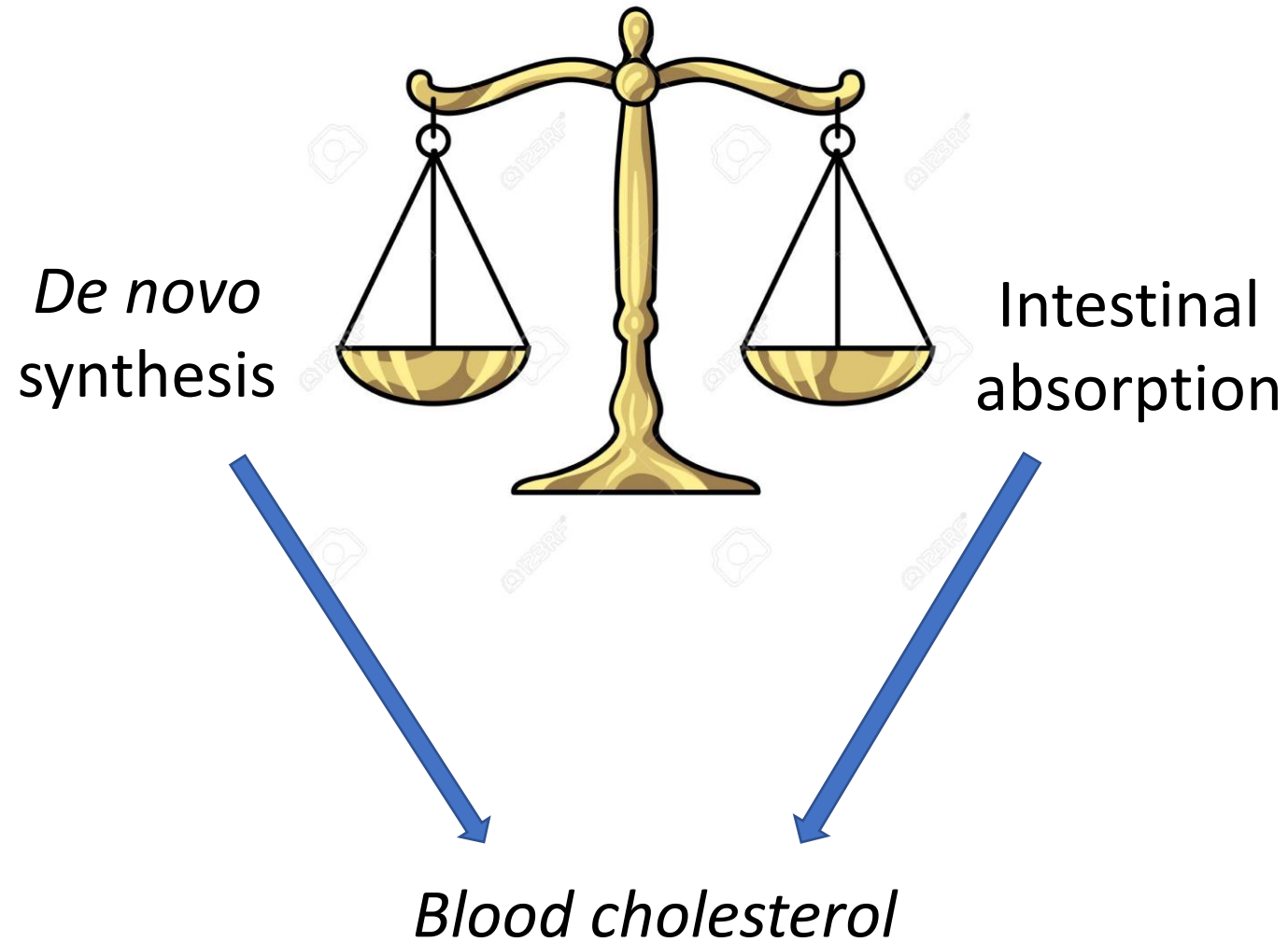


XXVII Congresso Italiano della Società Italiana per lo studio della Fibrosi Cistica
XVII Congresso Nazionale della Società Italiana per lo Studio della Fibrosi Cistica
Napoli, 20-23 ottobre 2021

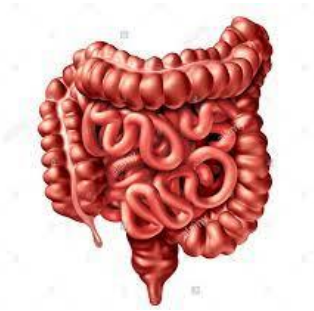
Metabolismo del colesterolo in FC:
dalla cellula al modello murino
al paziente in terapia con modulatori

Relatore:
Monica Gelzo

Cholesterol homeostasis



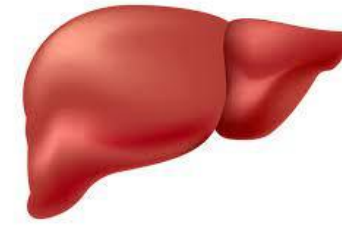
Surrogate markers of cholesterol metabolism



