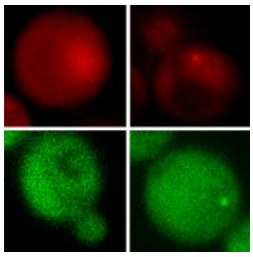
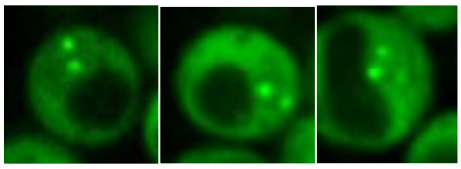
10 years of innovation in the virology field.

We are delighted to announce that NeoVirTech celebrates its 10 years of activity. It has been a wonderful journey and we are still expanding our applications. NeoVirTech was created in February 2014 with the goal to provide the best and easiest way to measure antiviral activities of innovative molecules. To achieve this goal, we developed the ANCHOR technology that allows us to visualize viral DNA replication in living cells. As we can see virus infection and replication, it is very easy to identify compounds that impact virus propagation using high content microscopy. To celebrate, here is our story of 10 years of innovation in the virology field, NeoVirTech facts in 2024 and a word from our CEO to all persons (especially PhD student and post-doc) that consider the opportunity to create a biotechnology company.

Genesis of the ANCHOR system, deriving a bacterial partition system into a eukaryotic DNA visualization tool.



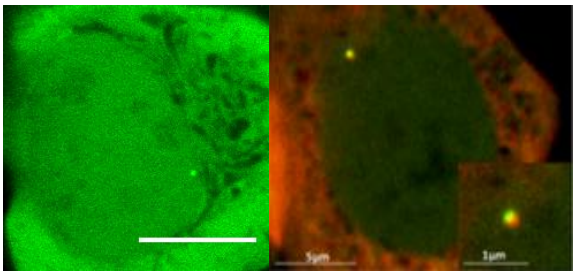
The genesis of the ANCHOR system started in 2010 in Pr K.Bystricky's laboratory. The goal of the ANCHOR program was to develop new DNA visualization systems that can be used in combination with preexisting tools and allow the visualization of DNA metabolism. By combining the expertise of Dr D.Lane laboratory, we have developed a first generation of ANCHOR systems derived from bacterial partition sequences that worked very efficiently in yeast (*S.cerevisiæ,* picture on the right). These first-generation systems allowed for the first time the visualization of DNA double strand break resection in living cells (Saad et al. Plos Genetics, 2014). As the ANCHOR system does not impact DNA metabolism (no fragile site, no modification of flanking gene expression), we thought it can be used to visualize unexplored DNA events in living cells. We asked ourselves if we could visualize the jump of a mobile genetic element. We cloned the ANCHOR system into a Ty1 retrotransposon and induced the jump of Ty1 from a donor plasmid to the yeast genome. Our jump condition should have triggered a 1 to 5 insertion into the yeast genome and most of the cells displayed 2 to 3 ANCHOR spots (picture on the left). We concluded as a proof of concet that the insertion of the ANCHOR system into a retrotransposon allows visualization of its propagation in yeast. Using mamalian cells, the first generation of ANCHOR systems failed to visualize DNA.



Development of second and third generation of ANCHOR system to visualize DNA into higher eukaryotes.

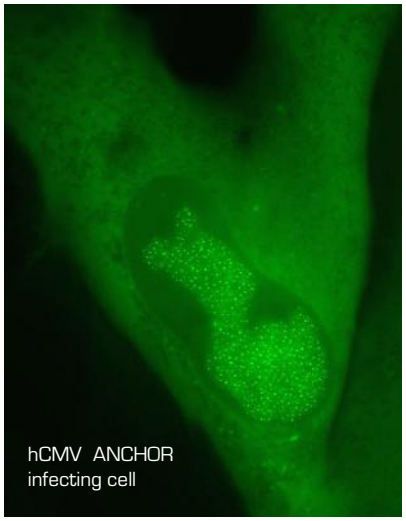
From 2010 to 2012, we used our experience to develop second and third generation systems of the ANCHOR technology. We have developed four ANCHOR systems that can be used alone or in combination. These systems were used to visualize gene position in living cells and its relationship with different biological mechanisms, from relation with transcription activation (Germier et al. Biophysical Journal, 2017) to chromatin looping dynamics (Gabriele et al., Science, 2022)

The ANCHOR sequence provides a bright fluorescent spot corresponding to the position of the tagged DNA. Combinations are also possible (see picture, right). It has been successfully used in numerous cells *in vitro* but also *in vivo*, for example in *drosophila* and in *planta*. <To date, more than 100 academic laboratories use the ANCHOR system in routine. However, the use of the ANCHOR system in an infectious human virus has not been tested yet.

