



Metabolomica nella prevenzione e diagnosi per la salute umana

Alfredo Miccheli

*Dipartimento di Biologia Ambientale,
Sapienza Università di Roma*



**NMR-based Metabolomics Laboratory of
Sapienza**

Le definizioni

Metabonomica “...misura della risposta metabolica dinamica multiparametrica di sistemi viventi a stimoli patofisiologici o modificazioni genetiche ...” J. Nicholson et al., 1999

Metabolomica “...il set completo di metaboliti od intermedi a basso peso molecolare, che sono contesto-dipendenti e variano secondo lo stato fisiologico, patologico o di sviluppo di una cellula, un tessuto, un organo od un organismo ...” Oliver 2002

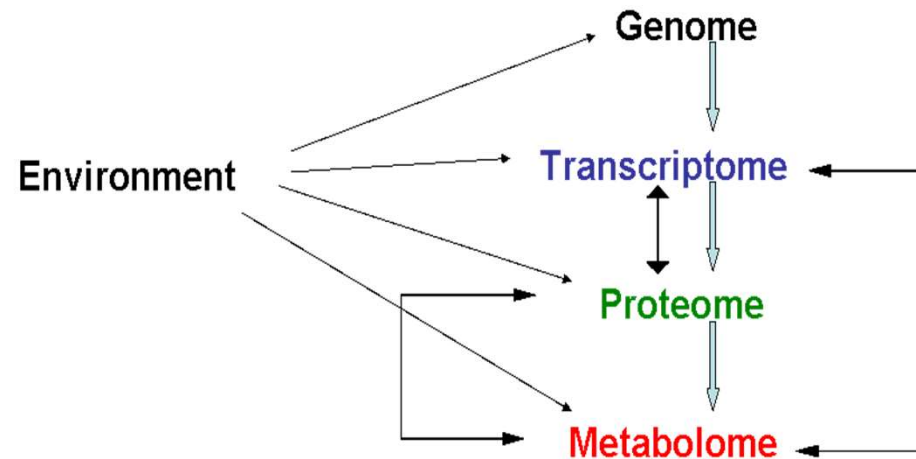
Journal of Magnetic Resonance in Biology and Medicine - Vol. 1 - n. 1/93

Multivariate data analysis as applied to NMR results: a window on biological complexity

A. GIULIANI, G. CAPUANI, T. AURELI, A. MICCHELI*, C. MANETTI*, F. CONTI*°

La Systems Biology e la nascita delle discipline “omiche”

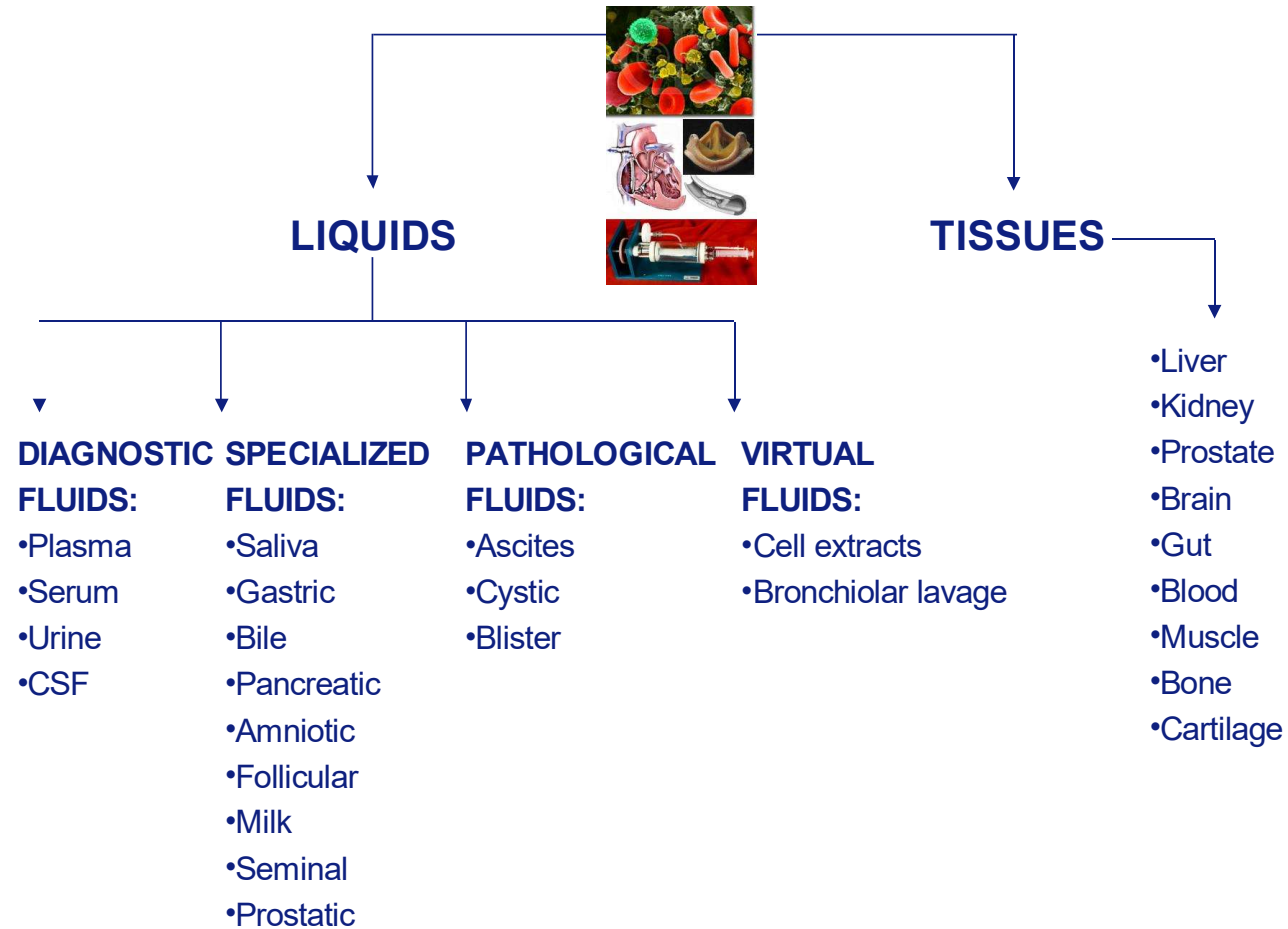
- **Genomica**
 - Studio dei geni – l’unica -omica non contesto dipendente
- **Trascrittomica**
 - Tutti gli mRNA in una cellula/tessuto/organo/organismo
- **Proteomica**
 - Tutte le proteine in una cellula/tessuto/organo/organismo
- **Metabonomica/Metabolomica**
 - Tutti i metaboliti in una cellula/tessuto/organo/organismo



