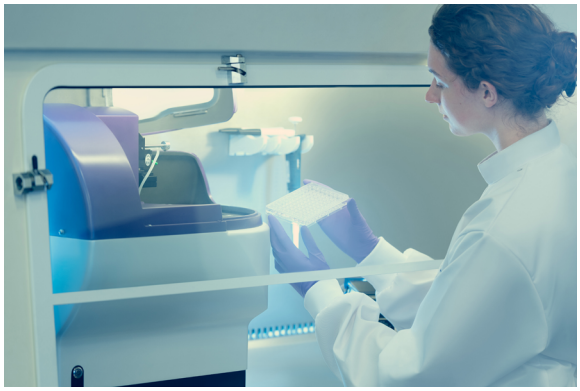
ADVANCED INSTRUMENTS

Solentim

Product Update

VIPS™ Updates:

Product improvements for an increased efficiency in single-cell seeding process



Recent updates to VIPS have resulted in an increase in the efficiency of single-cell seeding, for further acceleration of workflows. Here we provide a review of the benefits of VIPS, and an overview of the significant recent updates made to this product.

VIPS (Verified In-Situ Plate Seeding) is the high efficiency single cell seeder designed to accelerate single-cell cloning workflows. The instrument launched in 2017 with the ambition of combining single-cell seeding with assurance of monoclonality and has become an integral part of major cell line development (CLD) workflows around the world.

VIPS uses a low seeding pressure of less than one psi in the dispensing of droplets to seed single cells. The resulting increase in high cell viability, and subsequent increase in clonal outgrowth, is an important foundation for high efficiency cell seeding workflows.

Laboratories have confirmed that the increased seeding efficiency and percentage of wells confirmed with single cells, made possible with VIPS, results in a major transformational change to lab productivity. VIPS workflows regularly deliver ~80% seeding efficiency, accelerating workflows and reducing the number of plates required from the outset.

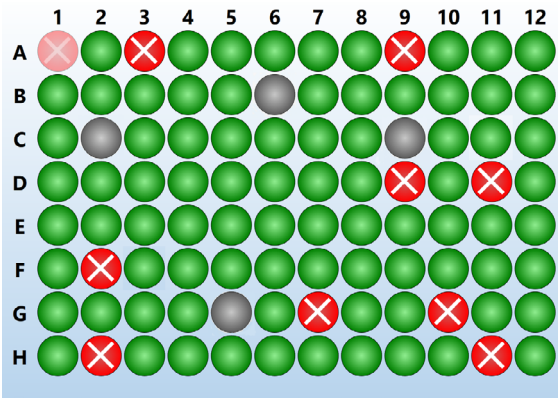


Figure 1. Example plate map overview from VIPS software, confirming clonal wells after seeding run. Green wells confirm clonal cells, grey wells are empty and red wells have more than 1 cell seeded within the well.

At its core, VIPS combines seeding with regulatory assurance. By imaging the droplet immediately after deposition VIPS captures quality evidence to support clonality. VIPS then automatically fills the well with media, and post settling, can provide a whole-well image ('day 0 image') to provide additional evidence of clonality. Together, these two pieces of visual evidence provide our 'double lock' of assurance. VIPS software wraps this data in a convenient clonality report pdf, linking whole well images of colony outgrowth right back to the images of the single cells dispensed in the droplet, which can be supplied to a regulator as part of an IND submission.

For customers previously using limited dilution approaches, the time savings are considerable. As VIPS requires only a single round of cell seeding, Solentim customers have reported that it more than halves the timeline for single-cell cloning workflows when compared to the traditional two-step limited dilution methodology. Instead of questionable probability statistics, VIPS provides the reliable, high quality image evidence that regulators are looking for within regulatory submission.

Due to these functionalities, the VIPS has contributed towards an acceleration of single-cell cloning and CLD workflows. High seeding efficiency of viable cells with good colony outgrowth, in combination with the assured identification of monoclonal wells gained through a single round of cloning, has enabled projects to be completed in less time, with the ability to decrease operational workloads.

