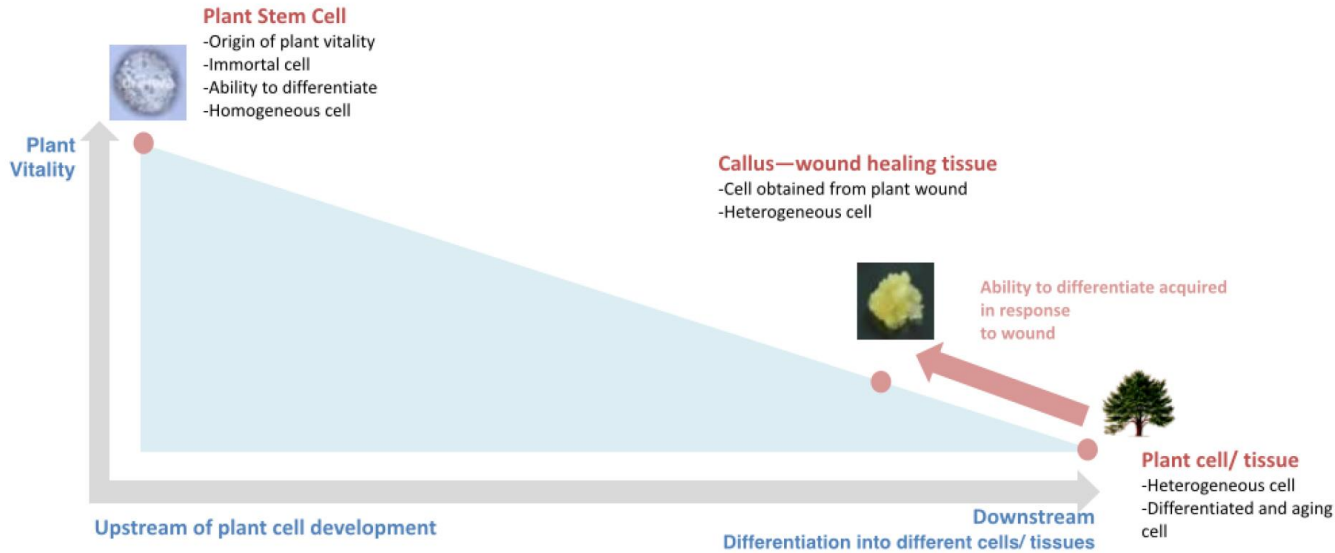
Callus was cultured for 160 years in order to produce plant useful compounds. Callus is **cells formed for the purpose of healing a plant wound and is also called dedifferentiated cell (DDC) or wound healing tissue.**





Plant Stem Cell vs. Callus

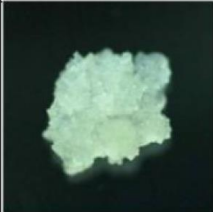



Callus is similar to plant stem cell in its ability to differentiate, however callus and plant stem cell are different in their origin. Furthermore, **ability to differentiate and proliferate are different that differences between plant stem cell and callus were prevalent in culture and research.**





Plant Stem Cell vs. Callus

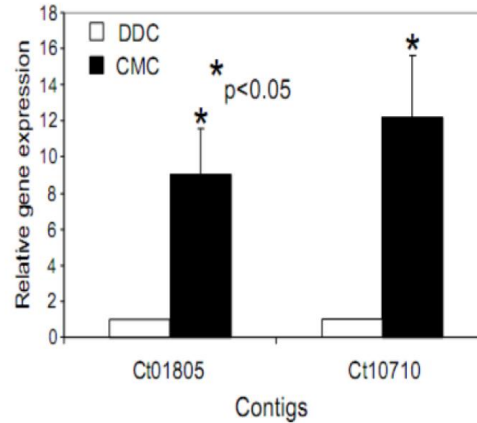
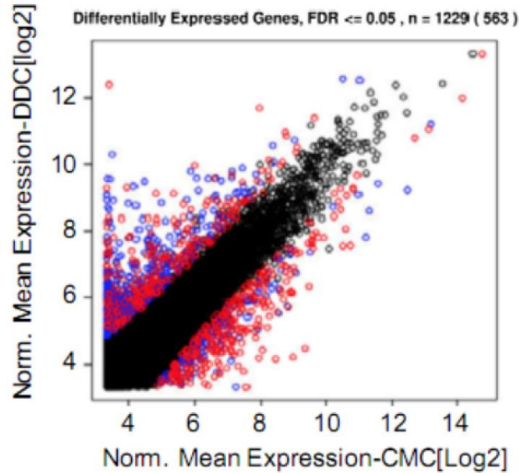
In long term culture, partial differentiation and browning of callus cells were observed and they were no longer dividing well. However no variation was observed in plant stem cell throughout the entire culture period.

