DIACCURATE

BioWorld™

BioWorld (correction): Could HIV be cured by tackling 'bumpy' CD4 cells? France's Diaccurate wants to find out

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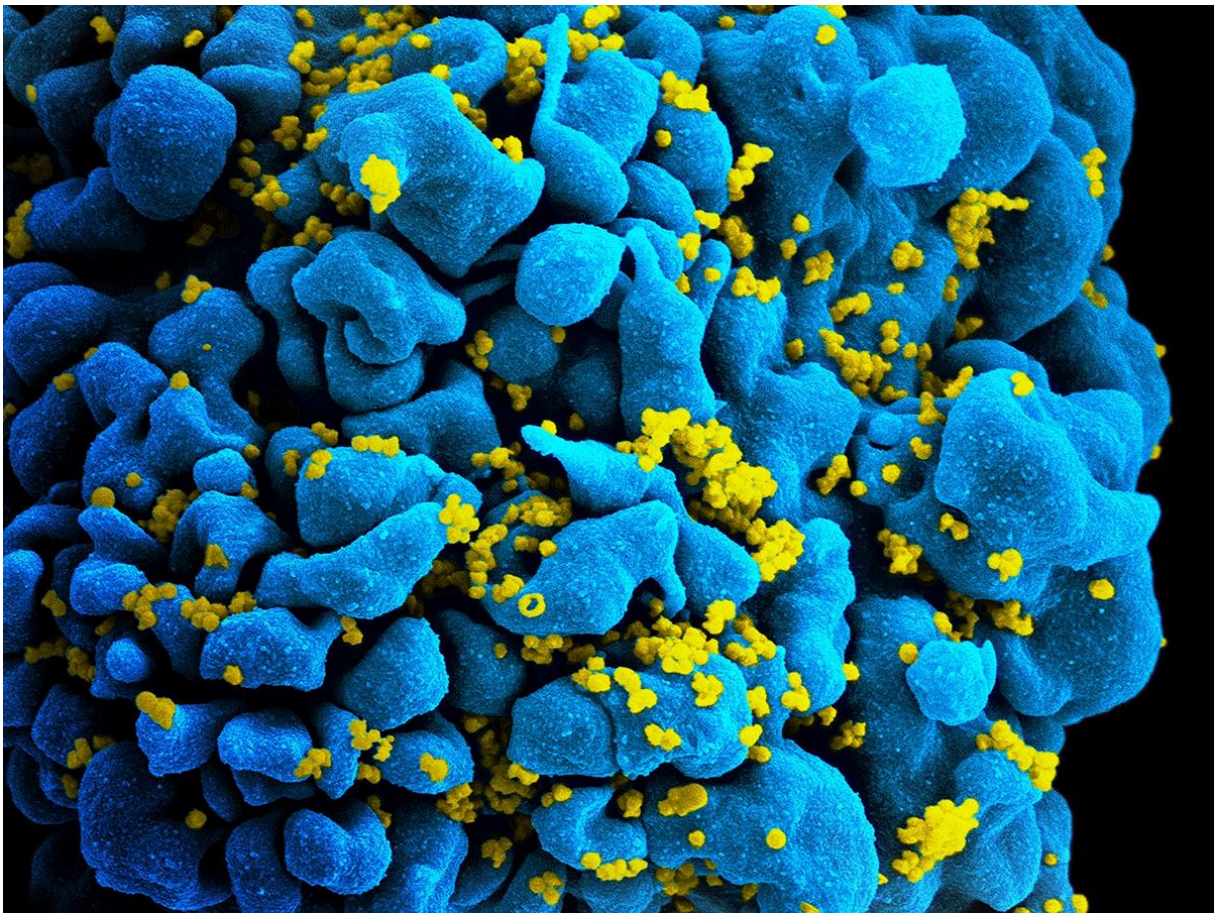
Link (article behind paywall): https://www.bioworld.com/articles/510378-could-hiv-be-cured-by-tackling-bumpy-cd4-cells-frances-diaccurate-wants-to-find-out?v=preview



HIV infected cell. Credit: NIAID

Finding a functional cure to HIV is one of the biggest challenges in modern medicine, a task made so much tougher because of the virus's ability to incorporate itself permanently into a host's genome. But Diaccurate SAB, of Paris, thinks it may have a solution – and it's all down to a discovery showing that the virus seems to make crucial immune CD4 cells go "bumpy", lose their function and die.

