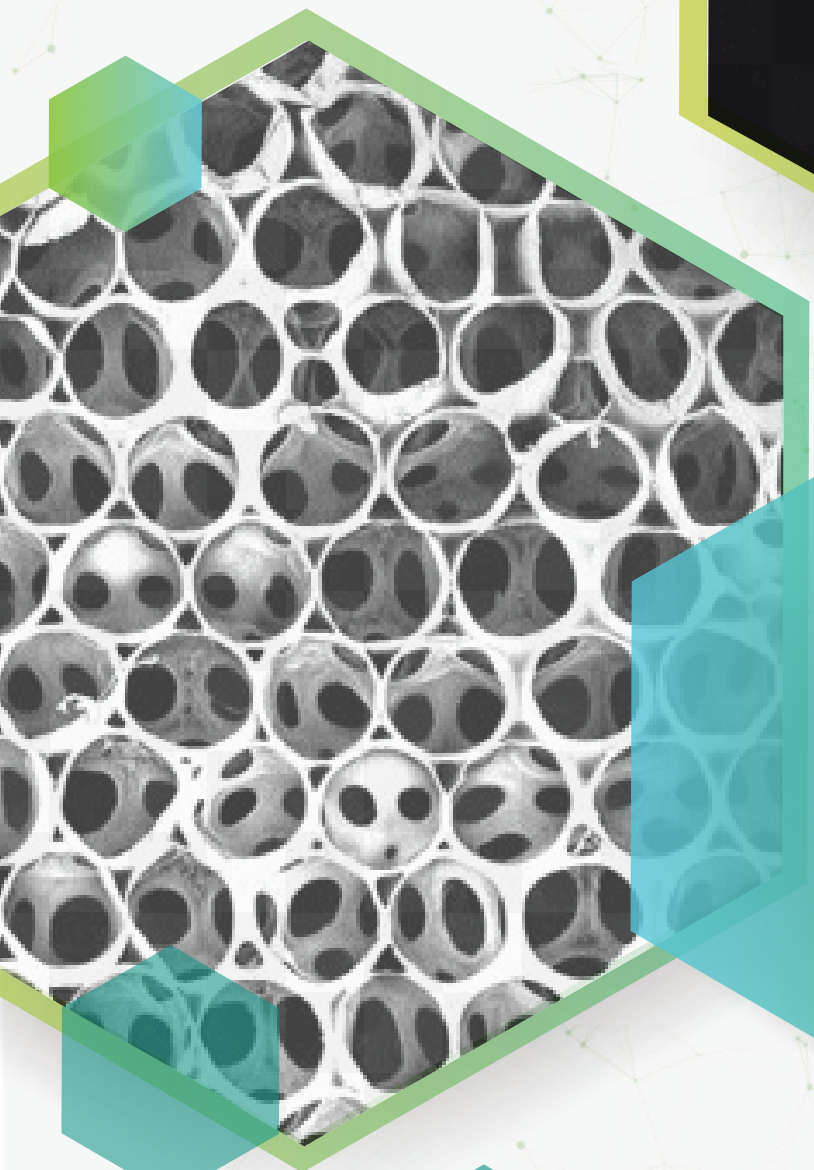

UniTantrix® Dissolvable Microcarriers

T A N T T I

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tantti

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Company

Tantti Laboratory Inc. ("Tantti") was founded in 2014 by eight distinguished professors in Taiwan with expertise in Chemical and Materials Engineering. Since its inception, the company has developed two platform technologies (Tantti® Monolith and Tantti® BioScaffolds) which use microfluidics and in-mold polymerization to create highly ordered micro- and nano-porous biomaterials.

▪Tantti® BioScaffolds, which include our UniTantrix® Dissolvable Microcarriers and 3D BioScaffold product lines, are our platform solution for the biomedical industry's growing needs for high-density cell expansion used in vaccine/viral particle production, cell therapy, tissue engineering, regenerative medicine, and high-throughput/content drug screening, among other applications.

▪Tantti® DuloCore™ represents a breakthrough in liquid chromatographic technology used in the separation and purification of large biomolecules, including DNA plasmids, mRNA, viral vectors, viruses and exosomes. Its applications target downstream process (DSP) of biopharma products in advanced therapies and vaccines.

