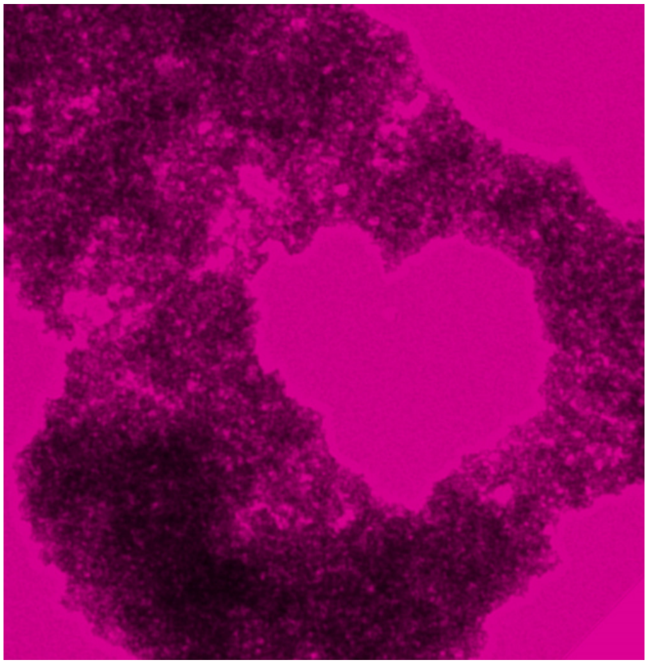
Cerium oxide nanoparticles may be of therapeutic value in chronic liver disease

What is this? We use Cerium oxide NPs (CeO_2NPs) to treat cirrhosis in model rats and we observe how it has dramatic beneficial effects in reducing inflammation and allowing tissue reparation What makes nanoceria very appealing is its high *capacity to buffer electrons* from an oxidant/reducing environment, followed by the capture or release of oxygen, or molecular oxygen species (as OH·) which are very reactive oxygen species (ROS).



Electron Microscope Image of a deposit of CeO2NPs onto a carbon coated cupper grid substrate

What have we observed? In principle CeO_2NPs decreases oxidative stress always present during inflammation. These NPs are similar to the used in the petrochemical industry and cars catalytic converters. Here, in the liver of cirrhotic rats, they do not only decrease the level of ROS, but also decrease all the inflammation. Therefore, in the field, CeO_2NPs have proven to behave as free radical scavenger and antiinflammatory agents.

How does it work? NPs have been designed to maximize catalytic activity (and decrease dose) and at the same time to localize in the inflamed area of the liver. This is done controlling interactions with proteins and tuning morphology (size and shape) of the NP to then control in-liver extravasation and in-inflammation accumulation. Then, once the target –inflammed area- is reached, the NPs start decreasing the local excess of ROS until it reaches healthy tissue levels and the whole inflammation decreases. The particles are active for few weeks and then they dissolve into innocuous Ce^{3+} ions. Ce^{3+} has been observed to be weakly bacteriostatic and to compete with Ca^{2+}. Due to the low amount of Ce and the abundance of Ca, interference of Ce with Ca has not been observed.

What is special here? I think that the most interesting thing here is that the NP is not an assistant to help current medicine, as a vehicle for drug delivery or radiotherapy-imaging contrast agent. Here, it is the NP itself the active principle. The aim of our study was to determine whether CeO_2NPs display hepatoprotective properties in chronic liver disease. Systemic and hepatic effects of nanoparticles were assessed in CCl_4-treated rats receiving CeO_2NPs. Thereafter, mean arterial pressure and portal pressure, among other, were assessed and serum samples obtained to measure standard hepatic and renal function tests. We observed that CeO_2NPs protects against chronic liver injury attenuating the intensity of the inflammatory response.

How all this started? This initially started 8 years ago when Dr. Casals point out to the biomedical benefits of CeO_2NPs recently discovered in in vitro experiments at that time. We were producing those materials to study their potential environmental impact. At that time, we contacted the group of Pr. Wladimiro Jimenez. We are synthetic chemist and they are clinical doctors, the learning to join multidisciplinary work was important. We focused on what does the body to the NP, how the passage through the body affect the NP, while Pr. Jimenez's team would work on what the NPs do to the body. Then, combining what does the NP to the body and what does the body to the NP, we could understandand design the use of CeO_2NPs to treat chronic cirrhosis.

What's next? Well, we have ambitious plans for the future, the liver is a complex and fundamental organ and the CeO_2NPs (and other NPs) may have useful effects in monitoring and treatment of the liver diseases and help to maintain it a healthy status. We foresee, Pr. Jimenez and us, to work together in all related to the liver and nanoparticles in the following years to come. It is not easy to find effective and efficient truly multidisciplinary teaming, therefore, once it is settled, it should last for many years.

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Cerium oxide nanoparticles reduce steatosis, portal hypertension and display anti-inflammatory properties in rats with liver fibrosis.
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