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profile feature



Marc Le Bozec, CEO of *Collectis biosearch*

Genome customization: generate the cells you want

Thomas Hobbes famously wrote that the life of man is “solitary, poor, nasty, brutish and short.” If the author of *The Leviathan* would write about generating cellular clones, perhaps he would have called the process time-consuming, imprecise, cumbersome, brutally expensive and short-term. The culprit? Traditional clone generation through cellular transfection - because the technique requires many months to achieve an often imperfect result. Cellular transfection often results in the modified gene integrating randomly, transiently and at less-than-optimal levels, which can't be easily regulated. Paris-based *Collectis biosearch* now offers a suite of genome customization kits that provide stable integration of a specific gene in a specific location of a given cell type, with the location chosen to optimize control of protein expression. The company offers kits for generating clones relevant to drug discovery (including drug screening), protein production, as well as basic science applications. Marc Le Bozec, *Collectis biosearch* CEO, tells *Nature* how these kits can make lab life easier than the pessimistic Hobbesian view.

Q: What technological tool drives your approach?

The main tools we use are the meganucleases. They are highly specific DNA scissors that can be engineered to recognize and cut virtually any DNA sequence. We created these 22-base-pair endonucleases with specific recognition sites. We want to take the guesswork and the time out of targeted integration, with kits specific to clones for drug discovery, protein production, basic science applications. A given meganuclease makes a cut at a precise genomic site and induces homologous recombination (HR), a natural repair mechanism to paste the gene of interest at the meganuclease genomic recognition site. We call this combination the “cellular Genome Positioning System” or cGPS®, because we know we can insert a given gene where our client wants it to be.

Q: What are the broad applications of this technology?

We call it “Genome customization”; we want to provide life science researchers with tools enabling them to customize the cell line or organism they want for a particular

purpose. Our product enables scientists to do something that is normally long, painful and cumbersome. Currently it is very difficult to generate a family of clones that have a new stable gene modified from a different cell. It takes at least a couple of months normally and you have no guarantee of the expected result. With our kits, you can get the results you want within four weeks.

at a very high level. We can also provide expression stability over time, unlike in transfection, which results in lots of variation in both expression and production. Also, with our product, you can modify the producer cell line so you can produce a more active protein. You can turn your product into a high-titre protein production machine.

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Q: What are the kits' strengths?

Because our integration is not random, it provides you with controlled expression. The targeting works quickly and the clones will be homogenous. You know in advance the level of expression. That way our results are reproducible and robust. That's important in research labs. Peer reviewers often ask, “Have you tried this with mutants in the same cell line?” If you try transfection with mutants, you get random integration; if you transfect at two different times, you get two different results. With our system, you can tell the gene “Go there, stay there, and be expressed.” You will get the same robust results multiple times—whether you use wildtype genes or mutants.

Q: How can your kits improve drug discovery?

In drug discovery, targeted integration speeds up the generation of cell-based assays. In 24 days it is possible to generate clones expressing functional drug targets like ion channels, for example. Since the clones are homogeneous, researchers do not need to screen a lot of them. Besides, since the generated clones are isogenic, drug profiling on these cell lines is much more robust.

Q: What about protein production?

With this dedicated product, you know that you will always have expression from the same locus - a locus selected for very high expression, a so-called “hot-spot”. We can guarantee that you will produce your protein

Q: And for basic science applications?

Reproducibility is key here. When labs use transfection, they often see random integration, so, for example, cells will often express different levels of, say, different G-protein coupled receptors. With our kits, they will have a single copy of a gene, integrated at the desired place.

Q: Any success stories so far?

Our first client, a French mid-size pharma, generated a few tens of stable clones in just 28 days. This company validated all those clones at molecular and functional levels. This client further selected some cellular clones to integrate into his high-throughput drug screening platform.

Q: What's next for your company?

We'd like to develop more kits for specific targeted integration applications. Then, we will work on using our technology for gene functional invalidation and individual gene modification. Our goal is to become a turn-key, off-the-shelf solution for both basic and applied biology, just as *Microsoft* has become a default operating system and *Intel* has become the default chip in computers. Researchers now spend a lot of time establishing stable cell lines, rather than focusing on their primary scientific objective. Our system provides a faster, easier, less expensive way to accomplish the same goal. So we want our systems to become the new industry standard.

tired of
using tools
that just don't
*** fit your needs?**

genome customization

is our promise to bring at your bench
easy and ready-to-use research tools
to generate the cells and organisms
with your desired characteristics

whether you want to study gene function, develop
cell-based assays for drug screening, or produce high titers
of the desired proteins, our meganuclease-engineered kits
are a fast and effortless solution. collectis-bioresearch.com



GENOME CUSTOMIZATION