Our technologies have received patent approvals around the world, including in the United States, Europe, Japan, Taiwan and China, and we continue to conduct extensive R&D in-house as well as with our academic and corporate research partners.

At Tantti, our mission is not only to develop innovative biomaterial technologies that provide the highest performing, cost- and time-effective solutions for our customers. We also aim to become a collaborative partner with our customers, assisting them in realizing their visions of developing innovative biologic therapies, whether it is in a small-scale research setting or at the commercial production stage. We distribute our products around the world, both directly to customers and through our distribution partners.

Ultimately, we hope our commitment to innovation, quality, and service will drive Tantti's long-term sustainable growth in the biomaterials industry. Together with our partners, we strive to become a world-class, global biomaterials company and we sincerely welcome you to collaborate with us, whether as a customer, distributor, research partner, employee or as an investor/shareholder.

About UniTantrix® Dissolvable Microcarriers

Microcarriers are support matrices that allow for high-density cell expansion in a bioreactor environment and are used in the biopharmaceutical industry for vaccine/viral particle production and cell/gene therapy. One of the major challenges associated with microcarrier-based cell expansion is the harvesting of the desired cell products. Typically this is achieved by filtration and/or centrifugation; however, these separation processes can result in sub-optimal cell yields and, as a results, reduced cost efficiency.

To address this challenge, Tantti has developed UniTantrix® Dissolvable Microcarriers, a patented product that can be dissolved with Trypsin or TrypLE™ solution for easy separation and harvesting of the desired cell products. Additionally, UniTantrix® is valued for its high porosity and high interpore connectivity. The highly connective macropores in UniTantrix® allow cells to adhere, proliferate and migrate within the microcarrier while simultaneously enabling the exchange of nutrients, oxygen and metabolic waste. Moreover, the denatured collagen-based material that comprises UniTantrix® provides high cell attachment rates, growth yield and cell viability. With all these unique features, UniTantrix® offers a highly efficient and cost-effective cell expansion solution for both R&D and USP production of biologics.

The advantages of UniTantrix®Dissolvable Microcarriers include:

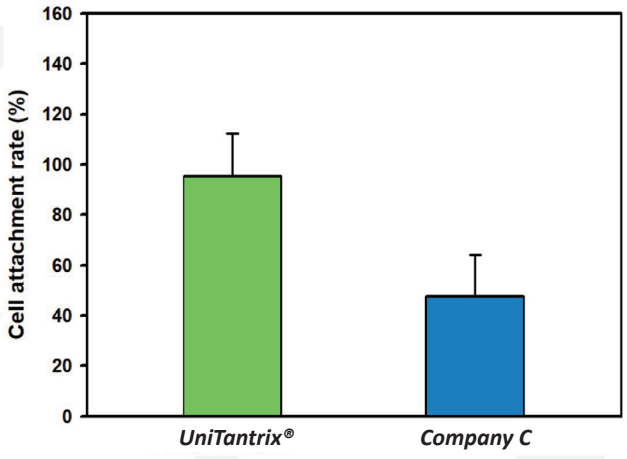
- Superior cell adhesion: composed of denatured collagen.
- High-yield productivity: effective surface area of more than 6000 cm^2/g.
- Macropores and inter-connected pores: protects cells from shear stress, increasing cell viability and yield.
- Dissolvable materials: easy cell harvesting with Trypsin or TrypLE™.
- Controllable lot-to-lot consistency.

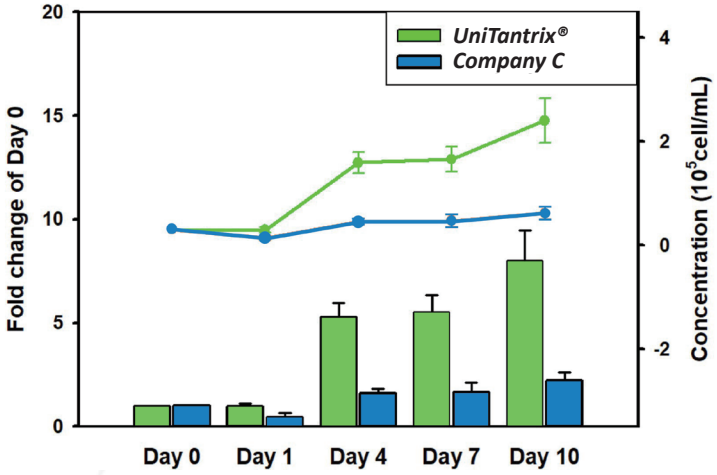
Product Name	UniTantrix® Dissolvable Microcarriers
Material	Denatured Collagen
Density	1.0-1.1 g/ml
Microcarrier diameter	Format-- Dry Powder
Average pore diameter	~150 µm
Average interpore size	~30-50 µm
Surface area	~6,000 cm^2/g
Dissolvability	Yes, with Trypsin-EDTA or TrypLE™"

