

## Magnetic 3D Bioprinting: Kits, Reagents, and Services For Growing Cells in 3D in a Petri Dish



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**CEOCFO: Dr. Souza, what is the focus at Nano3D Biosciences?**

**Dr. Souza:** The Nano3D Biosciences focus is on what we call magnetic 3D cell culturing. We have two main systems, magnetic levitation and magnetic 3D bioprinting. We have both approaches as kits, reagents, and we also provide services.

**CEOCFO: Would you explain what you are actually doing?**

**Dr. Souza:** First, one must ask why we use 3D cell culturing. We culture cells, and what I mean by culture, is growing cells, taking cells from the body, putting them in a Petri dish and growing them to do experiments, such as for developing drugs or toxicological testing. The traditional way is done as what we call 2 dimensional cell culturing. This is where we take the cells, put them in a Petri dish, they go to the bottom, stick to the plastic or surface and literally grow in 2 dimensions; they grow sideways. In the last 10 to 15 years, there has been a paradigm shift in biology on how to grow cells. This is because we are learning more and more that culturing the cells in 3D, instead of the traditional 2 dimensions, is key for cells to behave as they do in the body. Therefore, we have a process that enables us to grow cells in 3 dimensions by magnetic levitation or 3D bioprinting.

**CEOCFO: What is that process?**

**Dr. Souza:** The way we culture cells in 3D is by using the Nanoshuttle and magnetic fields. The Nanoshuttle are very small particles relative to the size of cells, so we can sprinkle a few of these nanoparticles to magnetize cells, and then apply very mild magnetic fields to bring these cells together, enabling them to grow and form 3D structures. We can work with cells of the same or different types, and generate a more complex structure to better mimic the complexity of in vivo tissue.

**CEOCFO: What are people able to understand about the cell when it is in 3D? What is the practical value?**

**Dr. Souza:** First, there are different applications for 3D cell culture. One application that people generally use 3D cell culture is for developing a drug, for discovering if a drug works well or does not, and if it is toxic or is not. Many of the drug development failures could be a result of the use of cells cultured in 2 dimensions to evaluate the efficacy or toxicity of compounds, which is often not predictive of what will happen once the drug is in the body. In other words, when using 2 dimensional cultures one does not really know very well if the compound is really toxic or if it really works. However, if you do such test using 3 dimensional cultures, the outcome should be more predictive of how the compound will work in vivo.

**CEOCFO: *Has 3D cell culturing been embraced? Is everyone onboard with the idea? If not, what are the impediments to wide adoption?***

**Dr. Souza:** Every paradigm shifting technology meets adoption resistance. Getting people change their ways, change practices that they have done for years and years, it is always a challenge. Therefore, different areas of biology and research are changing at different pace. For example, people doing cancer research, they have adopted it and they are transitioning into 3D cell cultures. They are getting great results and they understand the field is going in the right direction. Other areas, such as toxicology, are moving a little slower, but they are changing to the 3D cell culture, especially in Europe, where cosmetics now cannot be tested in animals. Therefore, in order to replace animal testing, and considering 3D is more predictive of in vivo toxicity than 2 dimensional culture, the field of toxicology is now starting to transition to 3D cell culturing.

**CEOCFO: *Are many companies creating products in the 3D culture arena? What is the competitive landscape?***

**Dr. Souza:** We started a few years ago, and today there are many different companies of different sizes working in this area. There are also many different techniques, such as gravity techniques, scaffold, bioprinting, and a few of the companies that our main competitors would be Corning, because they have Matrigel, which is the oldest product on the market for 3D cell culturing. There is also Insphero with Hanging Drop, a new company called Organovo in the 3D bioprinting space. Therefore, there are many different approaches to doing 3D cell culturing today.

**CEOCFO: *Has the industry been paying attention to Nano 3D Biosciences?***

**Dr. Souza:** Yes, they are starting to pay more and more attention. One example is last year we signed a partnership with Greiner Bio-One, which is a multinational company with over billion dollars in sales and they are selling our product under their label, co-labeled with ours. That is quite a milestone for a small company.

**CEOCFO: *Are you funded for what you would like to do? Are you seeking partnerships or investment?***

**Dr. Souza:** Yes, as a small company we are always looking for partnerships. We do have revenue from sales and grants, as we have been very successful in getting grants from NIH and NSF. We have a grant from CASIS, the Center for Advancement of Science in Space, which is flying our system to the International Space Station in December, to be used in the space station. Again, as a small company, we are always looking for partnerships and investments at different levels.

**CEOCFO: *How would a company decide the best approach, as you offer more than one way to look at tissue?***

**Dr. Souza:** That is a very good question. I tell our users that how they are going to use our systems should be framed around the question they are trying to answer. Different approaches can be applied for different experimental goals. For example, many researchers are looking at cell migration, which is how cells move, and we have a particular type of assay that looks at cell migration. This is a little different than the traditional spheroid generating approach, where one basically make a little ball of cells that mature and then you add a drug and check then check if the cells are dead or alive. You also need to consider the amount of resources you have available, and even some the amount of compound you have access to. Such compounds can be very expensive, so one may have to work with the approach that allows the use of small volumes. Another scenario, is If one wants to test several compounds at the same time, then higher throughput approaches are preferable. The latter is one of the key advantages of n3D's technology. Actually, we offer a fully scalable solution, meaning we are the only company where the same core approach is used in a single well all the way to 384 wells. We are actually developing a 1,536-well system, in which one will be able to test 1,536 cultures at the same time and in the same plate.

**CEOCFO: *When someone turns to you, do they know what they want or would they work with you to decide the best approach?***

**Dr. Souza:** We see both. Some people know what they want and some don't. We always try to understand what they are looking for before suggesting what approach will provide the best answer to their question. That is also part of one of the services n3D provides, method development services.

**CEOCFO: *What surprised you as you have been working in this particular arena?***

**Dr. Souza:** What surprised me is that as a scientist, one's practice in the laboratory is not always driven by methods that will provide be the best scientific outcomes. There is still a great deal of the "human factor" in what we do, which is a challenge. As I mentioned in an earlier answer, every paradigm shifting technology meets adoption resistance, getting people to change their ways, change practices that they have done for years and years, it is always a challenge regardless of how good the new tool is.

**CEOCFO: *What is next for Nano 3D Biosciences?***

**Dr. Souza:** We are planning to expand. The technology is validated, published in high-impact journals, we have the scalable throughput, from single all the way to 384, and we about to launch 1,536. More importantly, we have pharma that is starting to adopt, and now we need the resources to grow faster. These resources are coming through partnerships and investments. Therefore, we are ready to grow.