Solentim continues to build upon VIPS technology with the following recent announcements:

Product updates for improved single-cell seeding

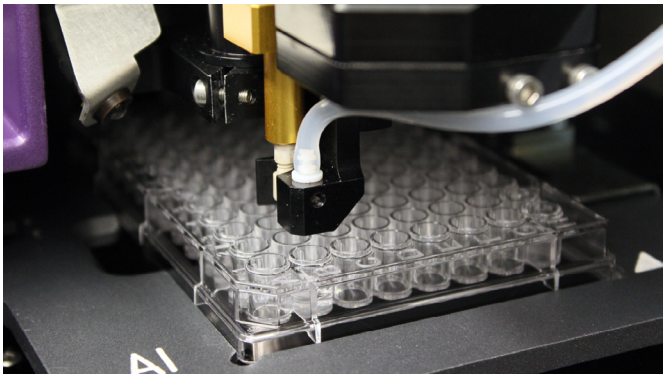
Over the last year we have incorporated a number of updates to VIPS to improve the efficiency of the single cell seeding process. This includes the use of 384-well plates, improved dispensing nozzles and sterile kits, artificial intelligence for automatic single cell detection and reagents for accelerated growth:

1. Project in a single plate: greater efficiency with384-well plates seeding on VIPS

It is now possible to increase the productivity of single-cell cloning workflows by using VIPS to seed single cells into 384-well plates. In our studies, clonal outgrowth increased by approximately 20% when using 384-well plates in comparison to 96-well plates (Table 1). Seeding efficiency was slightly reduced when using 384-well plates, but the number of wells with outgrowth increased by >3-fold when compared to 96 well plates. Maximal colony outgrowth is a primary focus for cell line development and the use of 384-well plates will greatly accelerate workflow productivity. In addition, 384-well plates enable a greater number of wells per incubator (or fewer plates per project), meaning more colonies can be established using the same space, further increasing productivity while using less plastic. In addition, smaller wells in 384-well plates also translates to a reduced volume of cell media and often costly cell growth supplements and reagents, saving money.

2. Improved project consistency with new V2 dispensing nozzles

Second generation V2 cell reservoir nozzles have been developed to enhance seeding efficiency and improve repeatability of consistent droplet dispensing for greater project stability.



	96-well plate	384-well plate
Time needed to seed a plate	11 minutes	30 minutes
Seeding efficiency	82%	56%
Clonal outgrowth of wells within a plate	30%	24%
Clonal outgrowth of seeded cells	37%	44%
Number of wells per plate with outgrowth	29	94

Table 1. Example comparison of seeding efficiency and clonal outgrowth of 96-well plate versus 384-well plate. CHO cells were seeded in Corning Costar 3596 96-well plates and Corning Costar 3701 384-well plates, and grown with EX-CELL CHO cloning media, 4mM L-glutamine and InstiGRO CHO PLUS.

3. Sterile VIPS Consumable Project Kits for single project use

Single project use consumable kits are now available for VIPS. These kits are supplied sterile and include all the consumable parts needed for use with VIPS for single-cell s eeding. Each kit includes a cell reservoir and a nozzle, media dispenser tubing and cell reservoir tubing. Two kits are available, one including V1 cell reservoir nozzles, and one including V2 cell reservoir nozzles, depending on your instrument set up.

These kits ensure a sterile set of consumables for each new project. The use of these kits significantly speeds up the cell seeding process, eliminating the need to complete sterilization procedures prior to seeding. A change of consumables for each new project can also be used to maintain optimal function of the cell reservoir, eliminate any potential for cross contamination between projects and prevent contamination of seeding batches.

4. InstiGRO™ growth reagents and MatriClone™ to boost cell growth

Accelerating single cell outgrowth is a primary factor in enhancing overall cloning workflows. Solentim's InstiGRO range of cell growth supplements enhance cell outgrowth of chinese hamster ovary (CHO) and human embryonic kidney (HEK) cells to enhance cell viability and clonal outgrowth after cell seeding.

The combination of VIPS and InstiGRO CHO PLUS growth reagent has been shown to produce a 7-fold improvement in total colony outgrowth of CHO cells per plate (Figure 3, left). In addition, the combination of VIPS and InstiGRO HEK supplement has been shown to generate over an impressive 11-fold increase on clonal outgrowth of HEK cells (Figure 4). Further supplements for workflows moving on from static to shake and storge conditions are also available.

For cell therapy workflows involving induced pluripotent stem cells (iPSC), the combination of VIPS and the new soluble matrix reagent MatriClone has been shown to produce a 3-fold improvement in clonal outgrowth of iPSC's per plate (Figure 3, right) and has enabled our customers to overcome the significant industry challenge of iPSC clone viability after single cell seeding.