Absorption

Phytosterols

Cholesterol



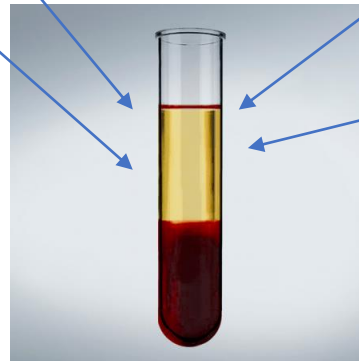
De novo synthesis



Lathosterol



Cholesterol



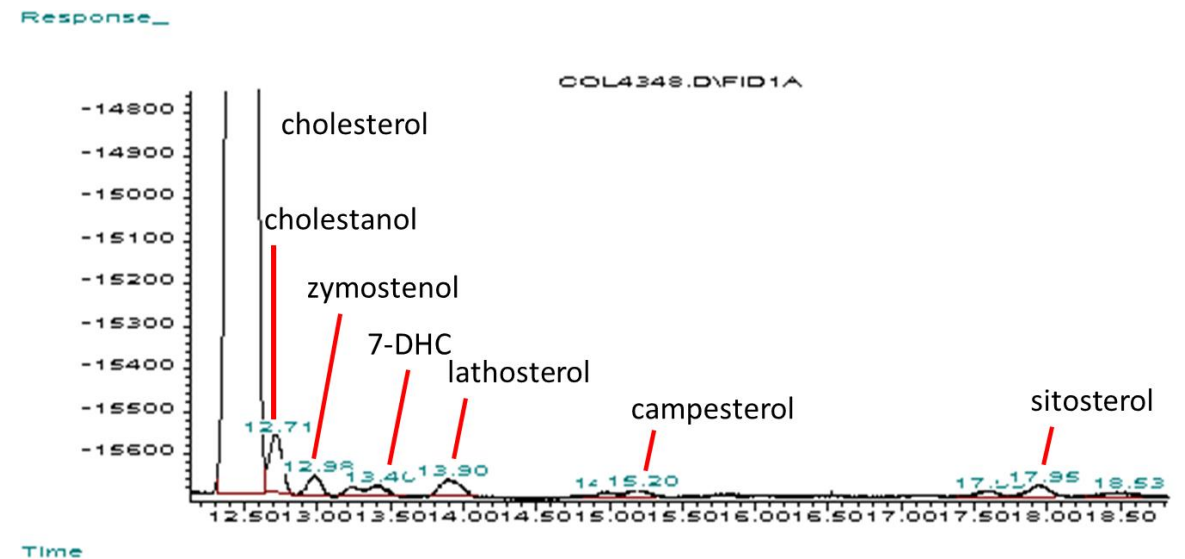
Sterol profile

Plasma sample



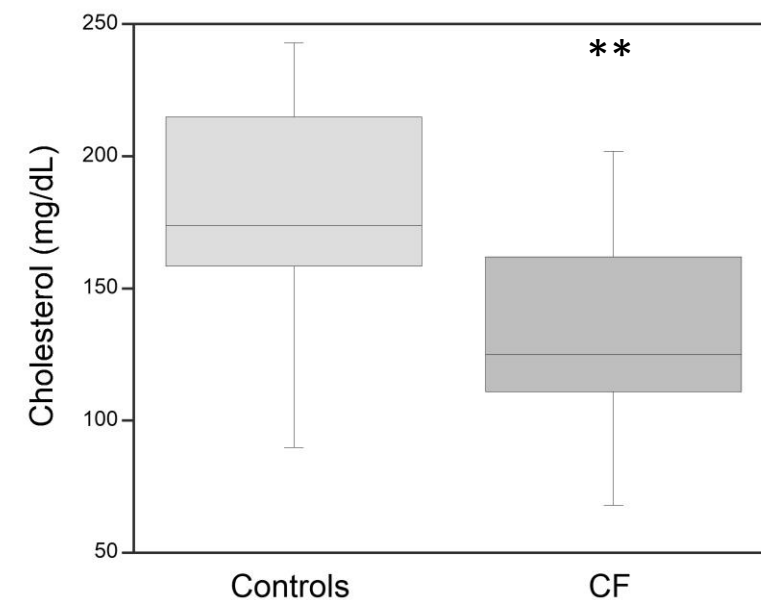
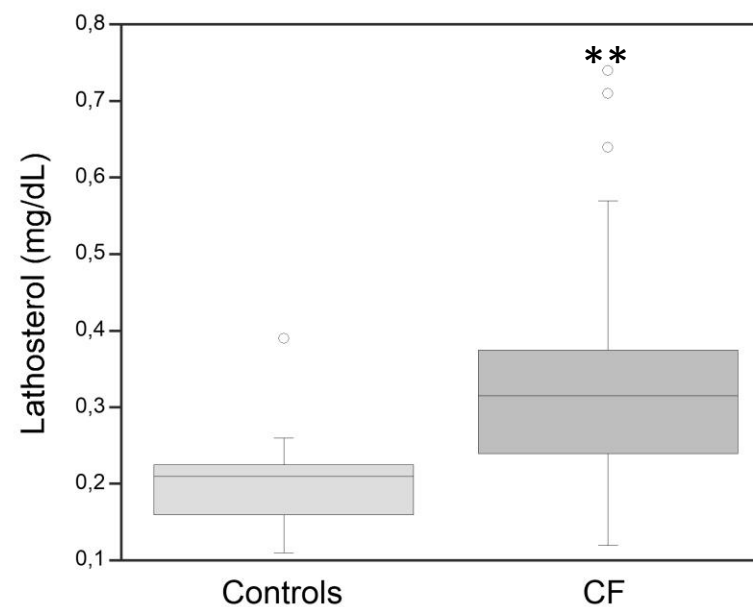
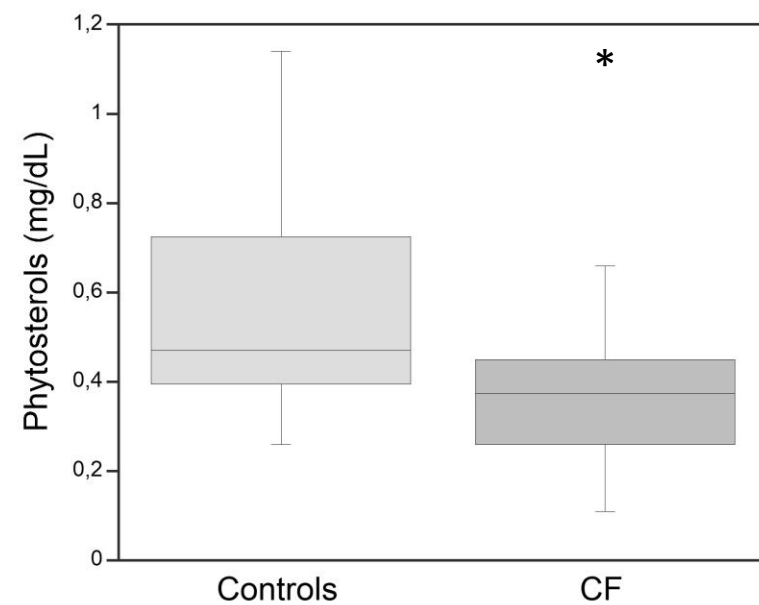
Sterol extraction

GC-FID

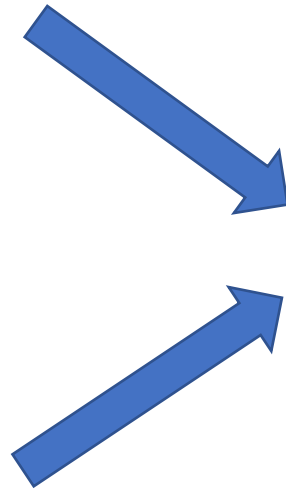
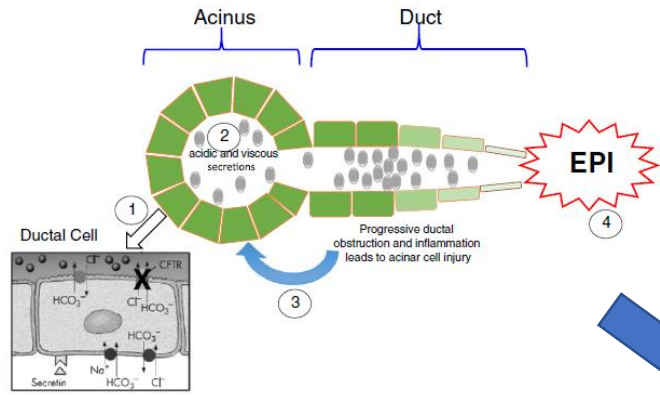


Monica Gelzo, Concetta Sica, Ausilia Elce, Antonio Dello Russo, Paola Iacotucci, Vincenzo Carnovale, Valeria Raia, Donatello Salvatore, Gaetano Corso* and Giuseppe Castaldo

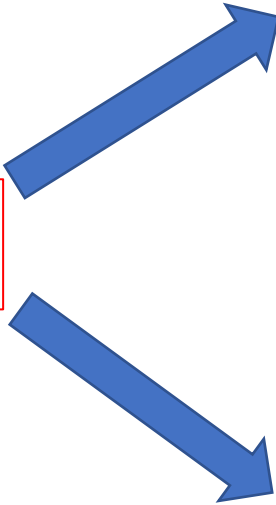
Reduced absorption and enhanced synthesis of cholesterol in patients with cystic fibrosis: a preliminary study of plasma sterols