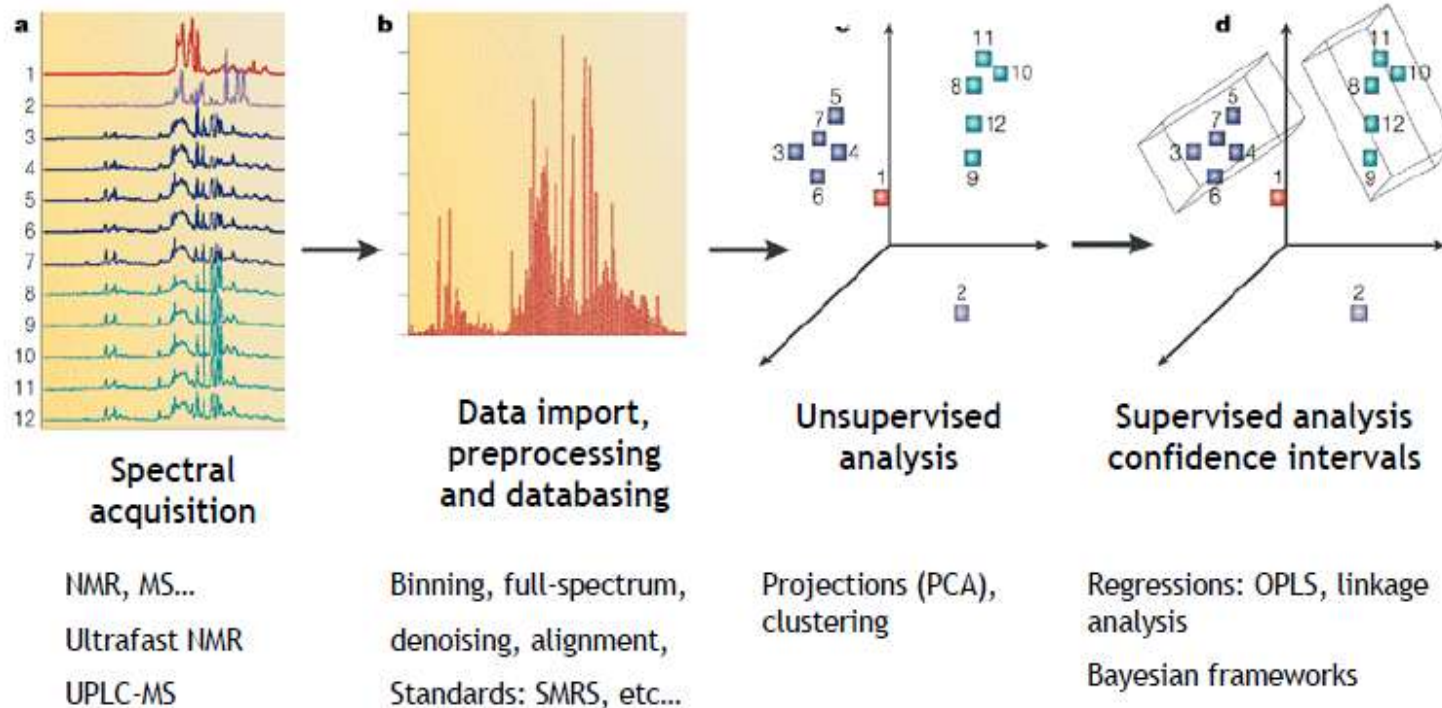
Different spectroscopic method used in metabolomic analysis

- Gas chromatography-mass spectrometry (GC-MS)
- Liquid chromatography-mass spectrometry (LC-MS)
- **Nuclear Magnetic Resonance (NMR) spectroscopy**
- Fourier-transform infrared (FT-IR) spectrometry
- Metabolite arrays