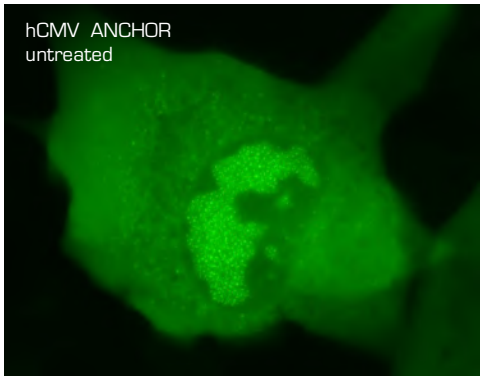


Construction and validation of the first autofluorescent human virus for its application in the discovery of antiviral molecules.

In 2012, we moved to the Advanced Life Science Technological Institute supported by the region Occitanie to develop industrial application of the ANCHOR system. One of our programs was to tag a human virus to see its replication in living cells. It took us two years to obtain the first validated ANCHOR recombinant Herpes virus (hCMV, picture on the right) where each fluorescent spot corresponds to the position of a viral genome. In parallel, we also worked on the development of ANCHOR tagged adenovirus in collaboration with Dr Harald Wodrich lab. These two projects were successfully concluded by a back-to-back publication in Journal of Virology in 2018 (Mariamé et al., Komatsu et al., J Virol, 2018). Having the ability to see virus replication in living cells opens new perspectives in terms of screening activity. Indeed, our readout should provide data on the kinetic of virus infection in the presence of a compound of interest, results being faster, multiparametric, qualitative and quantitative. The NeoVirTech story therefore begins.



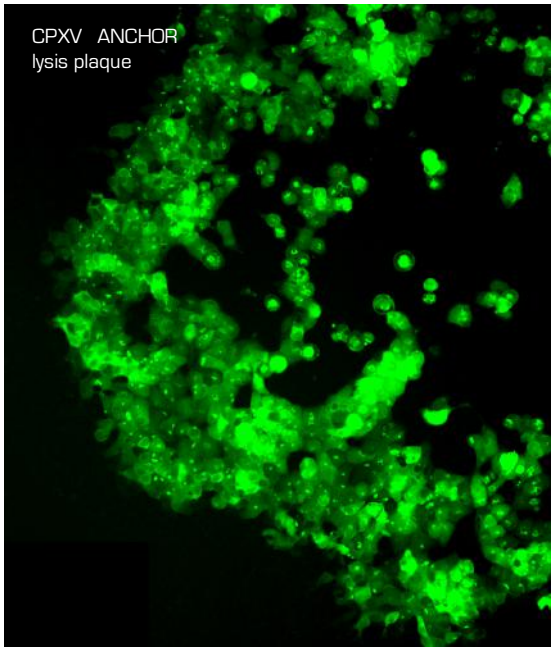
Translating from an academic research lab to the development of a biotech company is not an easy task. We had the chance to be supported by BPI France by winning the national contest for the creation of innovative companies in 2013, emerging category and 2016, development category. We received also support from Toulouse Tech transfer, our TTO, for the expansion of virus collection. From 2014 to 2018, we focused on the validation of our technology by performing robust controls and validation processes, to ensure that ANCHOR tagged viruses behave as the parental strain and respond to antiviral treatment. Indeed, high resolution imaging of cells infected with hCMV ANCHOR and treated with a known inhibitor of hCMV replication, Ganciclovir, triggered a complete disappearance of replication centers (see on the left).



Autofluorescent viruses for rapid and efficient antiviral screening & discovery

NeoVirTech, your partner beyond virology
Siège social: 1 place Pierre Potier, 31106, Toulouse, France. SAS au capital de 48.815€.
RCS Toulouse 800203739, TVA n°FR36800203739
SIRET : 800203739 00019 APE :7211Z

The largest collection of autofluorescent viruses for screening application.

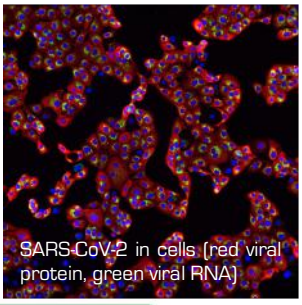


We focused our efforts to develop the largest ANCHOR tagged virus collection. The ANCHOR system has to be adapted in each case to fit with virus biology. For example, length of the construct and promoter choice were critical. Also, and specifically for poxvirus application, we had to adapt the ANCHOR system to work in the cytoplasm of cells, as poxvirus replication is strictly cytoplasmic. We could adapt the ANCHOR system to visualize infection and replication virus having different application both in the human and animal health, such as Herpes viruses (HSV1/hCMV/EHV1/PRV), pathogenous poxvirus (VACV, CPXV (see picture), MPXV (starting), MYXV T1, AFSV (pox-like)) and oncolytic poxvirus (MYXV SG33, VACV TG6002), lentivirus and retrovirus (HIV1), adenovirus (hAdv5), baculovirus (AcMNPV) and recently parvovirus (AAV2, H1 starting). Our goal is to tag all viruses having a dsDNA phase in their biology for screening applications.