Cystic fibrosis



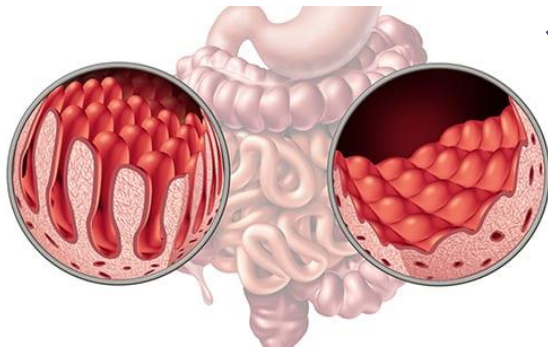
Malabsorption of lipids



Hypocholesterolemia

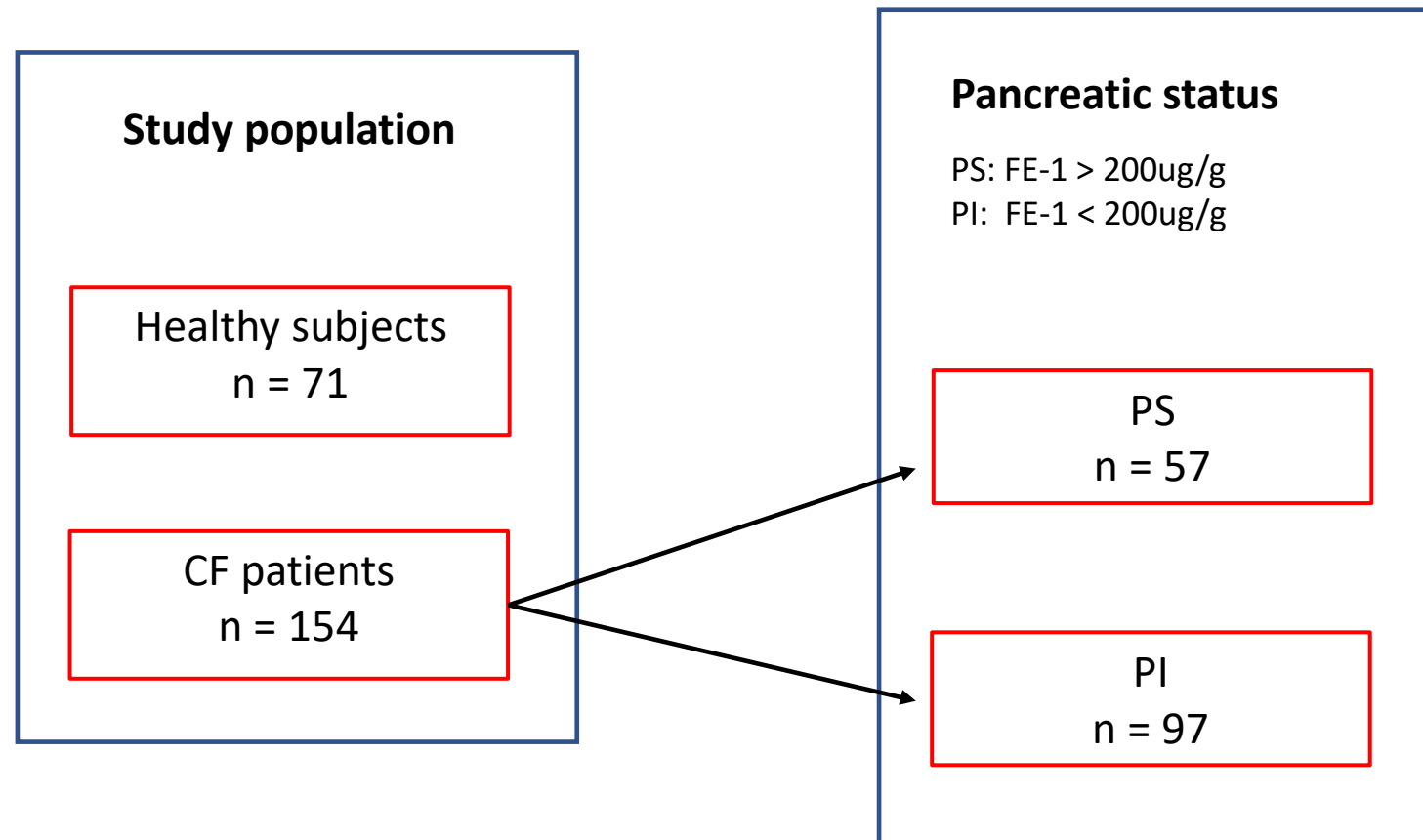
Normal cholesterolemia

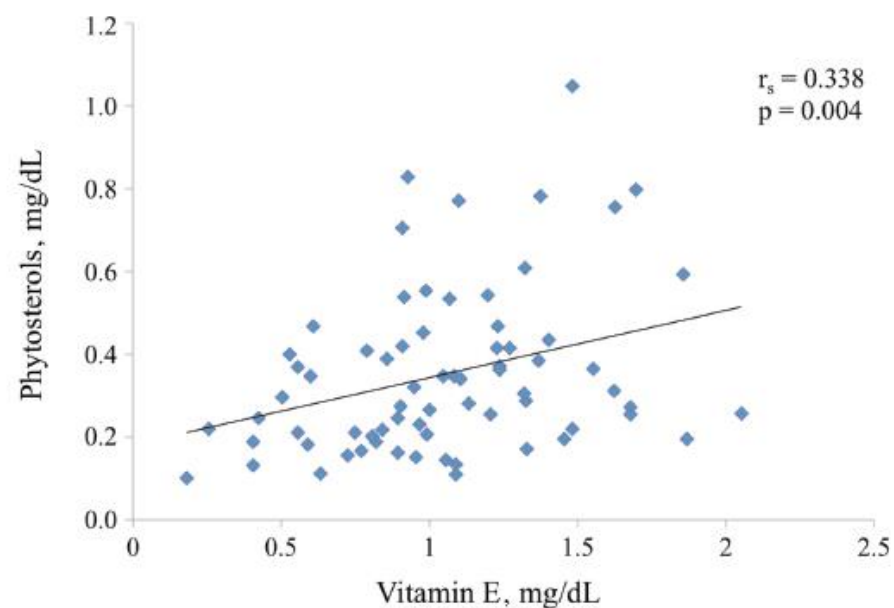
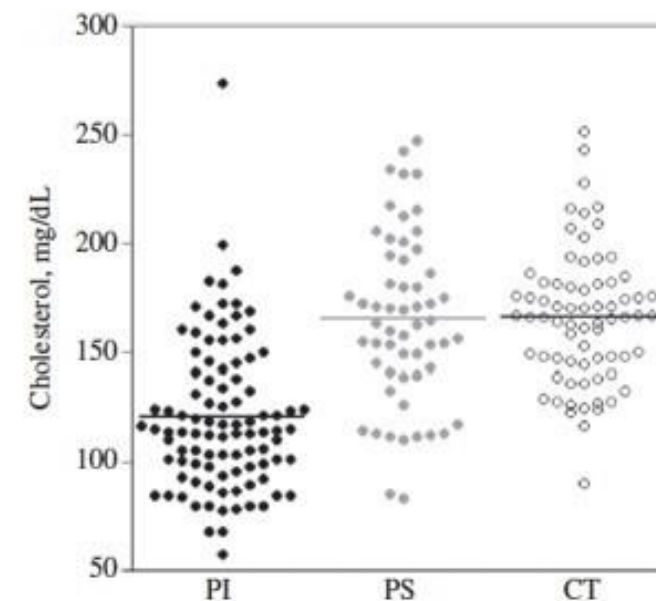
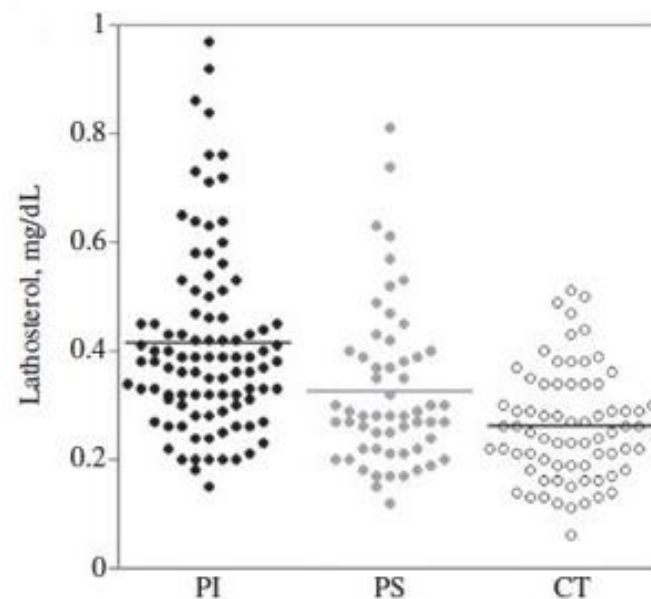
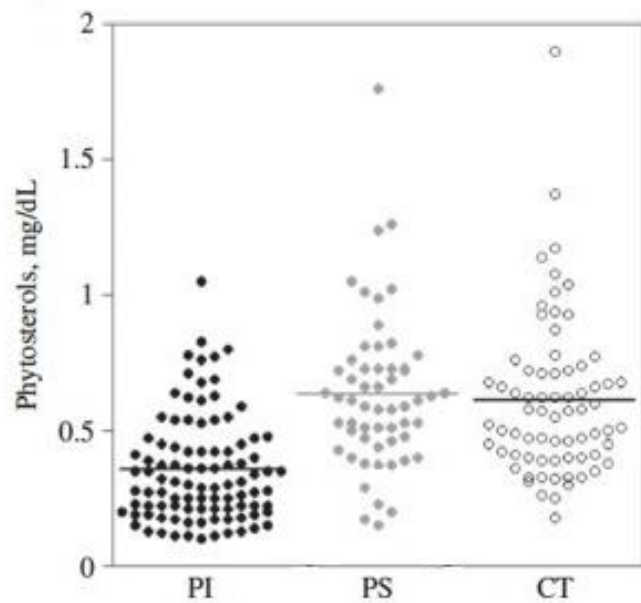
Celiac disease