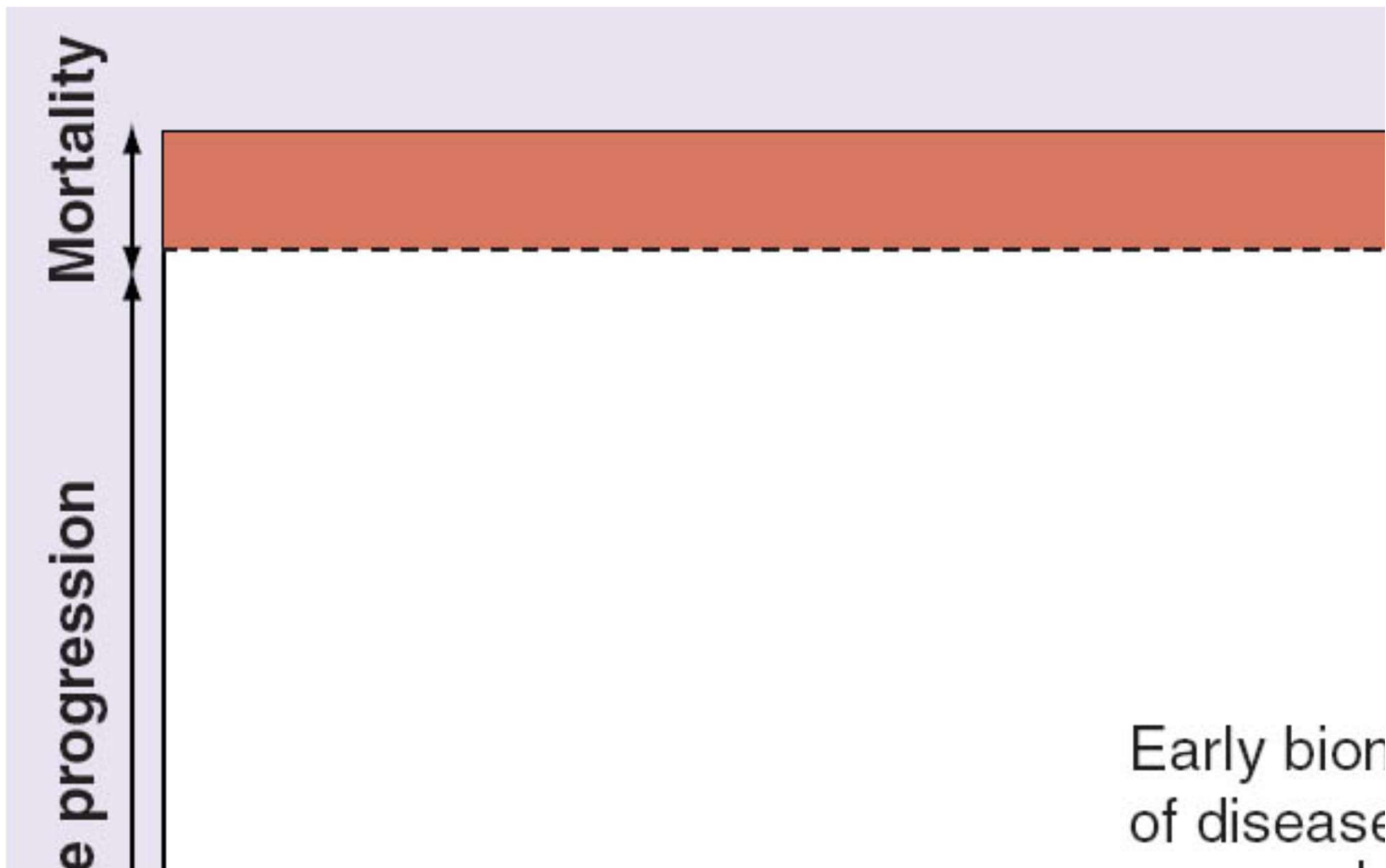
Biological samples and Biofluids



Metabon/lomics strategy



Nicholson JK, Connelly J, Lindon JC, Holmes E Nat Rev Drug Discov. 2002 Feb;1(2):153-61.



CLINICAL METABONOMICS

Diagnosis

- Identifying new biomarkers
- Clinical diagnosis where no simple test exists
- Screening subjects for clinical trials

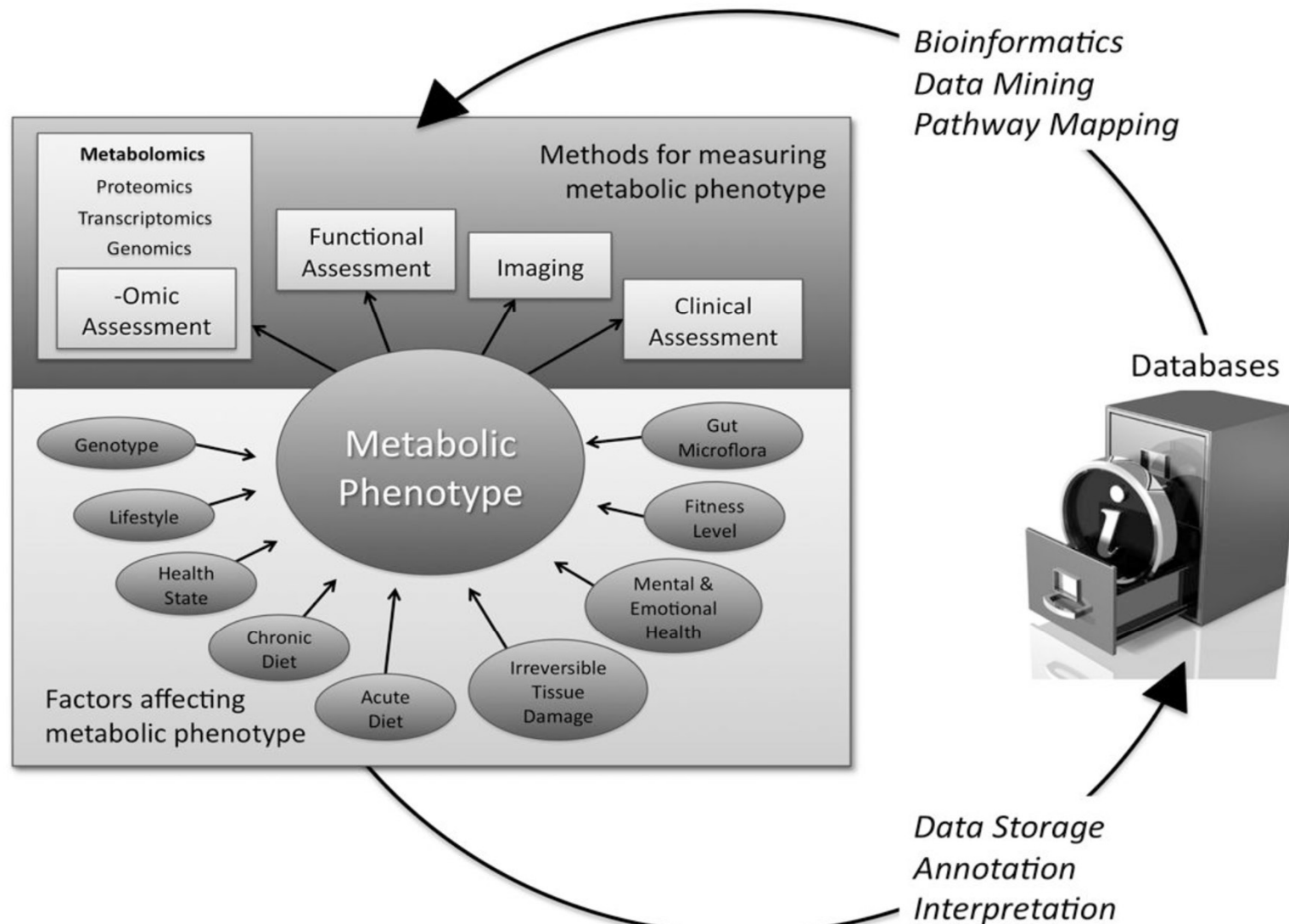
Prognosis

Monitoring therapy

- Understanding basis of drug efficacy
- Toxicology
- Pharmacometabonomics
- Clinical monitoring