UniTantrix® Dissolvable Microcarriers Applications

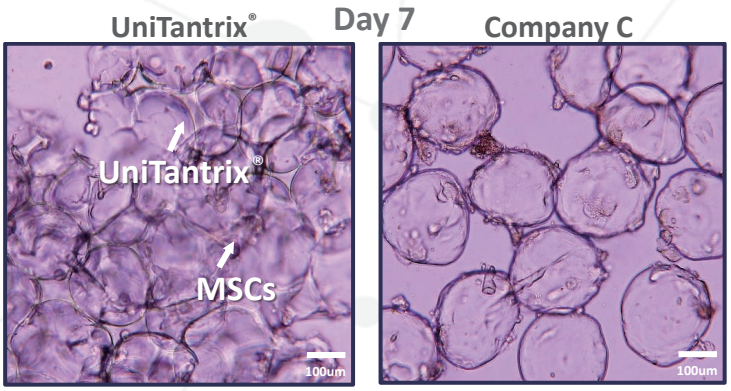
(A) hBMSCs Expansion on UniTantrix® Microcarriers

High surface area, high cell attachment rate and high cell yield

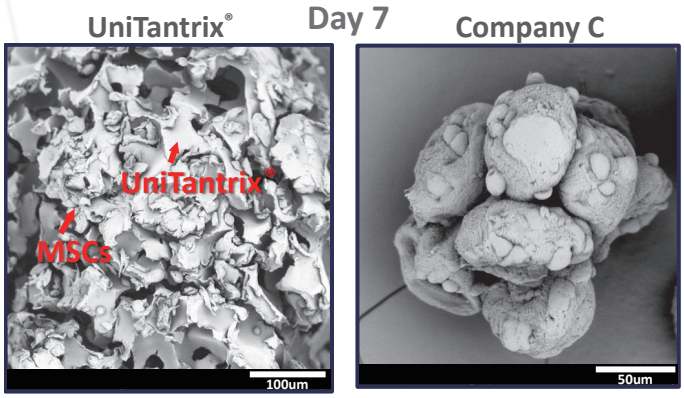




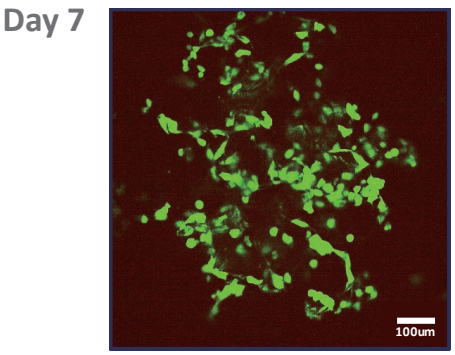
The images of hMSCs on UniTantrix® by optical microscope



The images of hBMSCs on UniTantrix® by scanning electron microscope



The image of hBMSCs on UniTantrix® by confocal fluorescence microscope



Characterization of recovered hBMSCs

Positive Markers	UniTantrix®	Company C
CD90	98.93%	94.75%
CD105	96.89%	55.17%
CD73	99.93	99.95%
Negative Markers	**UniTantrix®**	**Company C**
CD34, CD11b, CD19, CD45, HLA-DR	0.15%	0.16%

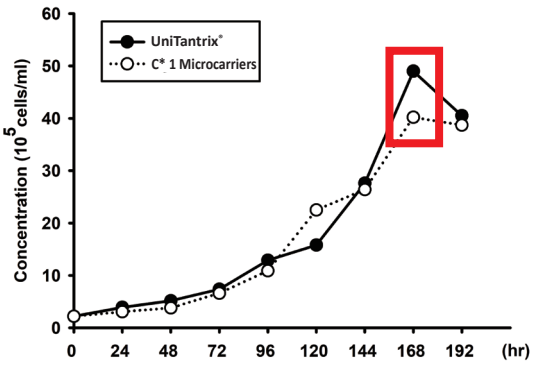
UniTantrix® Dissolvable Microcarriers Applications