	Plant Stem Cell	Callus from Needle	Callus from Embryo	Callus from Bark
<i>Time</i> ↓				
<i>Culture period</i>	64 months	9 months approx.		



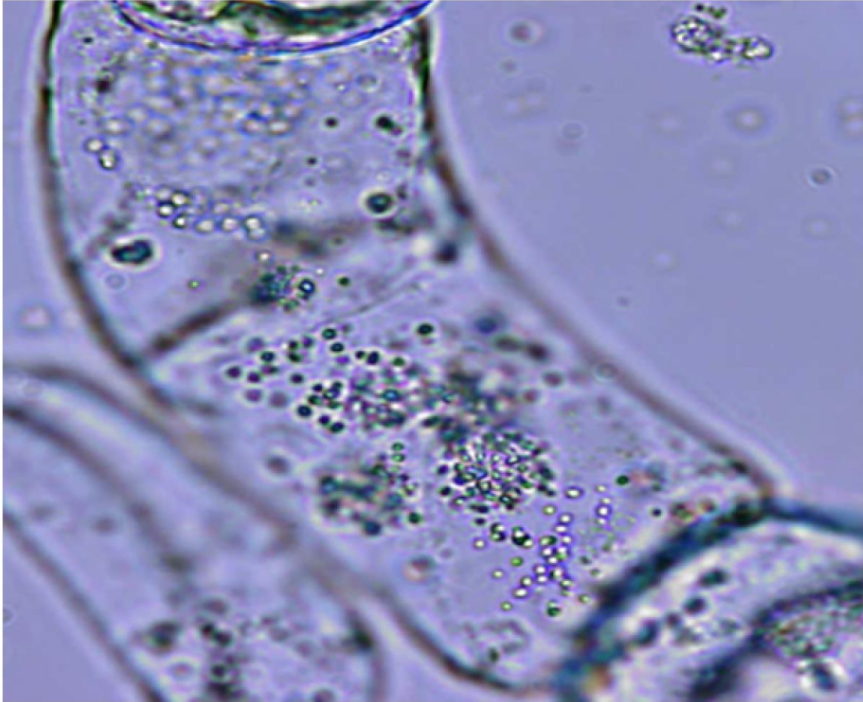
Plant Stem Cell vs. Callus

- Yew transcriptome that we acquired through a combination of deep sequencing technologies enabled us to use digital gene expression tag profiling to compare gene expression in CMCs (cambium stem cells) with DDCs (dedifferentiated cells).
- Digital gene expression tag profiling established that 563 genes were differentially expressed in CMCs (cambium stem cells), with 296 upregulated and 267 downregulated.
- Stem cell marker genes were also expressed in 9 or 12 folds in CMCs (cambium stem cells) compared to DDCs (dedifferentiated cells).





