Before travelling into the cells of our body under the guidance of Jean-Marc Sabatier and in order to understand the pitfalls of the current SARS-CoV-2 vaccines and their necessary evolution towards new generations, it is important to know that there are three types of antibodies:

- Neutralising’ antibodies, which fight and neutralise the virus. These are the most familiar to the general public. Their production is desired during a vaccination;
- Neutral’” antibodies, which recognise the SARS-CoV-2 Spike protein, involved in the infection of cells, but which are not protective;
- The "facilitating" antibodies which, contrary to the "neutralising" antibodies, will favour the infection of the cells by the virus (these antibodies are found during the vaccination of cats against the FIP virus, as well as during the vaccination against the SARS-CoV-2 at the origin of Covid-19 in humans). It is these antibodies that should not be produced during vaccination. However, all current vaccines based on the SARS-CoV-2 Spike protein produce these three types of antibodies. Hence the difficulties that we see after vaccination of some patients. Hence also the worrying vaccination strategy of the 3ᵉ or 4ᵉ dose recommended, including in France, for patients with co-morbidities (obesity, diabetes, hypertension, etc.). Jean-Marc Sabatier explains why.

In a previous interview, you demonstrated the strong similarities between the cat virus, known as FIP (Feline Infectious Peritonitis) virus, and the SARS-CoV-2 virus causing Covid-19. Yet vaccine trials in cats have been counterproductive. Why has this been the case? Because we have seen that the coronavirus that causes FIP (feline infectious peritonitis) in cats has strong similarities with the SARS-CoV-2 coronavirus that causes Covid-19 in humans. We have also seen that trials of vaccinating cats with an avirulent strain of FIP not only fail to protect vaccinated cats but, on the contrary, promote infection in cats subsequently exposed to a virulent strain of FIP virus. These data point to the existence (in this case) of a phenomenon called 'ADE' (antibody-dependent enhancement). In this mechanism, "facilitating" antibodies are present. These antibodies bind to the FIP virus and facilitate the infection of cells by the virus. Indeed, phagocytic cells (monocytes, macrophages, dendritic cells, etc.) have a receptor (called FcRIIa) capable of recognising the antibodies attached to the viral particle, which allows the infection of these cells by internalisation of the virus-antibody complex. ADE in respiratory infections is included in a broader category called ERD (enhancement of respiratory diseases) which also includes non-antibody based mechanisms (such as cytokine...
storms and cell-mediated immunopathology) that promote the infectious process and deleterious effects of the virus.
Recently, an abnormally high proportion of people vaccinated against SARS-CoV-2 have been shown to have more severe forms of Covid-19 than when unvaccinated people are infected with the virus.
By analogy with the FIP virus in cats, it seems conceivable that the "ADE" phenomenon (or "ERD" in general) could be found in vaccination against SARS-CoV-2.

What should be done?
The objective is to produce a vaccine Spike protein that is unable to bind to the ACE2 receptor in order to avoid the potential direct deleterious effects of the Spike protein and to avoid the "ADE" (or even "ERD") phenomenon.
The "challenge" therefore consists in preserving (as much as possible) the "key" elements of recognition of the Spike protein by the immune system, i.e. the regions of the Spike protein that will be recognised by the host’s immune system (the vaccinee) and that will induce a protective neutralising immunity.
More specifically, it is a matter of maintaining the protective B and T epitopes (specific regions of the Spike protein recognised by the immune system). B epitopes induce antibody production by activated B cells, while T epitopes are recognised by T cells (cytotoxic lymphocytes) responsible for fighting and destroying virus-infected cells.
It is therefore necessary to remove (as far as possible) the "facilitating" B epitopes that promote the infection of cells by SARS-CoV-2.