Combining ANCHOR viruses with HCS imaging

In 2019, we acquired our own screening platform, composed of pipetting robots and a Thermo CellInsight CX7 high content screening microscope, coupled with a 22To server for data archive. Since 2019, our HCS system is working almost every day to perform image acquisition and analysis. We have developed specific algorithm that automatically measure the toxicity of a compound, the infection rate and viral replication level. Compared to negative and positive controls (Gold standards), we can rapidly and in high throughput identify compound that display powerful anti-infective activities. We have screen thousands of compounds for the count of our customer and partners. These screening activities conducted to the discovery of a new family of acyclonuceloside inhibitors (DENALPOVIR project) and fluorocorroles (VIRCO project), backed respectively by the Defense Innovation Agency and the TTO Sayens.

The Covid era, development of disinfection activities.

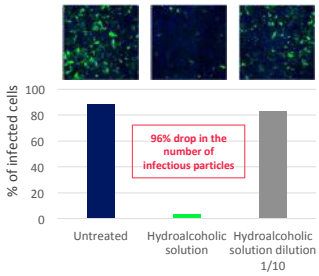

SARS-CoV-2 in cells (red viral protein, green viral RNA)

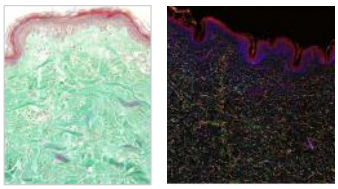
During Covid outbreak, we have been massively contacted to perform antiviral testing but also the measurement of disinfection procedure. We start testing antiviral against Covid as early as may 2020. Rapidly, we developed robust protocol using classical virology methods such as TCID50 and RT-qPCR. Next, we developed imaging techniques to increase the speed and quality of our readouts. We also developed numerous protocols to contaminate ad recover virus from different objects and surface such as metal, fabric, glass, leather and numerous materials from our customer. In collaboration with the company Syntivia, we

Autofluorescent viruses for rapid and efficient antiviral screening & discovery

developed a method to contaminate living human skin explants with a virus to simultaneously investigate disinfection capacities of a product of interest and its impact on skin physiology (irritation, morphology, DNA damage, etc....). For example, contaminating a living human skin with an ANCHOR tagged adenovirus and application of a hand sanitizer gel solution triggered an 96% drop of infectious particles in our condition.

The asset of ANCHOR tagged virus for the measurement of disinfection procedure lays on its reduced time to result, accuracy and absence of false positive.





High resolution imaging and quantification

NeoVirTech facts and awards, from 2014 to 2024

-6FTE working in BSL2, BSL2+ and BSL3, A2 and A3 animal facility
-Around 30 viruses in collection impacting human, animal and Defense market
-100 customers (world)
-8 patents
-18 articles, including five journal cover.

-Awarded at the national contest for the creation of innovative companies MESR/BPI France, Emerging category 2013

-Awarded at the national contest for the creation of innovative companies MESR/BPI France, Development category 2016
-Top 10 Drug Discovery company in Europe in 2019 by PharmaTechOutlook.
-Awarded by a RAPID grant from the French Defense Innovation Agency for the development of medical countermeasures in case of poxvirus outbreak, 2019.
-Awarded by a Readynov grant from region Occitanie for the development of disinfection procedure during Covid19, 2020.

A word from our CEO to all people that consider to create a biotech company.

"I developed the ANCHOR technology when I was in post-doc in K.Bystricky's lab back in 2010 after achieving a Ph.D at the Université de Montréal, Qc, Canada. It was a great challenge to generate the system and make it as powerful as it is to date. We clearly saw the industrial applications in numerous fields and we had the chance to be supported by the CNRS, our TTO, the ITAV and the Occitanie region. It was a critical decision to leave the academic field towards the private sector. I took this risk, because I had the will to do it. What you need is the will, support from friends and colleagues, an opportunity to develop high level science with a competitive advantage (in my case the ANCHOR system) and an extreme self-confidence. My objectives when I started were to create a sustainable company, to hire and maintain 6-8 people, to perform nice science and have fun everyday with what we do. If on top of that, I can discover something that cure an infectious disease (whatever the disease is), this will be the cherry on the cake. 10 years after my objectives are almost complete. I also decided to create the company to have nothing to regret. Back in 2014, I preferred to create NeoVirTech and maybe fail than spending the rest of my life saying "what if I had created a company at that time". If I can do it, everybody can do it."

Franck Gallardo, PhD. CEO NeoVirTech SAS.

Autofluorescent viruses for rapid and efficient antiviral screening & discovery