(B) Enterovirus 71 Vaccine Production

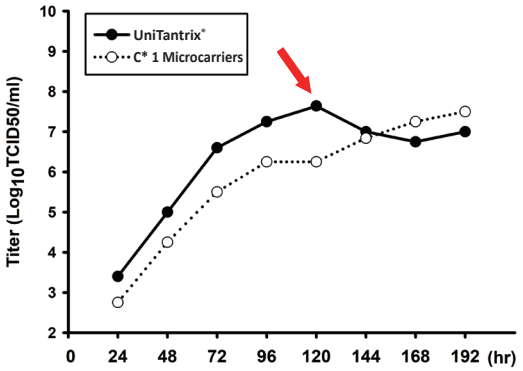
High production of cells and vaccines with less materials used per operation

125 mL of spinner flask

Growing curve for Vero cells (100 mL)

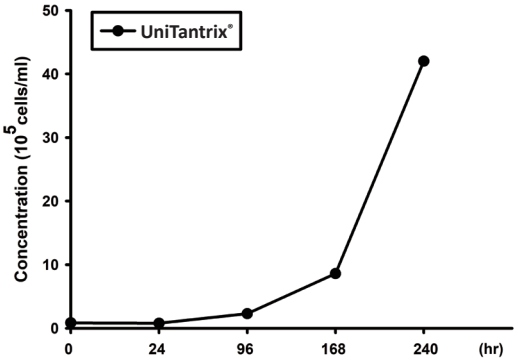


Enterovirus 71 (EV71) B5 production (100 mL)

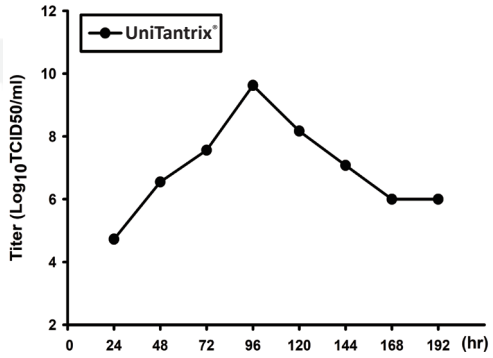


5 L of stirred bioreactor

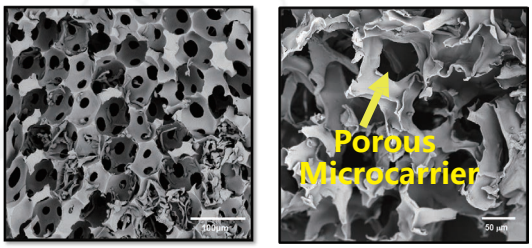
Growing curve (5 L)



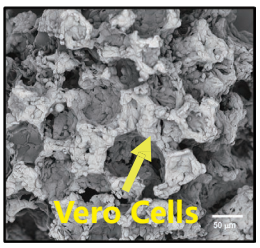
Enterovirus 71 (EV71) B5 production (5 L)



UniTantrix® (Blank)

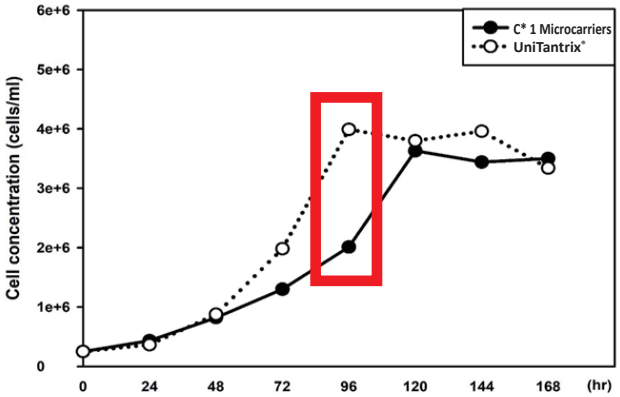


UniTantrix® (Vero Cell)