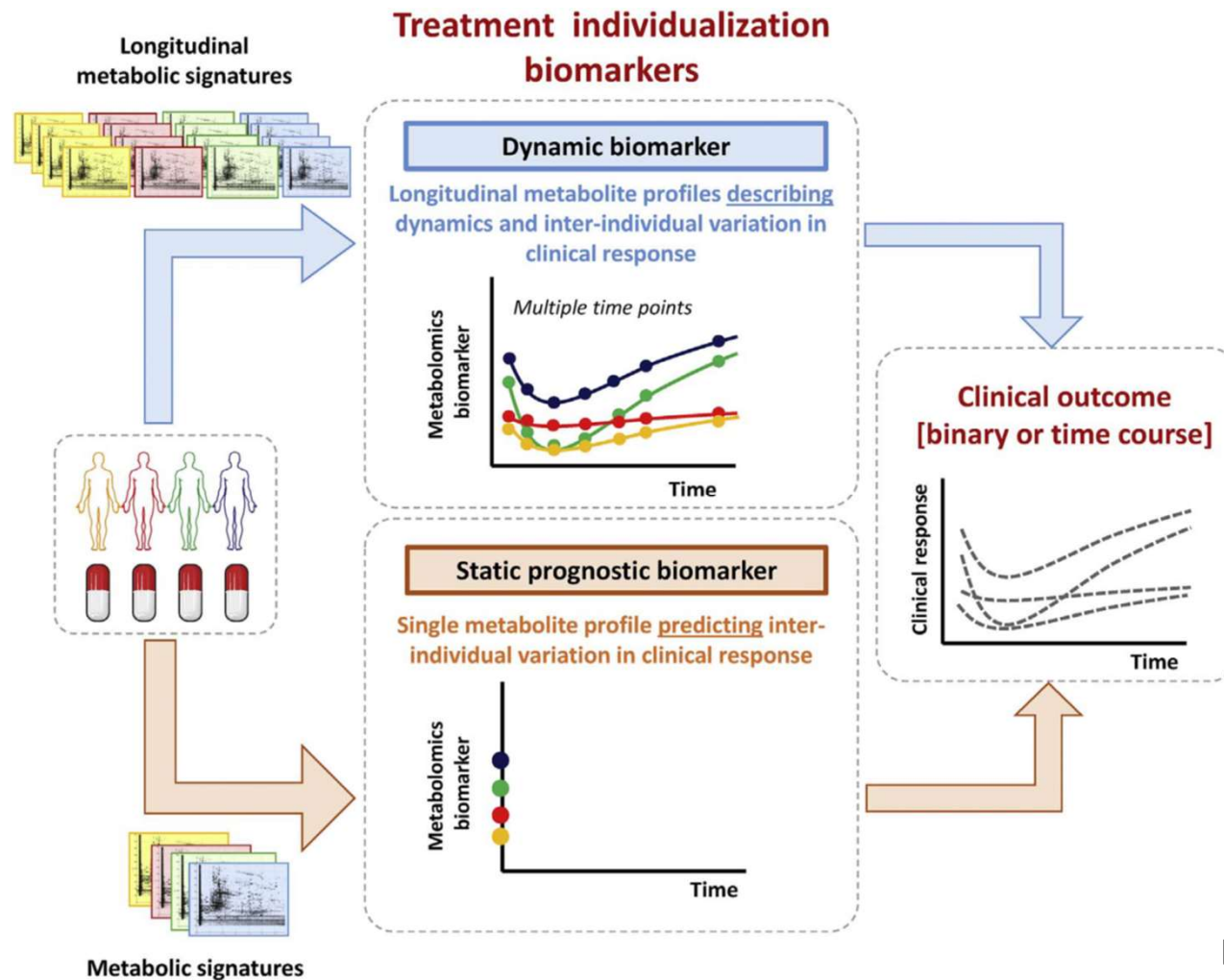
Designing therapy

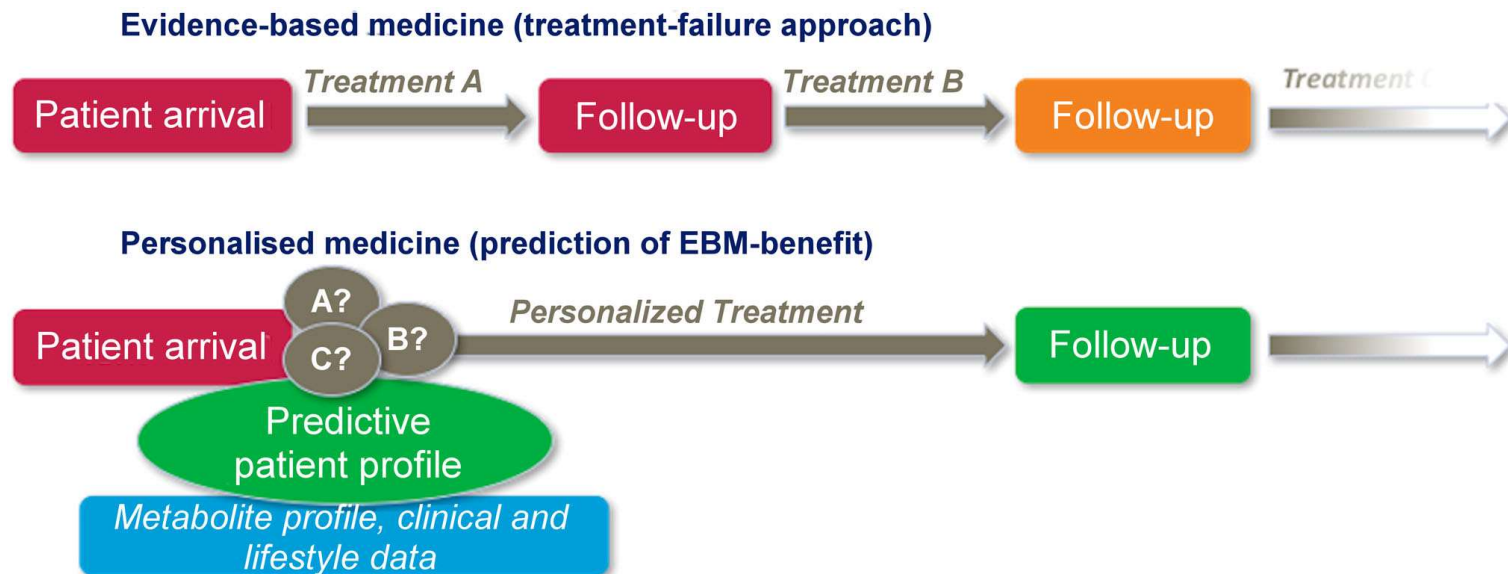
- New insights into physiology and pathology
- Validating animal models of disease



Metabolomics in precision medicine

Identification of prognostic and dynamic biomarkers which can be used to respectively predict and describe the inter-individual variation in disease progression and treatment response.