Plant Stem Cell vs. Callus



← Mitochondria in Plant Stem Cell



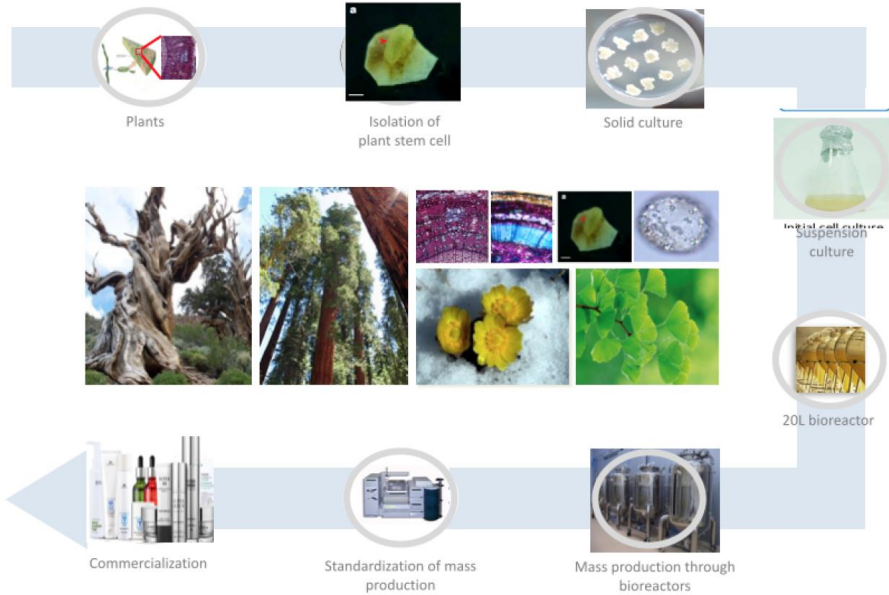
↑ Mitochondria in Callus





Plant Stem Cell Platform Technology: “Agriculture 2.0”

Plant Stem Cell Platform Technology is a plant stem cell isolation and culture technology that is utilized as standardized mass production system for commercializing highly added-value useful compounds and recombinant proteins.





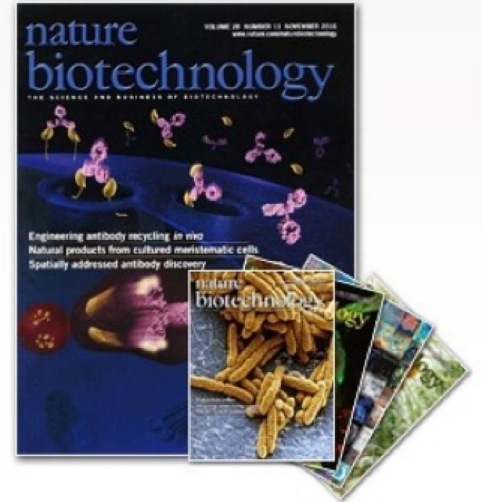
Plant Stem Cell (cont.)



In 2005, Mr. Youngwoo Jin and his fellow researchers succeeded in the world's first isolation and culture of plant stem cell.

Following the success of isolating plant stem cell, in 2006, Mr. Jin and his team began joint research with University of Edinburgh Institute of Molecular Plant Sciences, a world-renowned biotechnology research institute.

The research outcome of plant stem cell isolation and culture technology and the potentials of bioprocess innovation were published by a world-renowned scientific journal, Nature Biotechnology.





Publication in Nature Biotechnology



nature
biotechnology

Since 2006, Mr. Jin's team launched a joint research with University of Edinburgh Institute of Molecular Plant Sciences, a world-renowned biotechnology research institute. They identified the morphological and genetic characteristic of plant stem cell, which research was published as a cover thesis on the world-renowned scientific journal, Nature Biotechnology.

This research proved that cell which Mr. Jin's team has isolated from cambium is a genuine plant stem cell and proposed an infinite commercial potential of this technology.

LETTERS

Nature Biotechnology is an internationally recognized scientific journal with the impact factor of 39.08 (Thomson Reuters Journal Citation Reports, 2014). This places Nature Biotechnology first among journals in the field of biotechnology.