It's an idea that is so intriguing that Diaccurate has managed to bring aboard the Nobel prize winner Professor Tasuku Honjo, famously credited with the work establishing PD1 as a target in immuno-oncology, to chair its scientific advisory board.

Dominique Bridon, CEO, Diaccurate

Countless companies have tried and failed to find technology that can prevent the destruction of the immune system. But the team at Diaccurate, a spin-off from the Institut Pasteur in Paris, says tackling these bumpy and non-functional CD4 cells could be the answer.

Diaccurate CEO Dominique Bridon told *BioWorld* the foundation of the company is work done by the institute, which could also be the basis of therapies for other infectious diseases and even cancer.

At the center of the research is the discovery of the physical defect in CD4 cells, which leads to the immune system losing its function and the disease developing into full-blown AIDS.

As Bridon points out, CD4 cells are vitally important in the immune system because they provide supplies and support to the CD8 cells that do the dirty work and kill infected or malignant cells. Without CD4 to support, the "warrior" CD8 cells can't function for any period of time and the response to disease swiftly comes to an end.

Speechless

Bridon said he was "speechless" when he was presented with Diaccurate's preclinical evidence showing the immune deficiency seemed to be caused by these "bumpy" CD4 cells that do not respond to stimulus and perform their crucial supportive role.

"When you look at HIV 95% of CD4 cells are bumpy or lumpy. Nobody has seen it before," he said.

The work conducted by Diaccurate goes further than that as it also shows the mechanism that HIV is using to disrupt the cell membrane of CD4.

"What we have is evidence we can under certain circumstances we can block the insult that are made on the CD4," Bridon said.

Diaccurate has demonstrated that HIV gp41 protein binds with an enzyme called (PLA2G1B), which combines with a phospholipid that is present at trace levels in the bloodstream but is usually found in the gut.

This complex disrupts the membrane of the CD4 cells, causing it to deform and stopping it interacting with a range of chemical signals that tell it to take action against disease.

Diaccurate's lead drug, phospholimab, works by neutralizing PLA2G1B, breaking the cycle that leads to the breakdown of the CD4 cell membrane. It is the basis of the HIV therapy that could be in the clinic in early 2023 after publication of Diaccurate's discovery work in the *Journal of Clinical Investigations* in March last year.

Since then the company has been taking shape, with the appointment of Bridon and the input of Honjo and the scientific advisory board and a team of technicians with experience developing antibody drug.

Honjo agreed to help thanks to his long correspondence with Professor Jacques Théze, co-founder and initial CEO of Diaccurate.

“It’s the first time he came out of Japan and joined private company. It’s a huge honor,” said Bridon.

“They (Honjo and Théze) have been writing for quite a while, it was very easy to get him on board. I just had to ask. We need to challenge ourselves and go to the top.”

The biotech also has backing from Truffle Capital, which is led by Diaccurate’s chairman and cofounder Dr Philippe Pouletty.

Oncology and infectious disease applications

Diaccurate is testing whether the technology could have applications beyond HIV, as there is evidence that tumors could also be disabling CD4 in a similar way, allowing them to evade attack from the immune system.

“We think we could have proof of concept in HIV population. Then we will investigate which tumor we can apply it to,” Bridon said.

With the expertise of Honjo the company wants to test the hypothesis that the same bumpy CD4s are present in tumors and blood cancer, with pancreatic cancer at a starting point. They chose it as a first target in cancer because it secretes the PA2G1B enzyme and the lack of treatment options.

“It does not respond to current immunotherapy and it’s a terrible disease. We have preliminary data that say we should continue working down that line,” he said.

There is also potential for tackling infections caused by other viruses such as hepatitis B and C, lymphocytic choriomeningitis and COVID-19, the company said.

But for now Bridon is enjoying his work with Honjo and the other influential immunologists that are guiding development. “Each session flies by. It is exceptional,” he said.