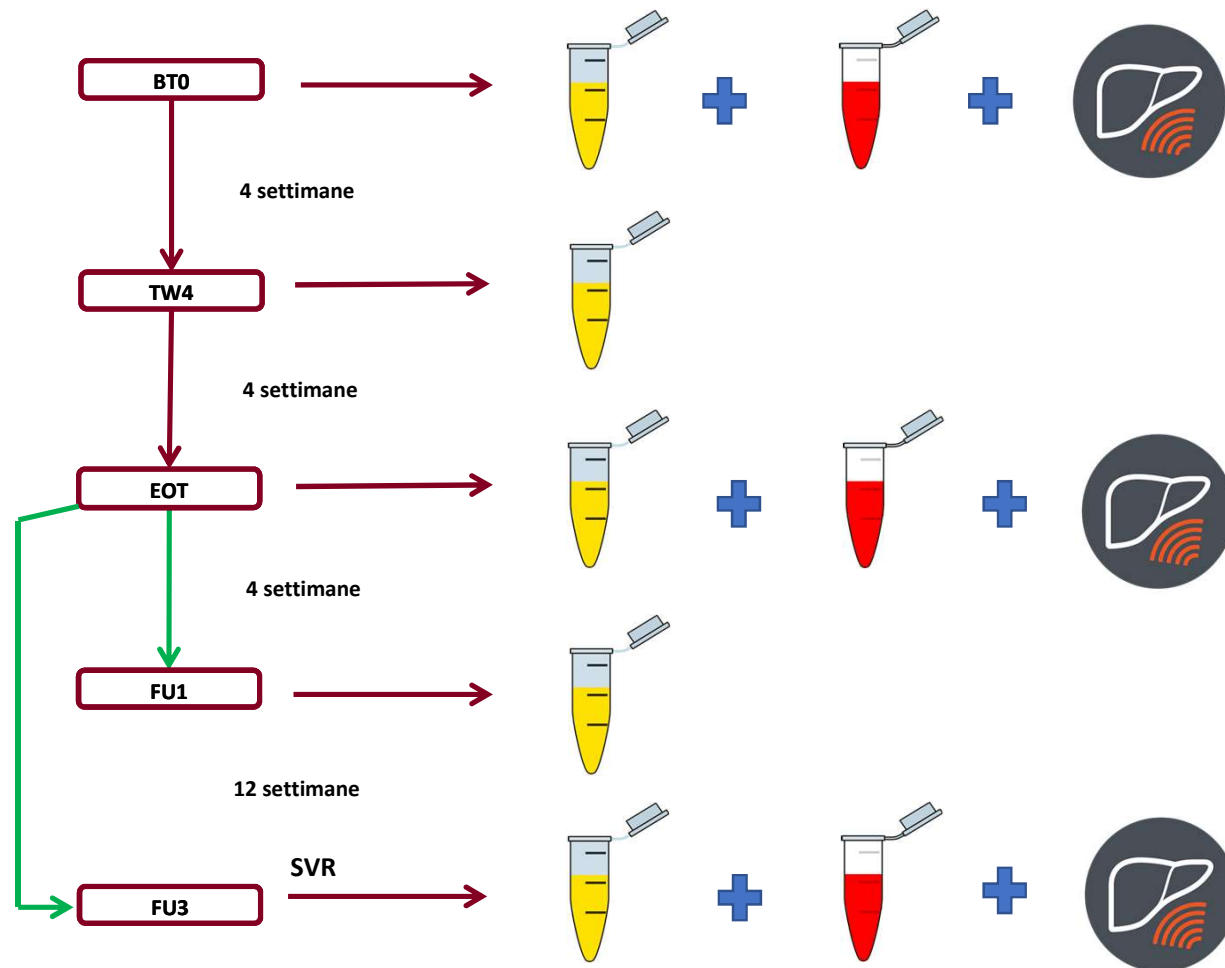




Precision medicine approach using metabolomics as compared to treatment-failure evidence-based medicine approach in clinical practice. 'Personalized profile' based on metabolomics as well as other clinical and lifestyle data will be used to predict the patients' responses to specific treatments and thus help select the best treatment regimens