Monica Gelzo^a, Paola Iacotucci^a, Concetta Sica, Renato Liguori, Marika Comegna,
Vincenzo Carnovale, Antonio Dello Russo^b, Gaetano Corso* and Giuseppe Castaldo

Influence of pancreatic status on circulating plasma sterols in patients with cystic fibrosis





DE GRUYTER




Clin Chem Lab Med 2020; aop

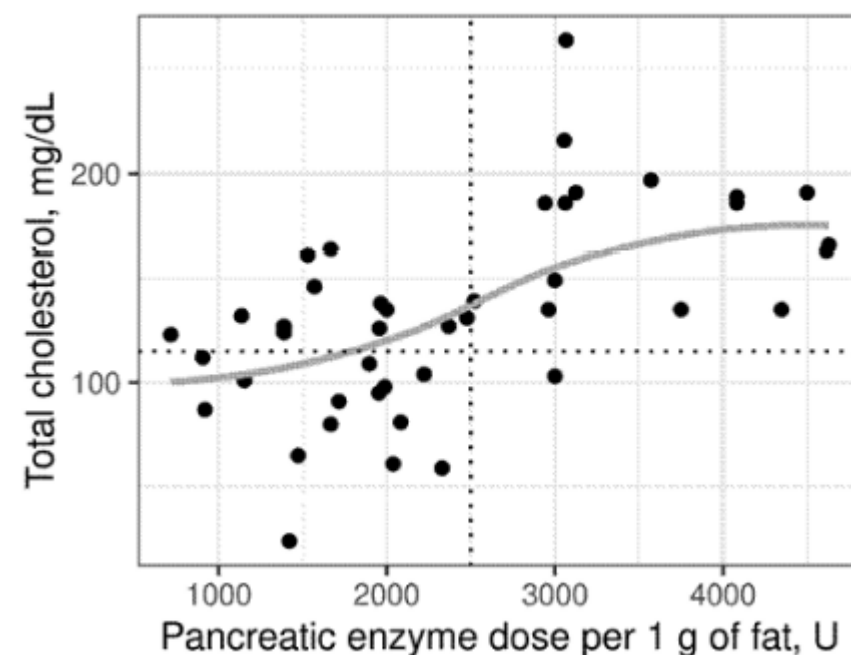
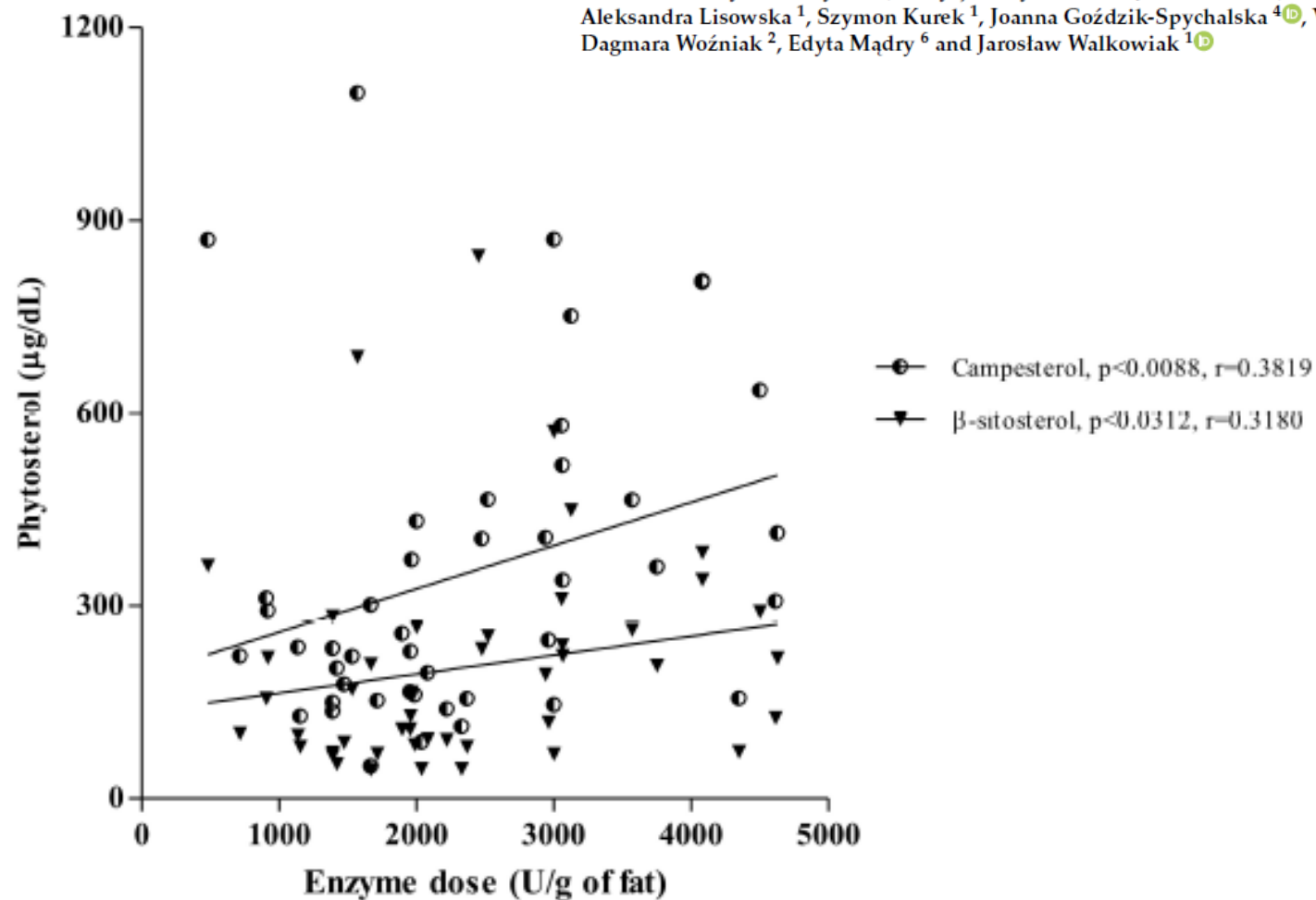
Monica Gelzo^a, Paola Iacotucci^a, Concetta Sica, Renato Liguori, Marika Comegna, Vincenzo Carnovale, Antonio Dello Russo^b, Gaetano Corso* and Giuseppe Castaldo