What about current vaccines?
The idea is to render the vaccine Spike protein inert by modifying it so that it is unable to bind to its ACE2 receptor and overactivate the renin-angiotensin system (RAS). This is not the case with current vaccines, either mRNA or attenuated viral vectors (adenovirus).
In other words, vaccines can produce the same effects as the SARS-CoV-2 virus and can be shown to lead to Covid-19 disease.
These vaccine proteins have been shown to have the potential to bind to the ACE2 receptor and overactivate the RAS that causes Covid-19 diseases. This means that a healthy individual could develop Covid-19-like diseases after vaccination.

Worrying. How can this be corrected?
By modifying the vaccine Spike protein so that it becomes unable to bind to its target (the ACE2 receptor) and trigger potential Covid-19 diseases. In addition, the Spike protein should ideally be modified to remove the regions that contain the 'facilitating' B epitopes.

Is this technically possible?
It is possible by identifying the regions of the Spike protein that are responsible for the production of the "facilitating" antibodies and removing them from the final structure of the vaccine Spike protein. This requires prior work to identify the 'facilitating' B epitopes.
Another approach is to produce synthetic vaccines based on peptides (fragments of the Spike protein) that mimic the protective B and T epitopes of the Spike protein.
Why haven't the big labs done this?
Because the labs went for the simplest (I guess it was already complicated) in creating their vaccines. The Spike protein is a large molecule that has two main parts: an outer S1 subunit (which allows binding to the ACE2 receptor) and an S2 subunit, which allows fusion of the virus and target cell membranes. Current vaccines are based on a Spike protein in which the S2 subunit involved in the membrane fusion process has been modified. Here, the outer S1 subunit should also be modified by removing the ‘facilitating’ regions that will promote infection of the cells by the virus.

So it is theoretically possible to produce new vaccines quickly?
It is also possible to produce synthetic vaccines based on molecules (peptides) that mimic the B ('neutralising') and T (protective) epitopes of the Spike protein. Peptides derived from other SARS-CoV-2 viral antigens (these antigens are the nucleocapsid protein N, the envelope protein E, the viral membrane protein M, and the fusion glycoprotein haemagglutinin esterase, which are essential for coronavirus infectivity) can be added. In other words, the majority of vaccines are based on the Spike protein: it is possible to add one or more other viral antigens in order to increase the effectiveness of the vaccines. For example, the Chinese vaccines Sinopharm (Eponym) and Coronavac (Sinovac) are based on inactivated SARS-CoV-2, which means that in theory they could provide superior protection to the others, as they have all the viral antigens. However, chemical inactivation of the virus results in changes to these antigens which can lead to a less effective protective immune response. This chemical inactivation of the virus leads (among other things) to changes in the three-dimensional structure of these viral antigens.

So vaccination does not fully protect?
The natural immunity conferred by infection with SARS-CoV-2 and its variants appears to be significantly higher than that conferred by vaccination. This natural immunity is based on the stimulation of the infected person's immune system against all viral antigens. Based on current data, it appears that the natural immunity conferred by SARS-CoV-2 is about ten times greater than that achieved by vaccination against the Spike protein.

What will the next generation of vaccines look like?
This suggests 'new' avenues for a future generation of effective vaccines that are free of side effects. In this new generation of vaccines, it will be necessary - in my opinion - to produce a Spike protein modified so that it is no longer able to bind to the ACE2 receptor of the target cells. 1. Preventing overactivation of the RAS should prevent the onset of potential Covid-19 diseases; 2. Suppressing the "facilitating" B epitope of Spike should result in a more effective humoral immune (antibody) response; 3. By adding one or more viral antigens to this vaccine composition, the protective potential of the vaccines could be increased. Such a strategy is also valid for the development of an effective vaccine against FIP virus in cats.

Are you therefore in favour of injecting a 3rd or even a 4th dose of vaccine, as soon as the school year starts, for patients with co-morbidities?
If the "ADE" (or even "ERD") phenomenon exists with current vaccination, it is likely that these booster vaccines (3ᵉ and 4ᵉ doses) would increase the proportion of "facilitating" antibodies, leading to a potentially opposite effect to that sought. The cure would then be worse than the disease.