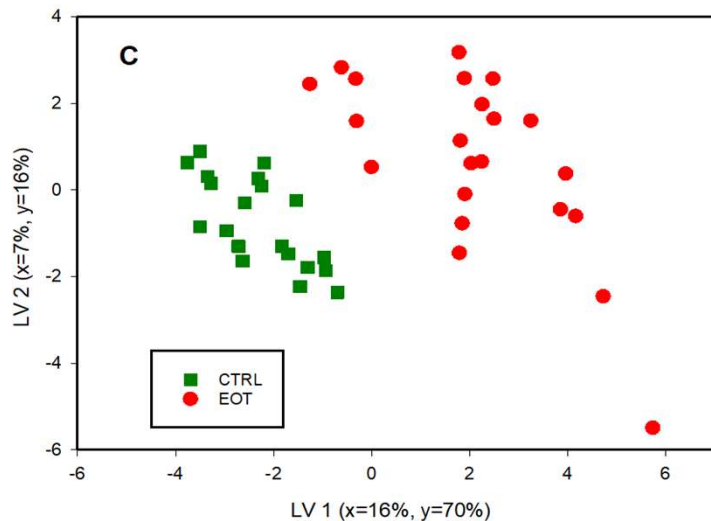
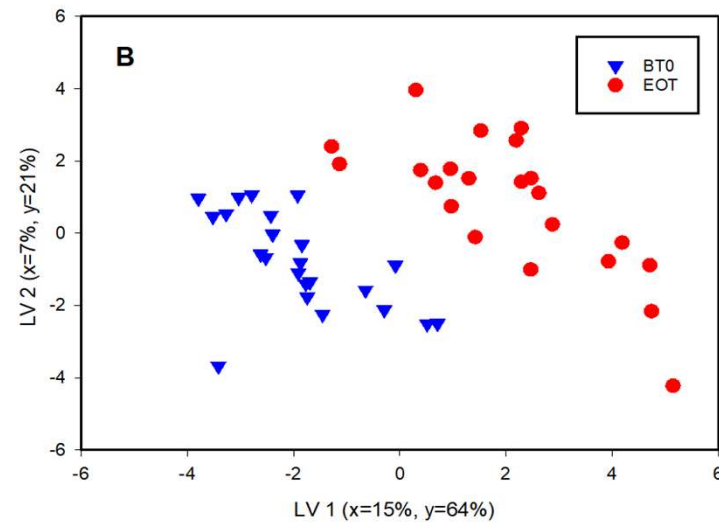
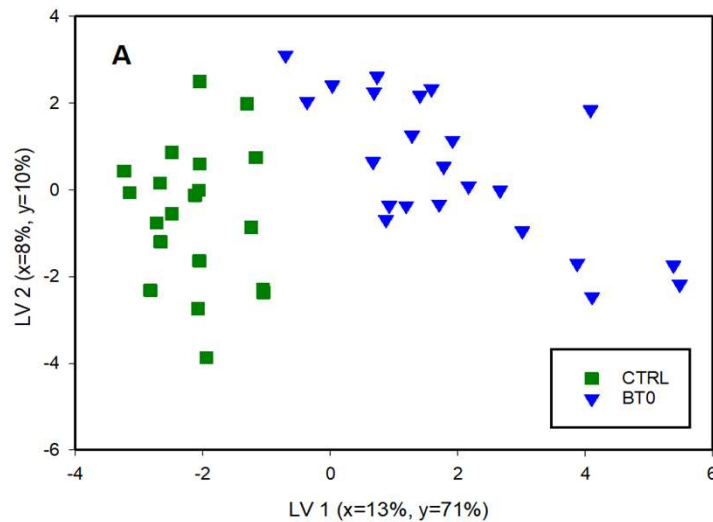
Beger RD et al Metabolomics 2016

- **Caratterizzazione del profilo metabolico urinario di pazienti con fibrosi da virus dell'epatite C (HCV) (23 maschi, genotipo virale tipo 1 a e 1b)**
- **Valutazione delle variazioni indotte dall'eradicazione farmacologica mediante farmaci antivirali diretti (DAAs) a 4, 8 settimane di trattamento e follow up 12 e 24 settimane**



Miccheli A. et al 2019

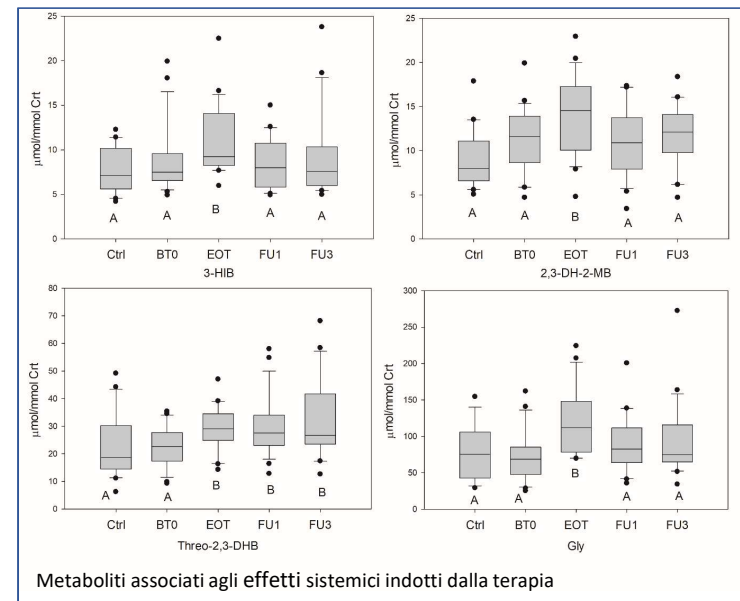
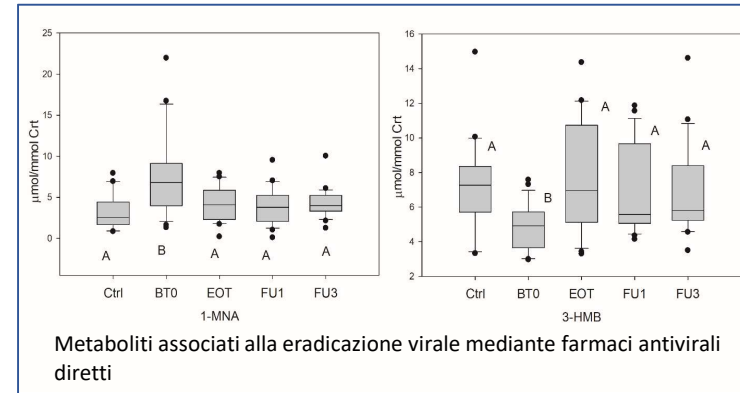
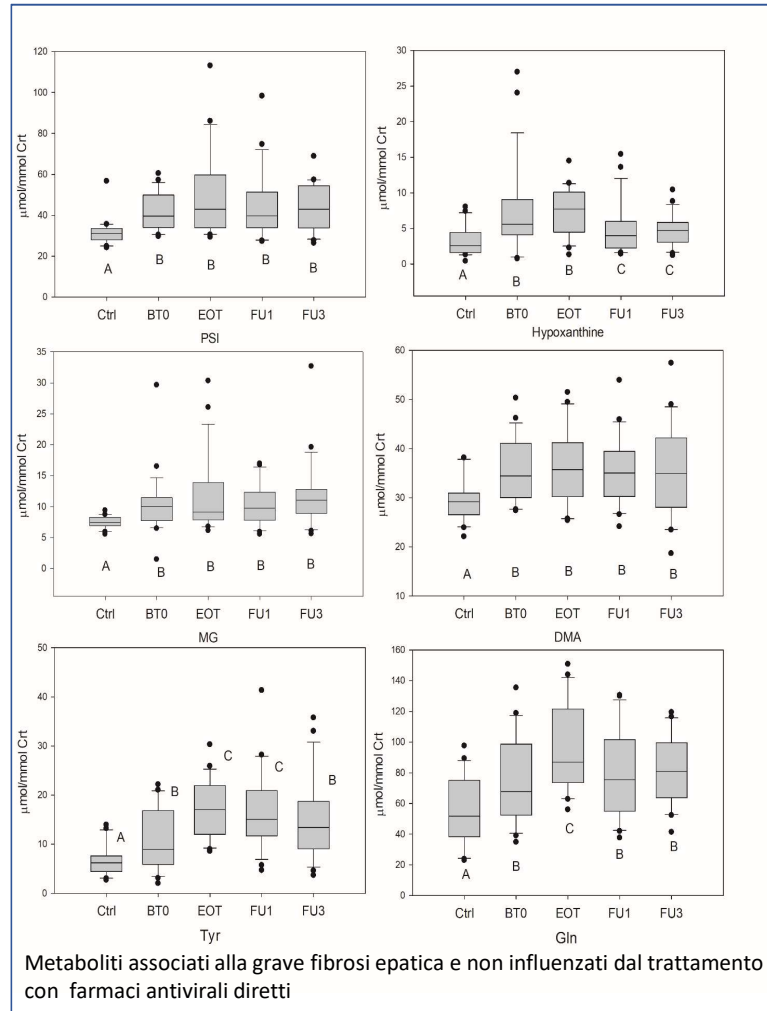
RISULTATI: Analisi Multivariata PLS-DA