(C) HEK293 cells Expansion on UniTantrix® Microcarriers

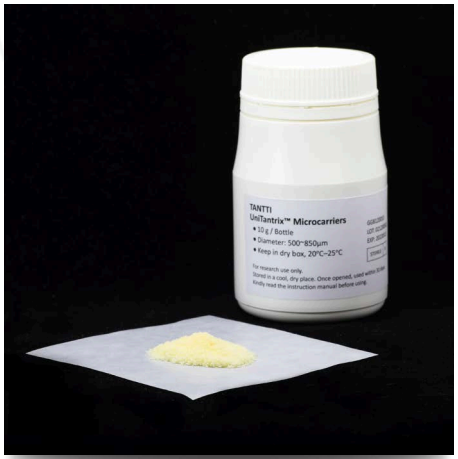
Growing curve for HEK293 cells

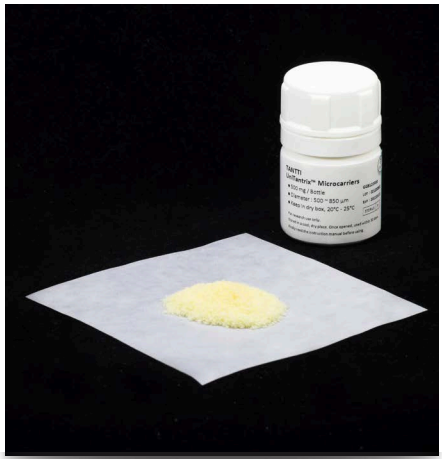


*The validity study was supported by National Health Research Institutes from Taiwan (Dr. Yung-chiu Hu)

Product List

PRODUCT NAME	PRODUCT CAT. NUMBER	PRODUCT SPECIFICATION
UniTantrix® Microcarriers Dry Powder, 300-1,000 µm	GGBB120001-01	UniTantrix® Dissolvable Microcarriers Collagen-based, weight 1 g/bottle, powder, sterile
	GGBB120005-01	UniTantrix® Dissolvable Microcarriers Collagen-based, weight 5 g/bottle, powder, sterile
	GGBB120010-01	UniTantrix® Dissolvable Microcarriers Collagen-based, weight 10 g/bottle, powder, sterile
	GGBB120020-01	UniTantrix® Dissolvable Microcarriers Collagen-based, weight 20 g/bottle, powder, sterile
	GGBB120011-01	UniTantrix® Dissolvable Microcarriers Collagen-based, weight 100 g/bottle, powder, sterile
	GGBB12G020-01	UniTantrix® Dissolvable Microcarriers Collagen-based, weight 20 g/bottle, powder, sterile, GMP grade
	GGBB12G011-01	UniTantrix® Dissolvable Microcarriers Collagen-based, weight 100 g/bottle, powder, sterile, GMP grade





Instruction for use

UniTantrix® Dissolvable Microcarriers

Sterilized by gamma irradiation

Note:

- UniTantrix® Dissolvable Microcarriers is only for *in vitro* use.
- Ship and store at +10 to +35 °C.
- It shall be used up after opening the bottle.

Instruction for use

※ The following instruction for use (IFU) to demonstrate how to use 2 g/L of UniTantrix® in a 100 mL bioreactor as an example. Generally, the concentration of UniTantrix® microcarriers used (g/L), cell seeding density (no. of cells/mL of UniTantrix®) or amount of Trypsin-EDTA (or TyrpLE™) added to dissolve UniTantrix® are suggested for a 100 mL bioreactor in the IFU which can be proportionally scaled up to other volumes of your desired bioreactors.

Materials and Equipment Needed

- UniTantrix® Microcarriers (surface area: ~6,000 cm^2/g)
- 125 mL siliconized BELL-FLO™ spinner flasks or 125 mL Corning® ProCulture® glass spinner flask (Whenever the glass spinner flask is used, the inside surface of the vessel should be siliconized to prevent the microcarriers attached to glassware surface)
- Cimarec™ Biosystem Slow-Speed Stirrer for cell culture agitation
- Cell culture medium for specific cell needs
- Sterile 1 x PBS (without $Ca2^+$ and $Mg2^+$)
- 0.25% Trypsin-EDTA (or 1 x TrypLE™)
- 37°C, 5%CO_2 cell incubator

UniTantrix® Preparation

UniTantrix® Hydration and Culture Medium Equilibration.

