"GREMI PRIZE - Michel CHIGNARD 2024": Floran BEGUE
Thesis done at La Réunion University, Research laboratory DéTROI
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High-density lipoproteins (HDL)
Diagnostic and therapeutic implications in COVID 19

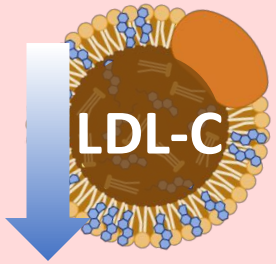
High-density lipoproteins (HDL) are crucial for maintaining good cardiovascular health due to their ability to transport cholesterol from peripheral tissues to the liver for elimination via a "reverse transport of cholesterol" mechanism. Moreover, HDL exhibits several other advantageous properties, including anti-inflammatory, antioxidant, and anti-infectious activities. In inflammatory situations, such as those encountered during viral infections, HDL can undergo both quantitative alterations, with a drop in circulating concentration, and qualitative alterations, such as a change in composition and loss of protective activities. Humanity is still struggling with coronavirus disease (COVID-19), characterized by acute inflammation and responsible for over 6.9 million deaths worldwide to date.

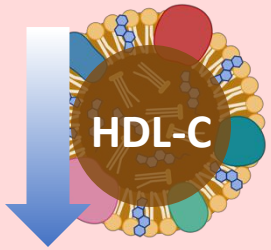
The aim of my thesis was to characterize the quantitative and qualitative changes in HDL during COVID-19, to identify specific biomarkers of the changes found in HDL, and to conduct a therapeutic trial of HDL mimetic supplementation during this disease.

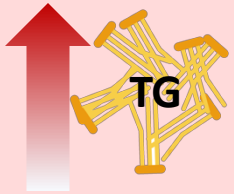
Quantification of circulating lipoproteins in the plasma of patients with severe COVID-19 shows a significant decrease in HDL and other lipoproteins, which may be predictive biomarkers of disease severity. Analysis of lipoprotein distribution shows a pro-atherogenic profile, with the presence of small, dense low-density lipoproteins (LDL) in the plasmas of patients with severe COVID-19.
Qualitative mass spectrometry analysis of the composition of both HDL and LDL showed an increased presence of proteins from the acute phase of inflammation, to the detriment of the apoprotein part of these lipoproteins when isolated from the plasma of COVID-19 patients.
When tested on human endothelial cells from primary culture, HDL demonstrated a significant alteration in their anti-apoptotic and anti-inflammatory properties when purified from the plasma of COVID-19 patients.
Finally, the anti-inflammatory properties of recombinant HDL injections were demonstrated in a patient admitted to intensive care with a severe form of COVID-19.

In conclusion, my thesis work provides some new insights into lipoprotein modifications during infectious disease, in this case COVID-19. It also opens up promising prospects for research into the use of HDL both as a biomarker of inflammatory disease severity and as a means of therapeutic control.

During acute inflammation of COVID-19

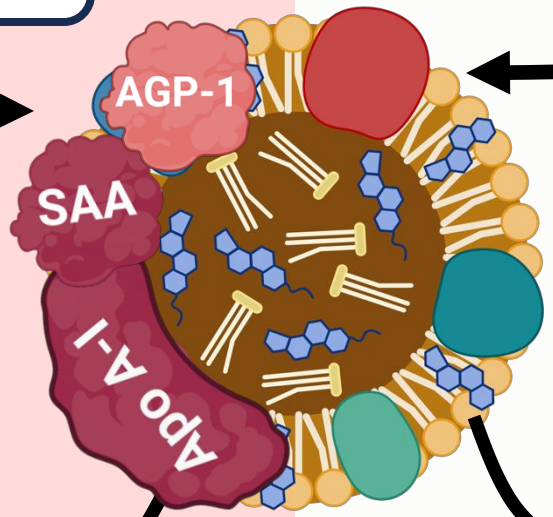






Enrichment in acute-phase proteins

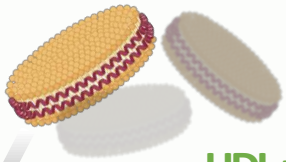
Depletion of antioxidant enzymes and apolipoproteins



HDL

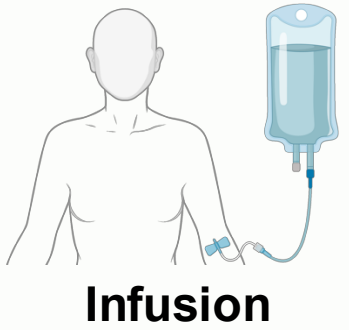
HDL dysfunction
↓ Anti-inflammatory
↓ Anti-apoptotic

HDL Therapies



HDL mimetics

Enrichment with Apolipoprotein A-I, antioxidant enzyme (Paraoxonase-1)



Infusion

Decrease in acute-phase proteins (SAA-1)

Improves HDL levels
↑ Anti-inflammatory