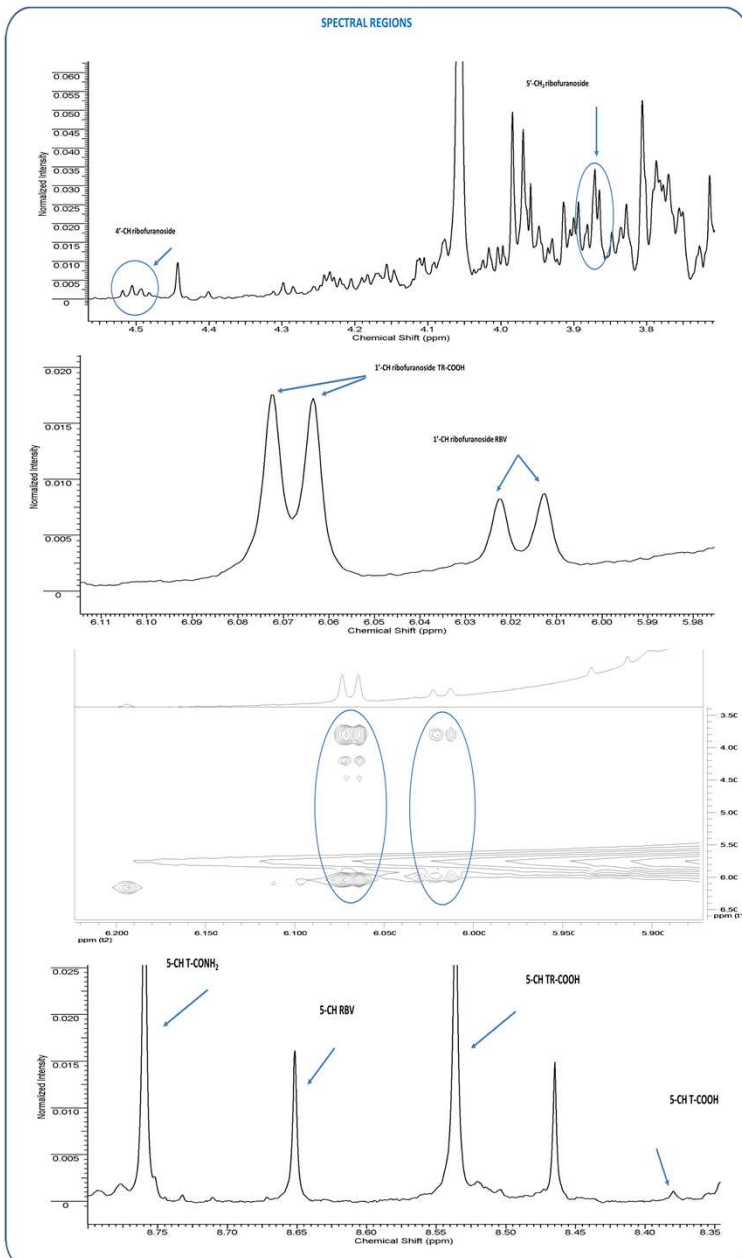


- Profili metabolici urinari dei pazienti con HCV con fibrosi epatica grave rispetto a CTRL (A)
- Variazioni influenzate dal trattamento con DAA sui profili metabolici dei pazienti con HCV (B; C);