1. Weigh 0.2 g UniTantrix® in siliconized glass spinner flask, and add to 100 mL 1xPBS.
2. Autoclave at 121°C for 20 minutes to hydrate UniTantrix®.
3. Cool down to room temperature before use.
4. Remove the PBS, add 30~50 mL fresh 1xPBS and mix. Repeat the wash step twice.
5. Replace PBS, add 50 mL fresh cell culture medium.
6. Place the spinner flask in the incubator at 37 °C and equilibrate at 40 rpm for at least 10 minutes.

Note:

a. hydrated microcarriers in PBS can be stored at 4°C for 7 days.

b. Pipetting carefully and not to aspirate microcarriers.

Instruction for use

Cell Seeding, Attachment and Expansion

A. Human Mesenchymal Stem Cells (hMSCs)

1. Trypsinize hMSCs from culture vessels and seed 6 x 10^6 (6 x 10^4/mL or 5,000 cells/cm^2) of total cell number into equilibrated spinner flasks containing UniTantrix® microcarriers.
2. Stir at 40 rpm for 40 seconds then 0 rpm for 30 minutes at 37°C, 5%CO_2 cell incubator for cell attachment.
3. Repeat the above step 48 times (24hrs).
4. After 24 hrs of intermittent cycles, add fresh cell culture medium to 100 mL of the working volume. And agitation condition was maintained at 40 rpm for cells expansion.
5. To avoid the cells-microcarrier aggregation and the stirring speed was adjusted to maintain microcarriers fully suspended during the cell's expansion (gradually increased to 50-80 rpm).

B. Vero Cells

1. Trypsinize Vero cells from culture vessels and seed 8 x 10^6 (8 x 10^4/mL or 6,600 cells/cm^2) of total cell number into equilibrated spinner flasks containing UniTantrix® microcarriers.
2. Stir at 40 rpm for 40 seconds then 0 rpm for 30 minutes at 37°C, 5%CO_2 cell incubator for cell attachment.
3. Repeat the above step 48 times (24hrs).
4. After 48 times of intermittent cycles, add fresh cell culture medium to 100 mL of the working volume. And agitation condition was maintained at 40 rpm for cells expansion.
5. To avoid the cells-microcarrier aggregation and the stirring speed was adjusted to maintain microcarriers fully suspended during the cell's expansion (gradually increased to 50-65 rpm).

Note:

a. Stirring speed should be adjusted promptly to adapt various cell types.

b. Culture medium exchanges were performed depending on nutrient consumption and metabolite accumulation and replaced 65~75% of the working volume.

Visualization on Cell Expansion

1. Homogeneously take 1mL of culture solution and transfer to a well-plate.
2. Visualizing the cells on microcarriers under an inverted optical microscope or staining the cells with a live cell fluorescent stain to observe cell morphology.

Instruction for use

Cell Counting

1. Take 1 mL of culture solution homogeneously into a microcentrifuge tube by slowly aspirating while the spinner flask was continuously shaking.
2. Allow microcarriers to settle and gently remove cell culture medium without disturbing microcarriers.
3. Wash microcarriers with 1xPBS at least 3 times.
4. Add 1 mL 0.25% Trypsin-EDTA (or TrypLE™).
5. Place in the 37°C incubator for 10~15 minutes (20~30 minutes for TrypLE™) for UniTantrix® dissolution (Once cells are detached, the harvesting solution should be diluted with a fresh culture medium to prevent cell damage).
6. Count cell numbers to estimate cell growth.

Cell Harvesting

1. Allow total UniTantrix® microcarriers were settled down (at least 10 minutes).
2. Wash microcarriers with 1 x PBS at least 3 times.
3. Add 30 mL (20-30% of the working volume) of 0.25% Trypsin-EDTA (or TrypLE™).
4. Stir at 100~120 rpm for 15~20 minutes at 37°C (30~40 minutes for TrypLE™) for UniTantrix® dissolution (Once cells are detached, the harvesting solution should be diluted with a fresh culture medium to prevent cell damage).
5. Place the harvesting cells into a 50mL centrifuge tube.
6. Centrifuge at 1,200~1,500 rpm for 5~10 minutes.
7. Discard the supernatant and add a fresh culture medium to harvest the total cells.

Tantti Laboratory Inc.