Plant natural products from cultured cambial meristematic cells as a source of plant natural products

Seungho Park¹, Donghyun Kim¹

Cultured cambial meristematic cells as a source of plant natural products

Nature Biotechnology

Plant natural products from cultured cambial meristematic cells as a source of plant natural products

Plant natural products from cultured cambial meristematic cells as a source of plant natural products

Plant natural products from cultured cambial meristematic cells as a source of plant natural products

Plant natural products from cultured cambial meristematic cells as a source of plant natural products

Plant natural products from cultured cambial meristematic cells as a source of plant natural products

Plant natural products from cultured cambial meristematic cells as a source of plant natural products

Plant natural products from cultured cambial meristematic cells as a source of plant natural products

Plant natural products from cultured cambial meristematic cells as a source of plant natural products

Plant natural products from cultured cambial meristematic cells as a source of plant natural products

Plant natural products from cultured cambial meristematic cells as a source of plant natural products

Plant natural products from cultured cambial meristematic cells as a source of plant natural products

Plant natural products from cultured cambial meristematic cells as a source of plant natural products

Plant natural products from cultured cambial meristematic cells as a source of plant natural products

Plant natural products from cultured cambial meristematic cells as a source of plant natural products

Plant natural products from cultured cambial meristematic cells as a source of plant natural products

Plant natural products from cultured cambial meristematic cells as a source of plant natural products

Plant natural products from cultured cambial meristematic cells as a source of plant natural products

Plant natural products from cultured cambial meristematic cells as a source of plant natural products

Plant natural products from cultured cambial meristematic cells as a source of plant natural products

Plant natural products from cultured cambial meristematic cells as a source of plant natural products

Plant natural products from cultured cambial meristematic cells as a source of plant natural products

Plant natural products from cultured cambial meristematic cells as a source of plant natural products

Plant natural products from cultured cambial meristematic cells as a source of plant natural products

Plant natural products from cultured cambial meristematic cells as a source of plant natural products

Plant natural products from cultured cambial meristematic cells as a source of plant natural products

Plant natural products from cultured cambial meristematic cells as a source of plant natural products

Plant natural products from cultured cambial meristematic cells as a source of plant natural products

Plant natural products from cultured cambial meristematic cells as a source of plant natural products

Plant natural products from cultured cambial meristematic cells as a source of plant natural products

Plant natural products from cultured cambial meristematic cells as a source of plant natural products

Plant natural products from cultured cambial meristematic cells as a source of plant natural products

Plant natural products from cultured cambial meristematic cells as a source of plant natural products

Plant natural products from cultured cambial meristematic cells as a source of plant natural products

Plant natural products from cultured cambial meristematic cells as a source of plant natural products

In addition, on News and Views in the November 2010 issue of Nature Biotechnology (a contribution written on monthly theses by prominent scientists in the given fields of study), Susan C. Roberts—the head of University of Massachusetts Institute for Cellular Engineering, Amherst, and the world's chief authority in plant cell culture—wrote in response to Mr. Jin's thesis under the title, "Plant natural products from cultured multipotent cells." There she wrote that (Mr. Jin)'s plant stem cell isolation and culture technology "marks an important departure from traditional plant cell culture" which was eclipsed by "uncertainties regarding the feasibility of large-scale manufacture...[and] [f]rom a commercial perspective, CMCs could supersede existing plant cell culture methods for generating natural products."



Intellectual Property Status

Rong Yu Biotech Intellectual Property Status:

- Secured an extensive international patent portfolio by applying for patents for plant stem cell isolation & culture platform technology in 10 major countries
- Established powerful patent portfolio by applying and registering about 84 patents (including 64 patents overseas) for substance, usage, and method



Patent Application & Registration Status		
KOREA	15 Registered	5 applied
GLOBAL	40 Registered	24 applied
TOTAL	55 Patents Registered	29 Patents applied

Rong Yu Biotech is a IP-focused company succeeded in developing a platform technology using plant stem cell. Rong Yu Biotech secures patents for its innovation and utilizes the same for commercialization of business.



Raw Material Development Through Various Process

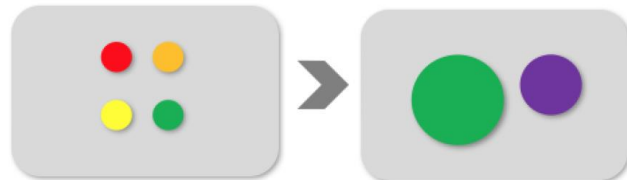
Rong Yu Biotech can produce various high-quality ginsenosides through wild ginseng stem cells. Diversifying the process allows production of various useful compounds and can increase the contents of useful compounds which scarcely exist or do not exist in ginseng or red ginseng and can mass produce specific compounds.