Influence of pancreatic status on circulating plasma sterols in patients with cystic fibrosis

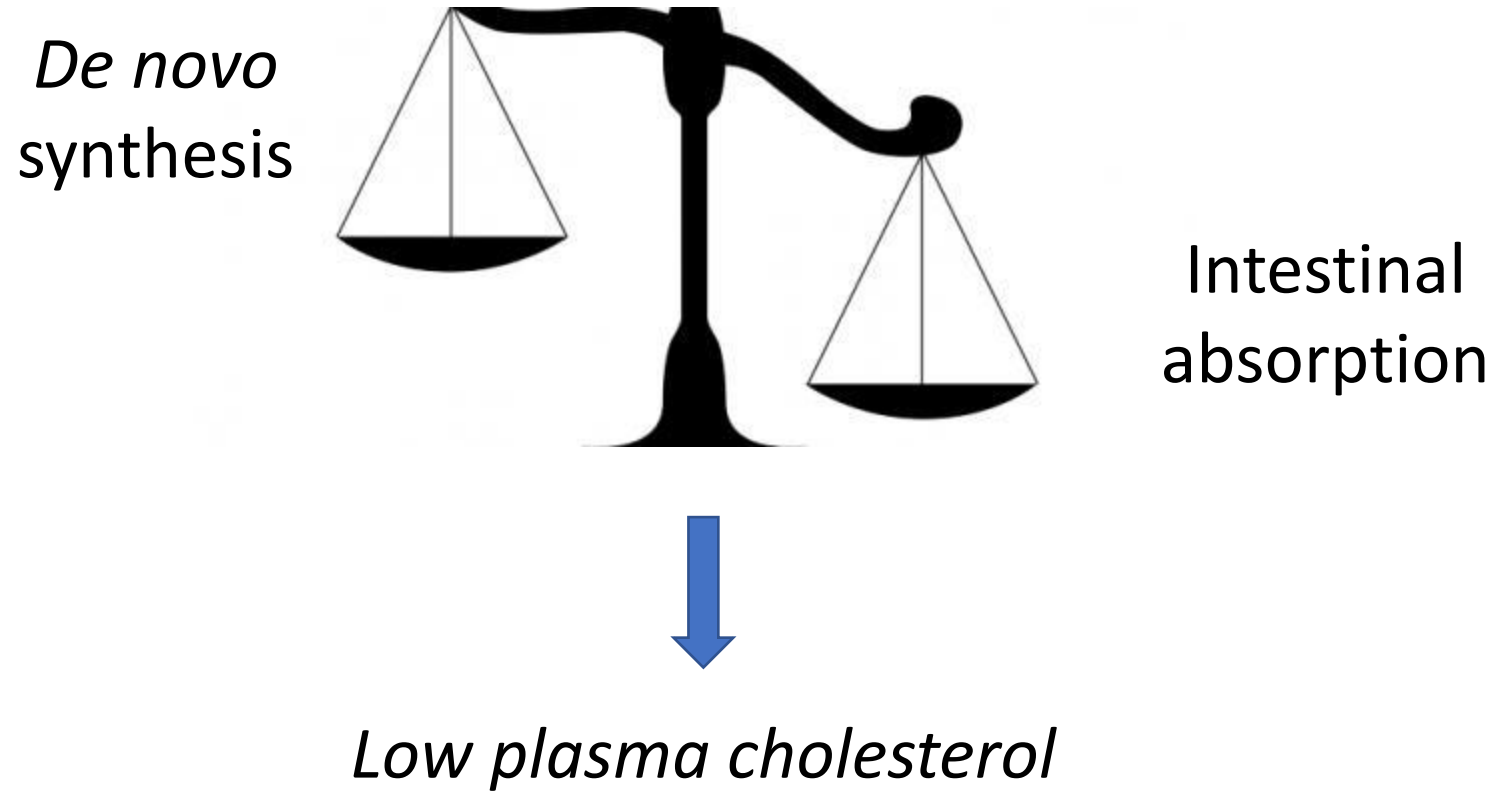
Article

Severe Genotype, Pancreatic Insufficiency and Low Dose of Pancreatic Enzymes Associate with Abnormal Serum Sterol Profile in Cystic Fibrosis

Sławomira Drzymała-Czyż ^{1,2,*}, Patrycja Krzyżanowska-Jankowska ¹, Krzysztof Dziedzic ^{1,3}, Aleksandra Lisowska ¹, Szymon Kurek ¹, Joanna Goździk-Spychalska ⁴, Victoria Kononets ⁵, Dagmara Woźniak ², Edyta Mądry ⁶ and Jarosław Walkowiak ¹



