

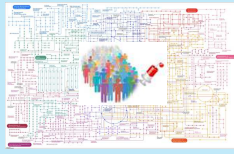
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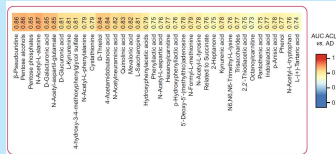
Background – Serum metabolomics to assess systemic inflammation and organ failure in patients with ACLF

- Patients with ACLF n = 181
- Patients with AD n = 650
- Patients with compensated cirrhosis n = 43
- Healthy controls n = 29

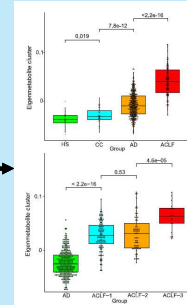
CANONIC study



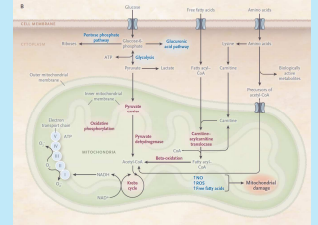
Serum Metabolomics



ACLF fingerprint of 38 metabolites



Correlation with systemic inflammation



Pathophysiology of ACLF (Mitochondrial dysfunction)

Moreau R et al, J Hepatol 2020

Objective of WP1 - task5: Better delineate cirrhosis decompensation using serum metabolomics

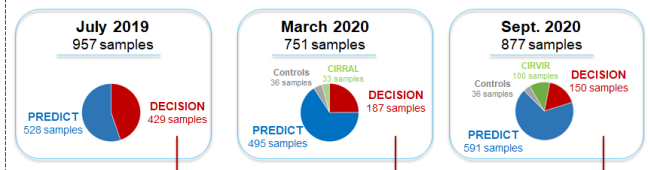
Work Performed so far

ACQUISITION OF SERUM METABOLIC PROFILES – 2500+ SAMPLES BY LIQUID CHROMATOGRAPHY COUPLED TO HIGH RESOLUTION MASS SPECTROMETRY (LC-HRMS)

- Standardized sample preparation protocols (standard operating procedures, SOPs)
- Randomization of sample preparation and analysis
- Internal standards added to all serum samples
- Quality Control (QC) samples injected every 10 samples
 - Pool of all studied serum samples (QC-Pool)
- Include diluted pooled QCs

LC coupled to high-resolution MS (x2)

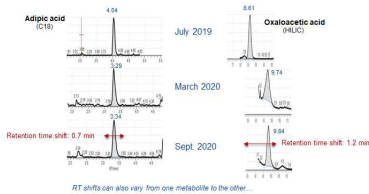
PREDICT COHORT / SUB-SET OF 766 SAMPLES (from 3 distinct batches over 1.5 yr)



766 samples

DATA TREATMENT – DIFFICULTIES ENCOUNTERED

Important chromatographic retention time shifts

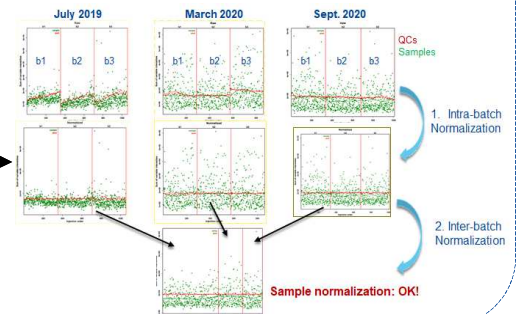


- Potential misalignment of peaks in case of fully automated treatment:
- Unreliable or incorrect metabolite quantification

Semi-automated targeted quantification of 360 metabolites



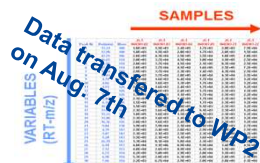
Batch-to-batch normalization



Results:

347 METABOLITES QUANTIFIED

766 Samples + 63 controls from PREDICT COHORT



What's next?

- Analysis of ACLARA samples: done, July 2021
- Data treatment, quality control check, ... : Sept. 2021
- Expected data transfer to WP3: Mid Oct. 2021



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