Diversity



Enhancement

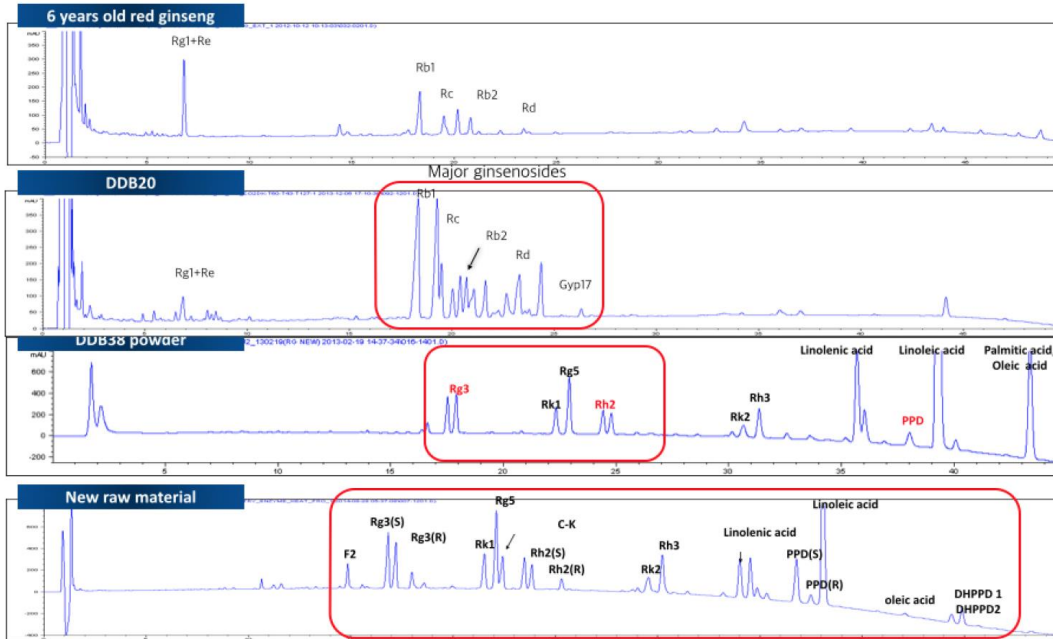


Specificity



Development of Food and Cosmetic Ingredient

Through the development of competitive raw materials, Rong Yu Biotech produces finished food and cosmetic products by using the developed raw materials. Rong Yu Biotech has developed raw material composed of rare ginsenosides which scarcely exist or do not exist in ginseng or red ginseng. Raw materials which contain more rare and more diverse rare ginsenosides are being developed.



Rare Ginsenoside as Nutrition Ingredient

Content of Wild Ginseng Stem Cell Culture Mix

Place	Substances	Compound	Efficacy	Compound	Efficacy
Cell containing compounds	Rare Metabolome Ginsenoside	Rg3	-Controlling Central nervous system -Improving blood circulation -Restraining cancer metastasis -Reducing anti-cancer drug side effect -Improving Liver functionality -Anti-Atopy	Rh2	-Anti-Cancer, Anti-Cancer metastasis -Expediting Cancer cell differentiation -Vitalizing anti-cancer medicine -Anti-Osteoporosis -Anti-Atopy
		Rk1, Rg5	-Anti-Cancer -Anti-Anxiety -Advancing Brain activity -Anti-Diabetic -Suppressing hepatitis C	Rh3	-Anti-Cancer -Anti-inflammation -Anti-Dementia
		Rk2	-Anti-Cancer effect -Expanding Vascular	PPD	-Anti-Cancer -Expediting anti-cancer medicine vitalization strongly -Anti-Dementia
	Saturated & unsaturated fatty acid	Palmitic acid	-Anti-Cancer (Skin cancer) -Strengthen immunity (Anti skin bacterial) -Antioxidative -Insulin resistibility	Oleic acid	-Anti-Cancer (Breast Cancer) -Decreasing production glucose -Antioxidative -Preventing Cardiovascular Disease -Preserving nerve cell
		Linoleic acid	-Immunomodulator -Anti-Cancer(Osteosarcoma, Gastric cancer cell)	Linolenic Acid	-Decreasing production glucose -Antioxidative -Preventing Cardiovascular Disease -Preserving nerve cell
Extract Liquid Containing Compounds	Polyphenol	Chloro genic Acid	- Restraining lipopeptide production - Restraining Cholesterol synthesis - Antioxidative - Anti-Cancer	3-O-Feruloyl quinic acid	- Antioxidative Action - Anti-Cancer