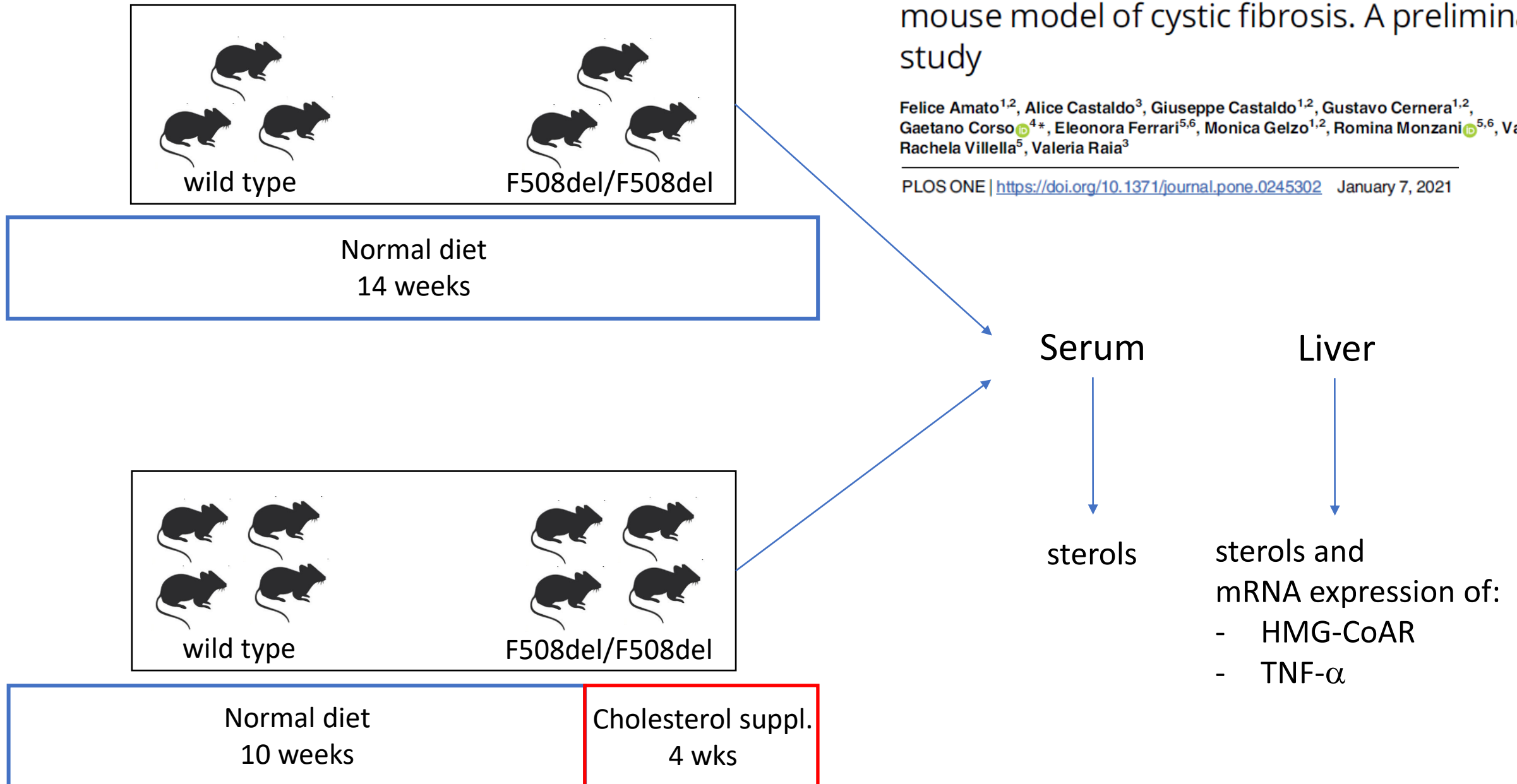
Cholesterol metabolism in CF patients

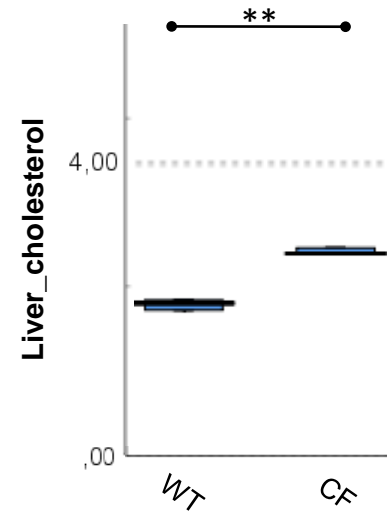
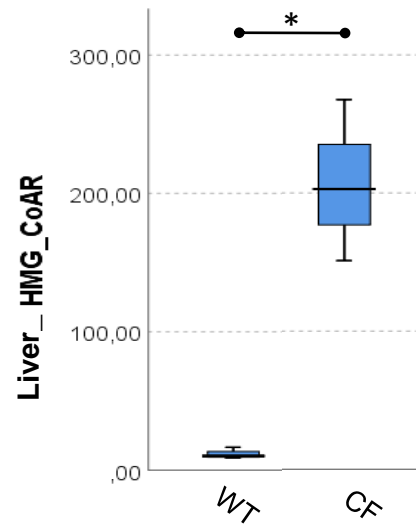
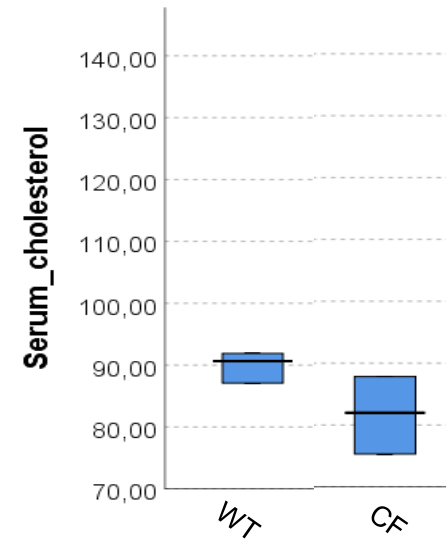
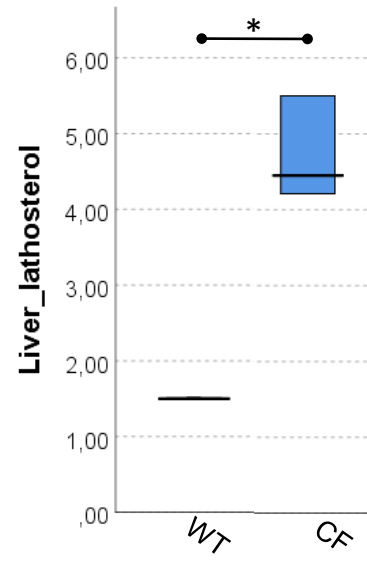
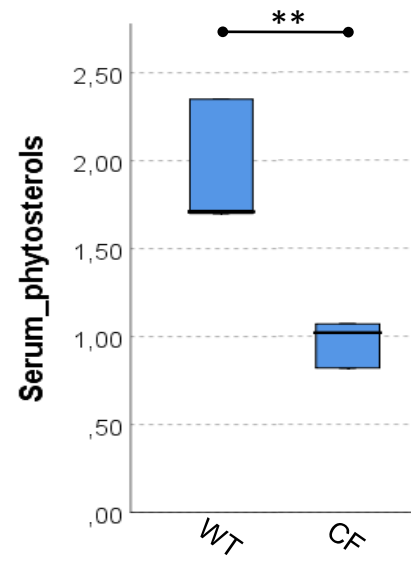