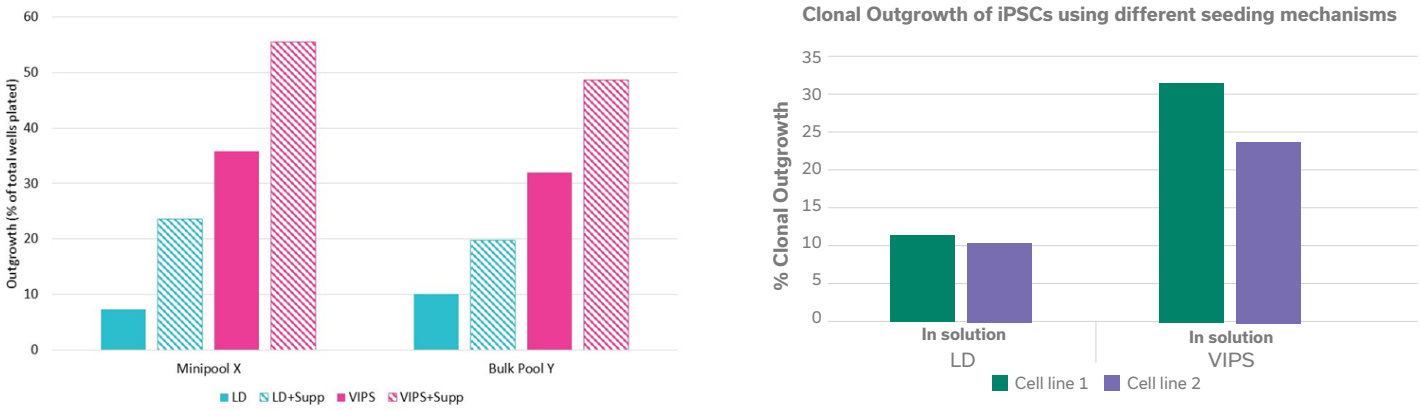


Figure 3. Comparison of clonal outgrowth of CHOZN cells selected through manual limiting dilution versus VIPS +/- InstiGRO CHO PLUS (Left). Comparison of clonal outgrowth of iPSC's selected through manual limiting dilution versus VIPS +/- MatriClone (Right).

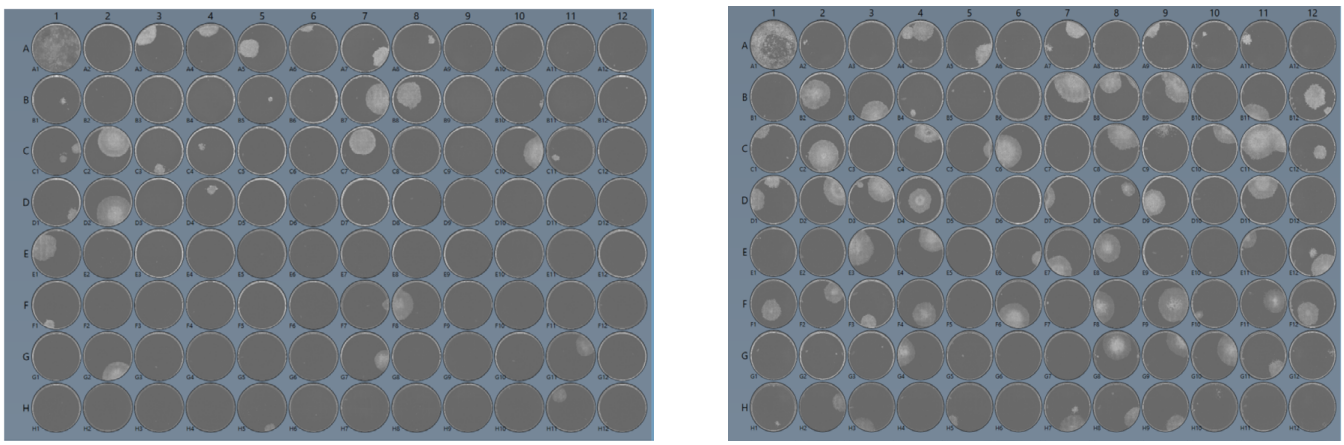


Figure 4. Clonal outgrowth images after 14 days of seeding with (right) and without (left) InstiGRO HEK supplement.