- Above Metabolome Ginsenoside, unsaturated fatty acid and Polyphenol are isolated and identified by Rong Yu.
- Extra isolation and identification is possible (Polyphenol).
- Classic activity is Anti-Cancer.





New Drug Development Business – Botanical Drug

Botanical drug development is one of Rong Yu's future business. Plant stem cell isolation and culture technology allows optimization of efficacy, consistency of quality, competitive mass production. With the aim of blockbuster botanical drug development, Rong Yu is collaborating with various world-renown researchers and institutions globally.

Efficacy Study

With the aim of new drug development, Rong Yu is collaborating with various schools and institutions in domestic and overseas for research and development of new drug by discovering the efficacies on various diseases and safety tests



Efficacy study on liver-damage protection

Efficacy study on metabolic diseases

Material Study

Based on the isolated plant stem cell, materials that have high potential for new drug development are continued to be discovered through various studies such as genetic study, compound analysis and transformation study , etc.



Identification of plant stem cell identity
Enhancement of high added-value secondary metabolites
Study on recombinant protein production

Mass Production Study

For safety and competitiveness, studies on biomass enhancement and specific target compound mass production based on 3Q quality control are going on.
(Bioreactor Capacity : 50 ton)

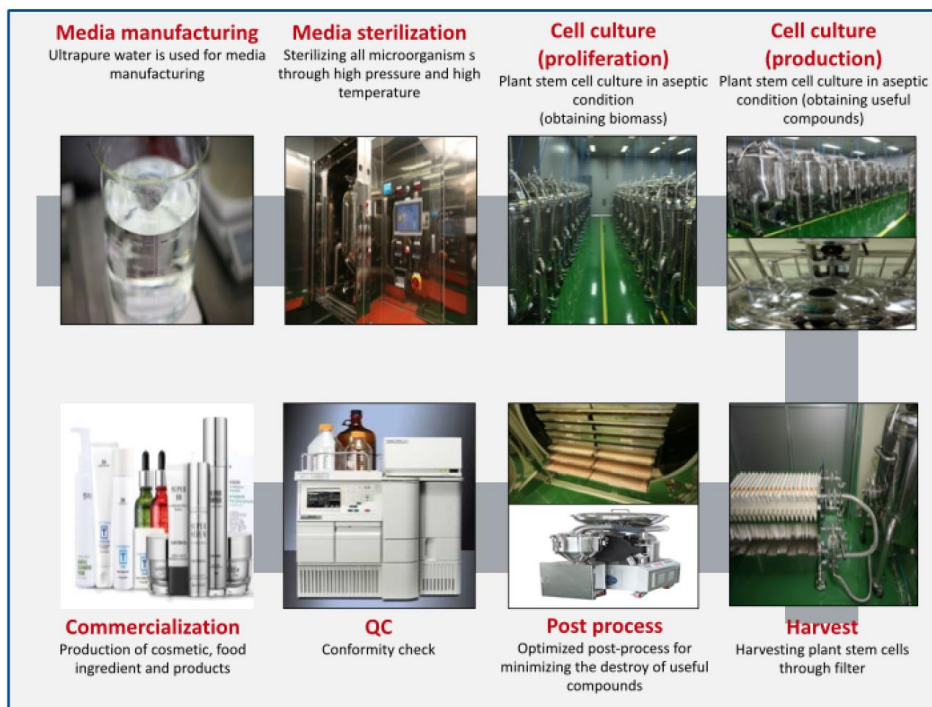
Mass production of raw material

Studies on production of specific compounds



Management of Quality Control System

Rong Yu Biotech produce consistent raw materials by intensifying the quality control standards throughout the whole process from material purchase step to production. It is produced in aseptic condition without any microorganisms and its safety is guaranteed since pesticide, heavy metals and hormones are not used. Also, whole production process is documented for management, thus maintenance of quality and stable and consistent production is possible.