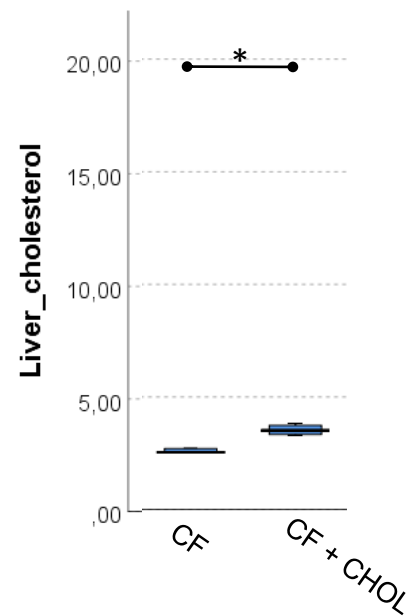
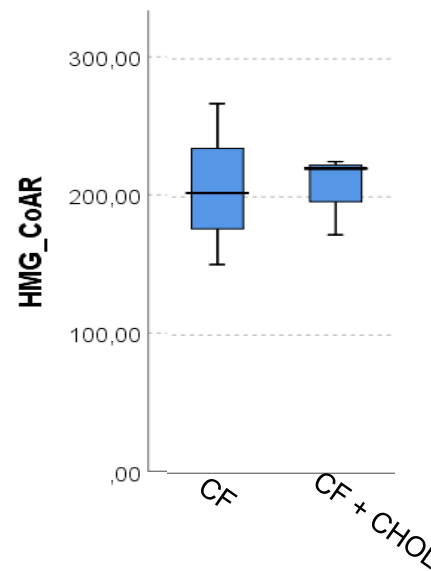
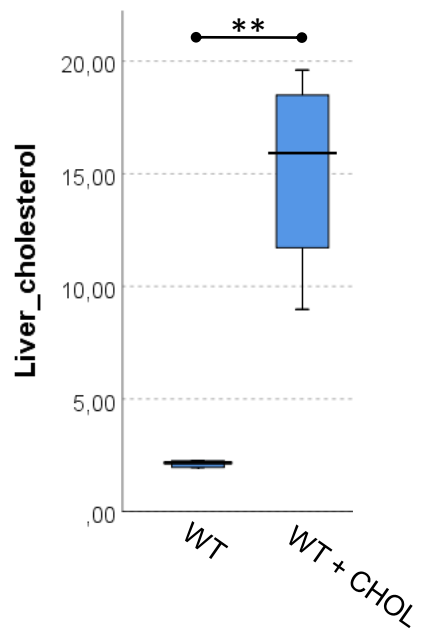
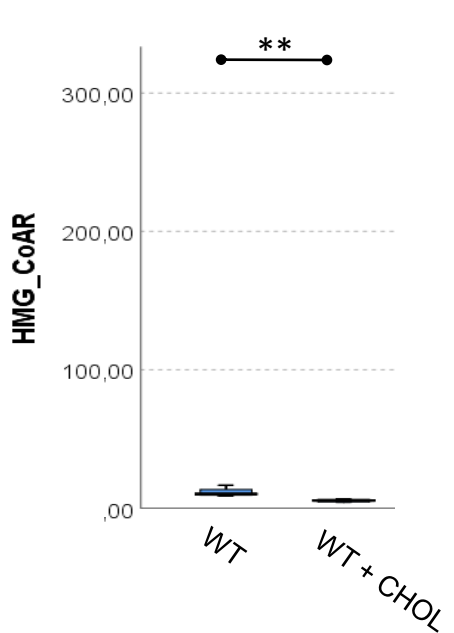
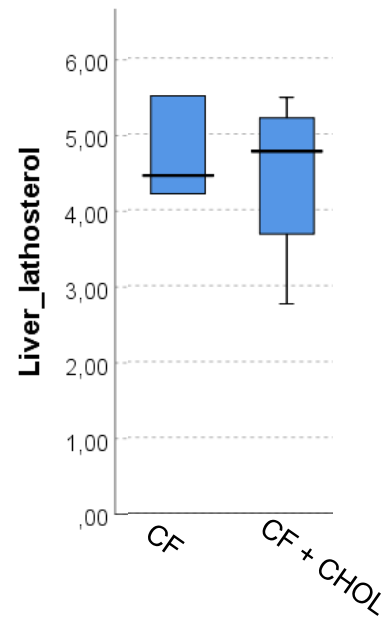
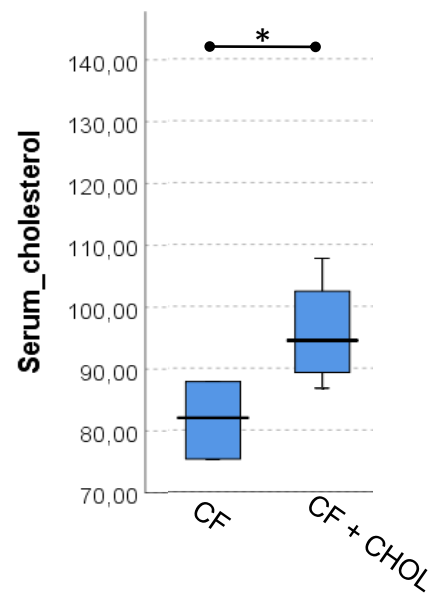
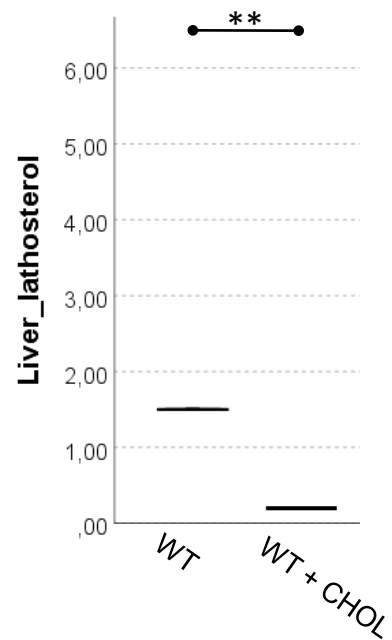
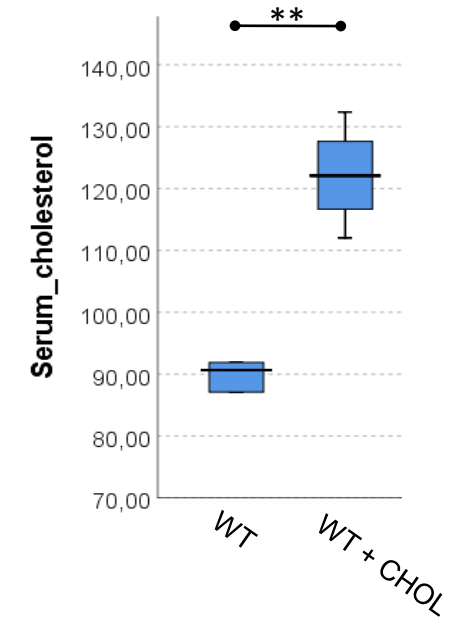
Impaired cholesterol metabolism in the mouse model of cystic fibrosis. A preliminary study

Felice Amato^{1,2}, Alice Castaldo³, Giuseppe Castaldo^{1,2}, Gustavo Cernera^{1,2}, Gaetano Corso^{4*}, Eleonora Ferrari^{5,6}, Monica Gelzo^{1,2}, Romina Monzani^{5,6}, Valeria Rachela Villella⁵, Valeria Raia³

