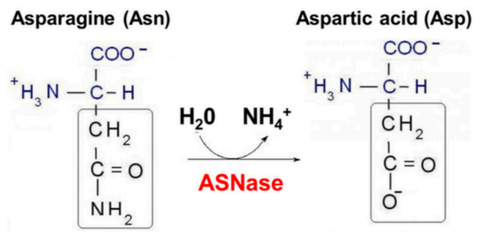
# Using metabolomics and lipidomics to crack the code on asparaginase-associated pancreatitis (AAP)

Chaitanya Srinivasan, Li Wen, Amitava Mukherjee, Sohail Z. Husain
Department of Pediatrics, Children's Hospital of Pittsburgh and the University of Pittsburgh

## BACKGROUND

- **Drug-induced pancreatitis is an important iatrogenic problem.**
- **Asparaginase (ASNase) is a cornerstone therapy for leukemia (ALL), but an unacceptably high number of patients taking the cancer drug develop the complication of pancreatitis.**
- **There is a major unmet need to decipher the mechanisms underlying ASNase-associated pancreatitis (AAP).**
- **A clue to AAP is that ASNase affects amino acid asparagine.**




## AIM

- **Using a comprehensive metabolomic and lipidomic platform and an unbiased, non-targeted approach, we sought to determine whether there are unique metabolomic or lipidomic biomarker signature, that will predict the development of AAP.**

## HYPOTHESIS

- **Patients with AAP will manifest a differential metabolomic signature at baseline, before receiving ASNase. The signals will be detectable in plasma, and the plasma metabolomics data can be used to guide therapy with ASNase in a personalized fashion.**

## METHODS

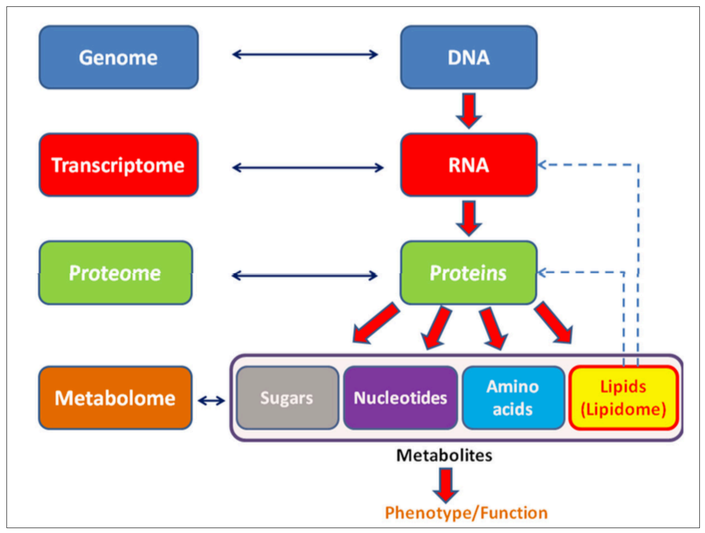



**Figure 1. Schematic of how metabolomic and lipidomic profiles fit into the framework of the metabolome and systems biology.** In this study, we will analyze a large metabolomics dataset in an unbiased fashion for biomarkers that could predict pancreatitis with ASNase exposure.

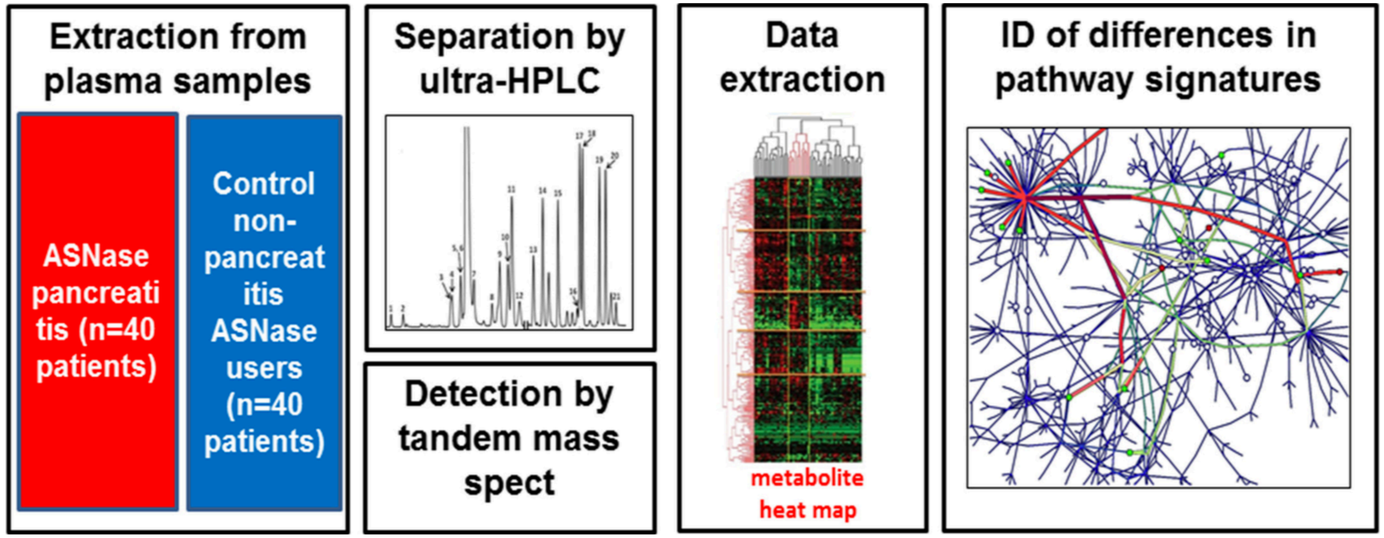



**Figure 2. Schematic of the methods we will use to perform a plasma metabolomic and lipidomic profile of plasma samples, from 40 patients with AAP and 40 ASNase users who did not develop pancreatitis.** The samples have been obtained by our collaborator at the Dana-Farber Cancer Institute. The samples were taken before ASNase exposure, but after the mild stress of an overnight fast.

## EXPECTED FINDINGS

- **We expect to find that patients with AAP will have a differential metabolomic and lipidomic signature.**
- **This study will help crack the code on AAP and help devise rescue therapies.**