5. Automatic single cell detection

Image analysis using VIPS can identify single cells and moreover recognise the absence of cells, aggregates, and debris using artificial intelligence, further optimizing the seeding process. This application runs automatically and is visualized through color coding: cell locations (identified in green), aggregate locations (identified in blue), or non-cell locations (identified in red).

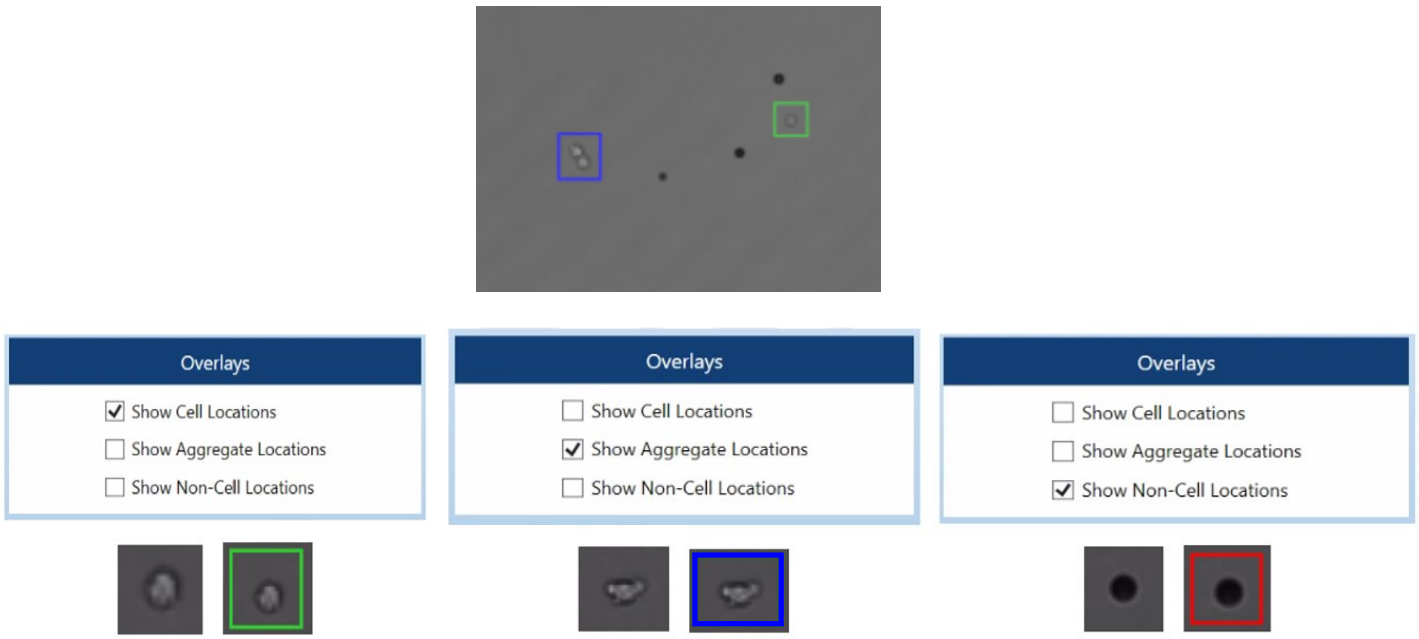
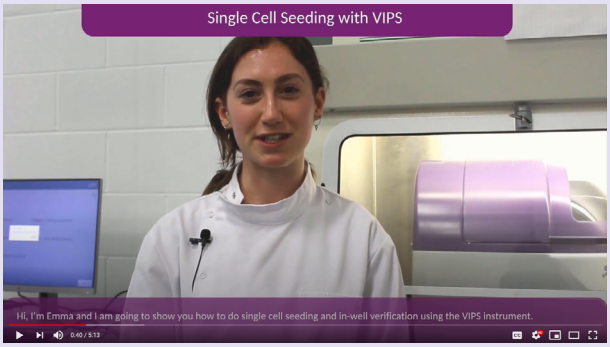


Figure 5. Identification of cell locations (green), aggregates (blue), or non-cell locations (red).

To learn more about recent developments in VIPS, visit **https://www.solentim.com/products/vips/**, or see our virtual demo for a walkthrough of VIPS in action **https://www.youtube.com/watch?v=PeLEk1G3gGA**. This virtual demo provides an overview of the practical steps of setting up VIPS and the process of single-cell seeding, and the generation of image-based clonality assurance. Together with the recent product updates reviewed here, you can now further enhance your productivity while reducing project timelines.



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