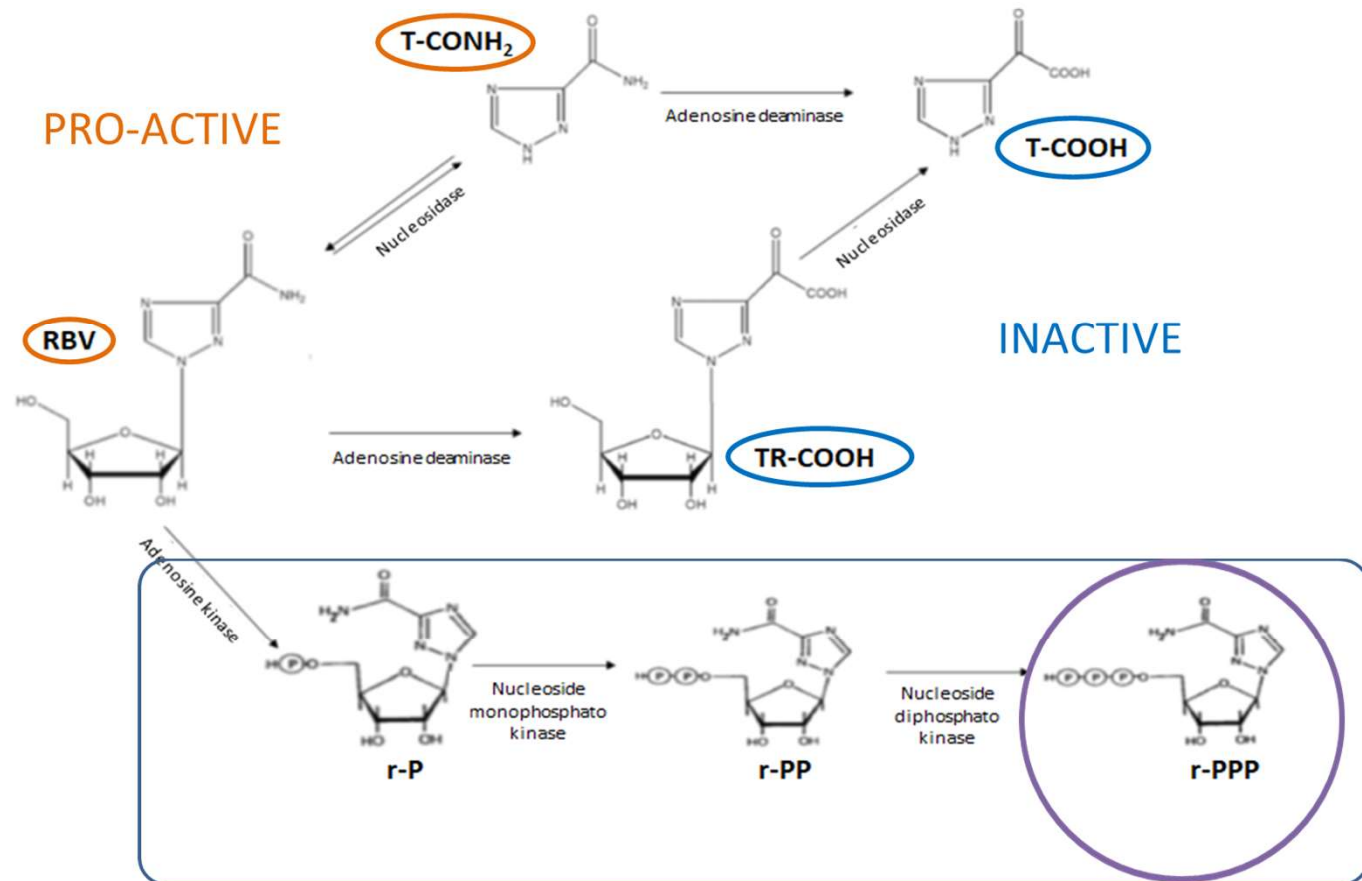
RISULTATI: Analisi Univariata

Natura provvisoria o persistente dei metaboliti discriminanti (analisi univariata delle modifiche che confrontano CTRL, pazienti BT0, EOT, FU1 e FU3)



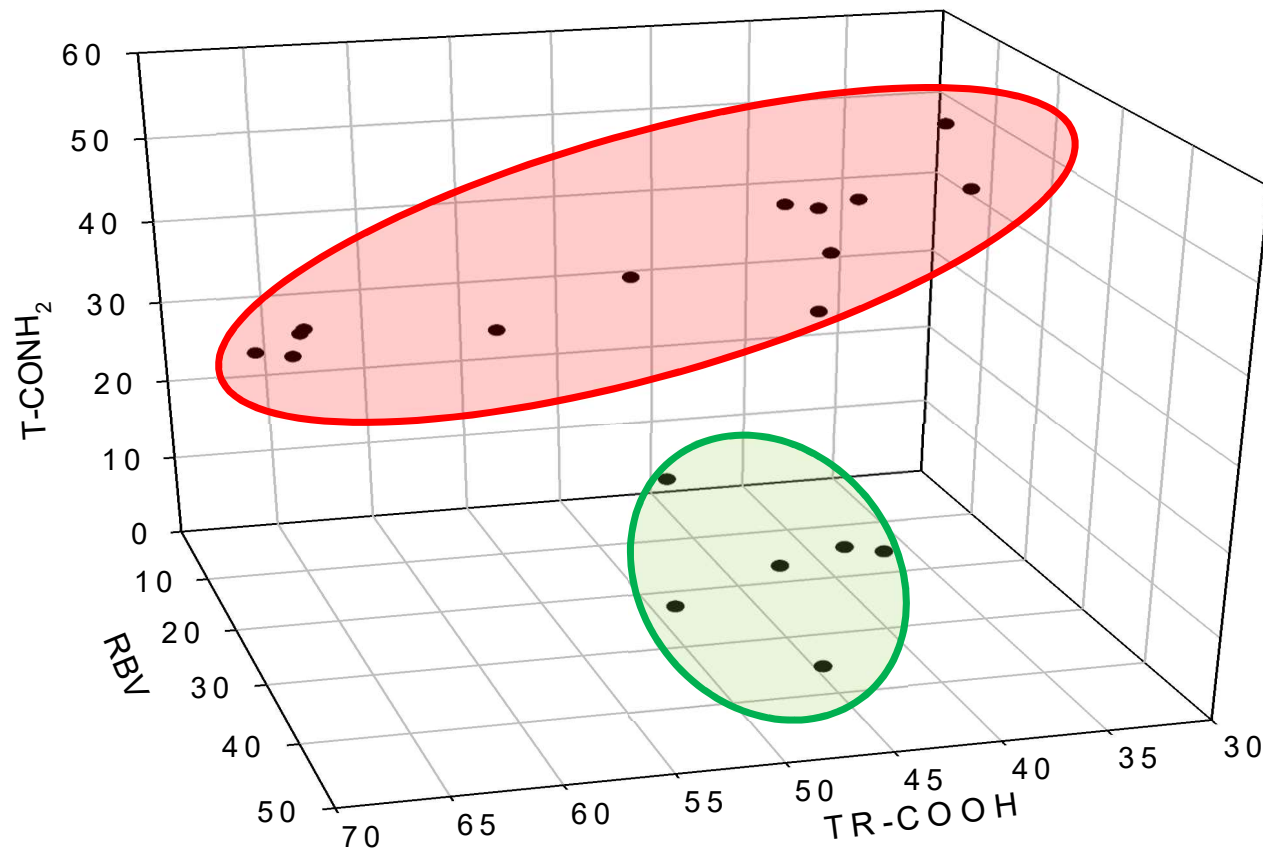


Urinary identification of active and inactive RBV metabolites in HCV patients: towards the personalized therapy



Miccheli A. et al 2019

Individuazione di due cluster di pazienti HCV con fibrosi sulla base della capacità metabolica della RBV



Miccheli A et al 2019

Grazie per l'attenzione



La parola alla dottoressa Giovanna Tranfo

ATMOSFERE IPERBARICHE: Fattori di rischio e Modelli di Prevenzione. 14 ottobre 2019