ENDOCANNABINOID AND POLYUNSATURATED FATTY ACID PROFILES ARE ALTERED IN CROHN'S DISEASE

Dorboz R, Riahi A, Ben Mustapha Y, Ben Fradj MK, Serghini M, Sanhaji H, Fekih M, Feki M.

Laboratory of Biochemistry & Service of Gastroenterology A, Rabta Hospital, Tunis, Tunisia.

INTRODUCTION AND OBJECTIVES

Crohn's disease (CD) is an inflammatory bowel disease of unknown etiopathogenesis, which remains challenging to treat. CD is characterized by innate and adaptive immunity dysregulation and gut dysbiosis. Endocannabinoids (eCBs) are bio active lipid mediators deriving from polyunsaturated fatty acids (PUFAs), which regulate inflammation, immunity, and gut physiology.

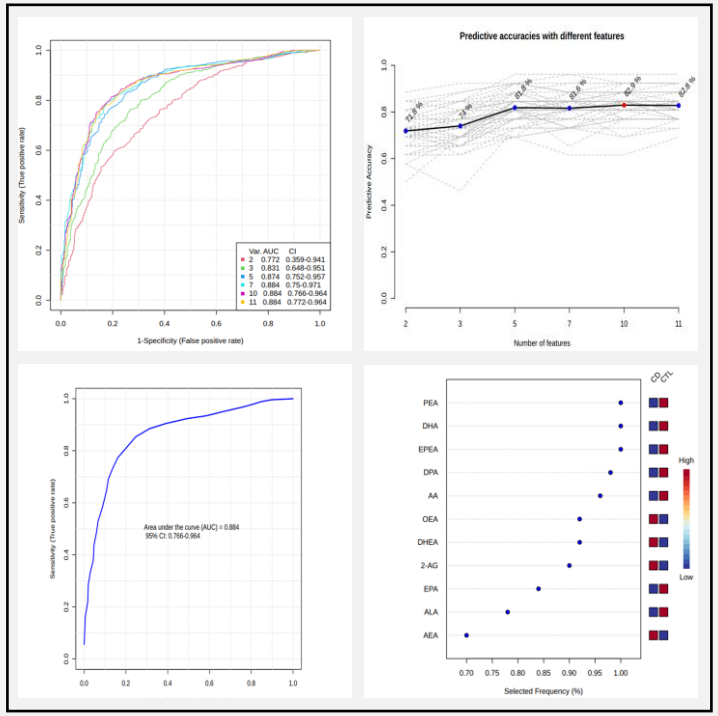
The study aimed to determine circulating eCB and PUFA profiles in CD patients and define a lipidomic signature for acute CD .

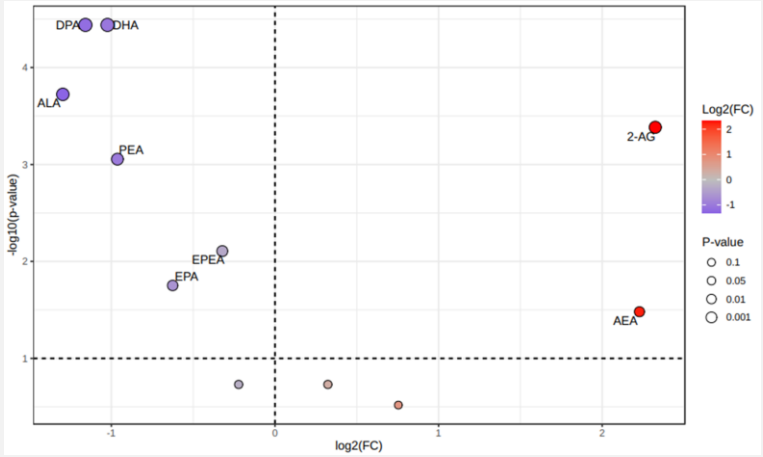
PATIENTS AND METHODS

- **Case-control study** : **26** CD patients and **35** controls.
- **Targeted LC-MS/MS** : quantification of 7 eCBs (PEA, OEA, ALEA, AEA, 2-AG, EPEA, and DHEA), and 5 PUFAs (ALA, ARA, EPA, DPA, and DHA).
- **Data analysis** : Volcano plot, univariate ROC, and multivariate ROC-based exploratory analyses.

RESULTS

✓ **Volcano plot analysis** : CD patients: increased eCBs (2-AG, AEA), and decreased eCB-like mediators (PEA, EPEA) and n3 PUFAs (ALA, EPA, DPA, DHA).





✓ **Univariate ROC analysis** : Most discriminant mediators were DPA [AUC (95% CI), 0.85 (0.76-0.93)], DHA [0.84 (0.72-0.92)], ALA [0.81 (0.68-0.89)], 2-AG [0.78 (0.66-0.89)], PEA [0.77 (0.63-0.89)], and EPEA [0.72 (0.56-0.86)].

✓ **Multivariate ROC-based exploratory analysis** : PEA, ALEA, and DHA demonstrated a **selection frequency of 1** in the best biomarker combination model. The combination has a good discriminatory power for CD; AUC=0,88 [0.77-0.96].

CONCLUSIONS

The profiles are characterized by the upregulation of n-6-derived eCBs and downregulation of eCB-like mediators and n-3 PUFAs. The combination of decreased PEA, DHA, and ALEA discriminates CD and may be a lipidomic signature for the disease. The findings suggest that eCB metabolism is disrupted in CD and that eCB and PUFA profiles are useful biomarkers for CD. Further research is needed to evaluate whether modulating eCB metabolism could be an adjuvant/alternative therapeutic option in CD.