ISO 9001 Certification



Documents for whole process management





Production Center

Rong Yu Biotech enables standardization and stable production of products based on the technology of Plant Stem Cell Institute (PSCI) with mass production and optimization system.



View of Production Center



PSCI : 213 bioreactors



PSCI : 67 bioreactors
Production Center : 168 bioreactors



Quality Control Team.



3 ton scale culture. Successfully completed pilot test for mass production (Chungbuk, Technopark)



Production Center Facility Status

cGMP pilot process, production process, Quality control analytical lab.

Scale : 1,516 m²

Annual productivity : 250T





Excellence of Technology

CMCs Culture Technology: Solution to CMC

CMC²™

Cambial Meristematic Cell Culture Technology, as a total solution to Chemistry, Manufacturing, and Control

Chemistry

- Various polychemical preparations
- Highly consistent chemical fingerprint
- Marker compound identification

Manufacturing

- Stable & sustainable process development
- cGMP : CMO services
- Cell line bank

Control

- Advanced QC methodology
- Manufacturing process control
- Metabolomics & bioinformatics

CMC Culture Technology

- highly consistent quality control
- stable and reproducible manufacturing system

Regulatory Approval Guidelines

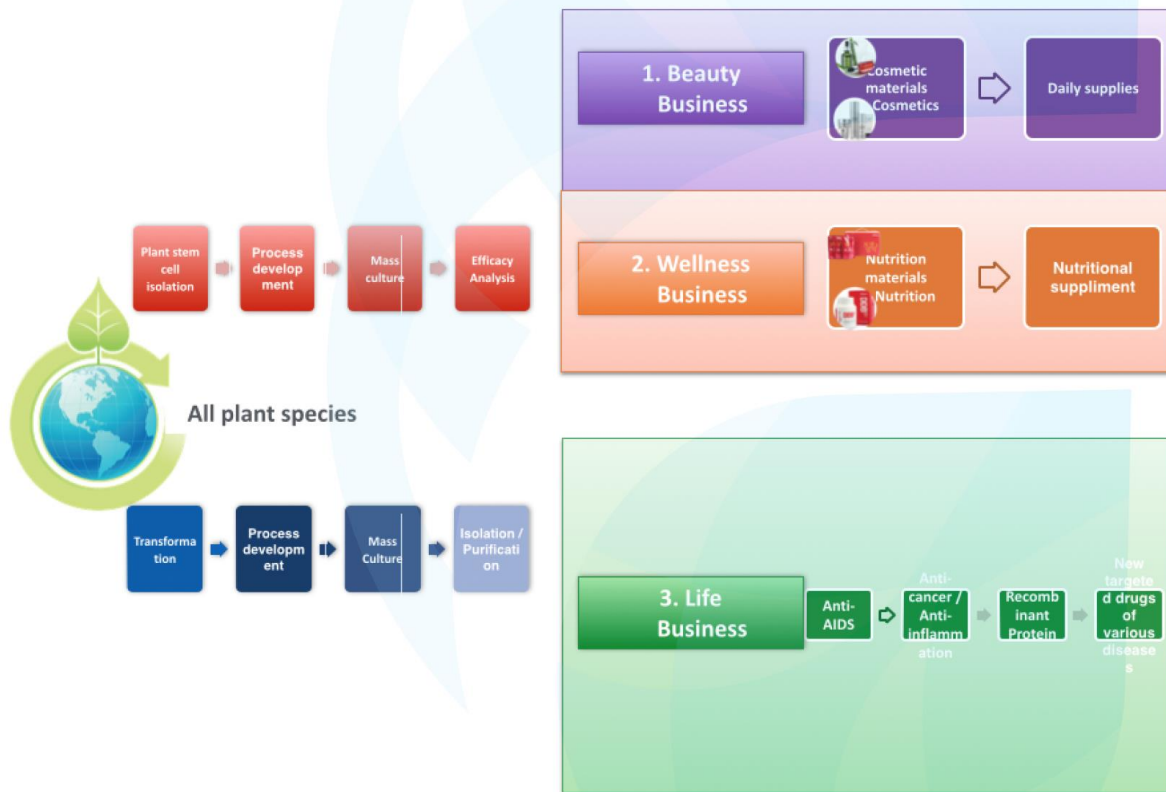
Standards & Platform Technology





Plant Stem Cell Technology applied Business Models

Rong Yu Biotech utilizes plant stem cell technology to develop botanical drugs, develop new biomaterial for pharmaceutical, nutrition, and cosmetic industries and simultaneously fosters its own nutrition and cosmetics business.

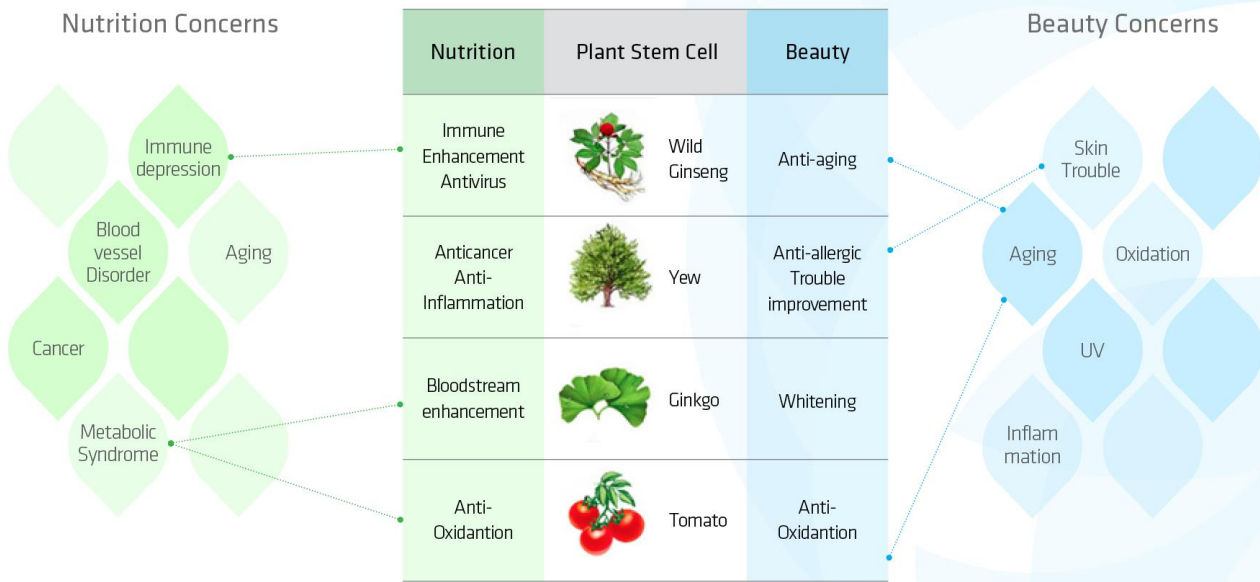




Cosmetics & Food Business

Rong Yu Biotech promotes various types of business in nutrition & beauty area such as raw material, semi-product/formula, ODM, branded product, etc. utilizing plant stem cell originated materials which hold the genuine vitality of plants.

[Product Scope for All Rare Plant Contents]





Rong Yu Biotech's Plant Stem Cell Platform Technology provides total solution to you

Quality & Standardization:

Get the best nutrition ingredient on earth with no compromise

Quantity, Speed & Stability:

Enjoy the most trustworthy supply system without limitation in time or quantity

Safety & Morality:

Say bye-bye to all types of pesticide, heavy metal, antibiotics, bacteria, GMO or pollution


(**BEYOND THE LIMIT**)
CMCs Platform


(**BEYOND THE NATURE**)
Rare Plant Content


(**BEYOND THE QUALITY**)
ODM Solution