PLOS ONE | <https://doi.org/10.1371/journal.pone.0245302> January 7, 2021

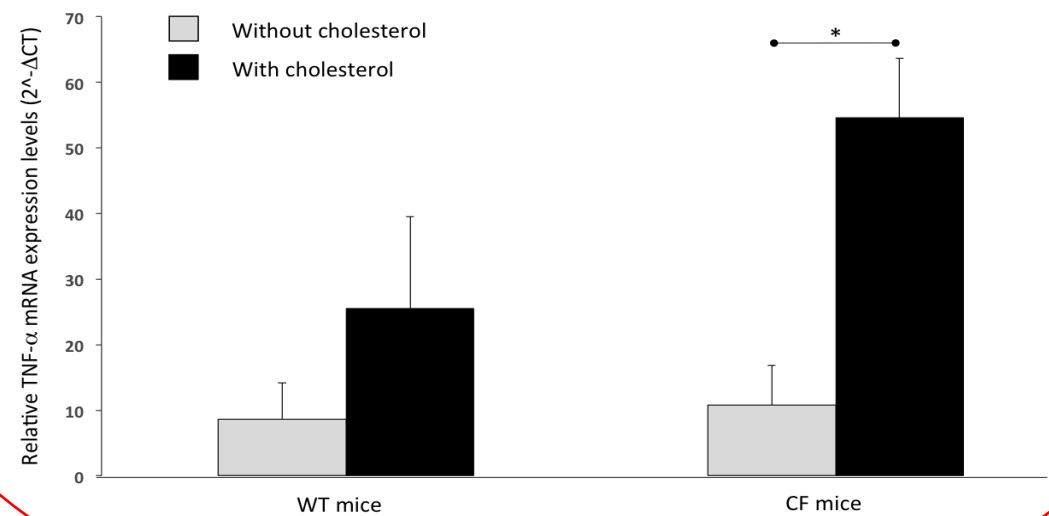




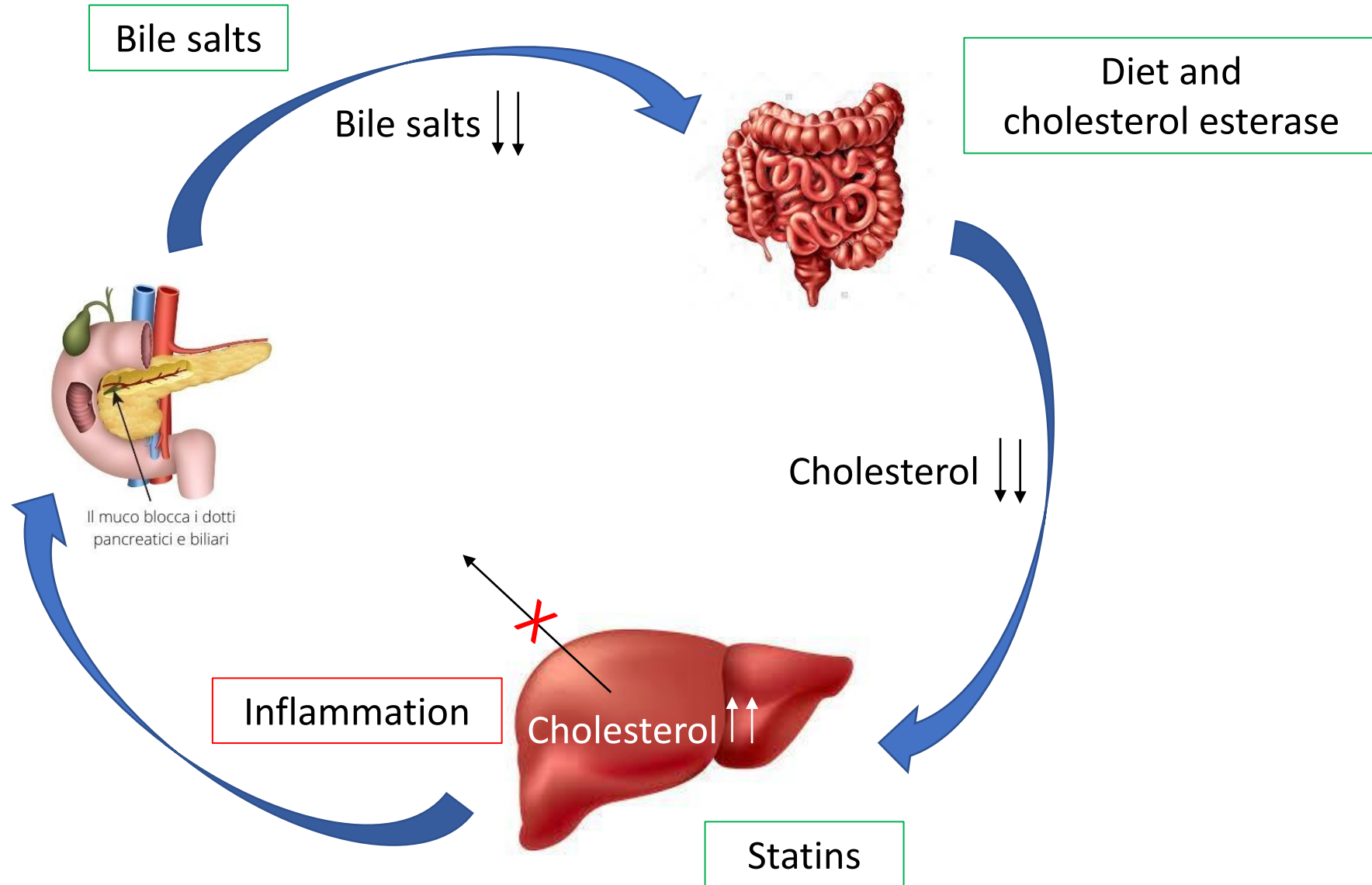


Liver inflammation

TNF- α



Vicious circle in CF



Lumacaftor/ivacaftor improves liver cholesterol metabolism but does not influence hypocholesterolemia in patients with cystic fibrosis

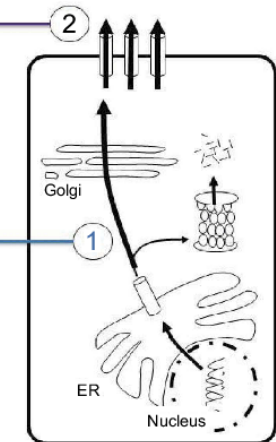
Monica Gelzo^{a,b}, Paola Iacotucci^c, Mafalda Caputo^a, Gustavo Cernera^{a,b},
Marika Comegna^{a,b}, Vincenzo Carnovale^c, Gaetano Corso^{d,*}, Giuseppe Castaldo^{a,b}

CFTR Potentiator: Ivacaftor

Potentiates the channel-open probability (channel gating) of CFTR at the cell surface

CFTR Corrector: Lumacaftor

Facilitates the processing and trafficking of CFTR to increase the amount of CFTR at the cell surface



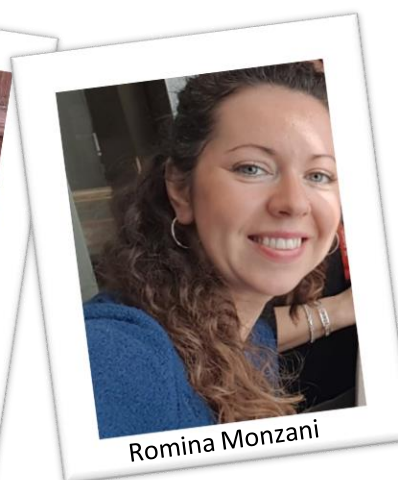
Effects of lumacaftor/ivacaftor on cholesterol metabolism and hepatobiliary injury/function in homo-deltaF508 patients (n = 20).

	Before	After	Reference intervals
Lipids (mg/dL)			
Cholesterol	112 (26)	99 (14)*	121–232
HDL-cholesterol	43 (37–53)	50 (42–58)	> 40
LDL-cholesterol	58 (47–72)	53 (49–60)	< 115
Triglycerides	62 (54–73)	64 (54–69)	< 150
Phytosterols	0.27 (0.13)	0.24 (0.06)	0.26–1.22
Lathosterol	0.40 (0.14)	0.23 (0.07)***	0.12–0.49
Cholestanol	0.24 (0.12)	0.32 (0.07)*	0.09–0.45
Vitamin E (μg/dL)	886 (215)	1112 (309)**	500–1800
Liver parameters			
AST (U/L)	20 (18–24)	22 (19–27)	0–34
ALT (U/L)	21 (17–25)	18 (14–26)	0–55
γGT (U/L)	14 (10–18)	12 (10–15)	12–64
AP (U/L)	110 (98–118)	68 (60–84)**	40–150
Total bilirubin (mg/dL)	0.60 (0.40–0.82)	0.36 (0.33–0.53)	0.20–1.20
Direct bilirubin (mg/dL)	0.29 (0.22–0.36)	0.18 (0.16–0.21)	0–0.40
Albumin (g/dL)	4.3 (0.3)	4.6 (0.4)	3.5–5.2

Conclusion



- ✓ CF patients have a reduced intestinal absorption of cholesterol (that could be corrected by cholesterol and cholesterol esterase supplementation)
- ✓ There is an enhanced de novo synthesis that does not normalize serum cholesterol (because the altered CFTR likely impairs cholesterol exocytosis)
- ✓ There is a significant accumulation of cholesterol in liver cells that triggers inflammation
- ✓ The cholesterol supplementation does not correct the enhanced de novo synthesis because the key enzyme is not responsive in CF (suggesting the use of drugs that inhibit endogenous synthesis)



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UNIVERSITÀ DEGLI STUDI DI NAPOLI FEDERICO II - DIPARTIMENTO DI ECCELLENZA (2018-2022)

MEDICINA MOLECOLARE E
BIOTECNOLOGIE MEDICHE



Cystic Fibrosis Research Lab



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