



METABOLOMIC MEDICINE®
HEALTH CLINICS FOR AUTOIMMUNE AND CHRONIC DISEASES

www.metabolomicmedicine.com

PRECISION MEDICINE ADVANCES IN CHILDHOOD ATOPIC DISEASES: RESULTS FROM ATOPIC DERMATITIS & ASTHMA

5th World Summit on Pediatrics Berlin 2019

Dr. Dimitris Tsoukalas, MD

Board Certified Family Physician

President European Institute of Nutritional Medicine

Associate Member of the World Academy of Sciences (WAS)

Scientific Director of Metabolomic Medicine Switzerland Medical Group

Licensed to practice in Switzerland, Italy & Greece

What I am going to talk about

- Precision medicine
- Atopic diseases and modifiable risk factors
- Metabolomics: a tool of precision medicine
- Our experience in using metabolomic analysis for prevention and treatment of asthma and atopic dermatitis



Precision Medicine

personalized or individualized medicine

“Precision Medicine, is an innovative approach that takes into account **individual differences** in people’s:

- **Genes**
- **Environments** and
- **Lifestyles**

- US Food and Drug Administration, Medical Devices, Precision Medicine
- US National Research Council. NIH U.S. National Library of Medicine



METABOLOMIC MEDICINE®
HEALTH CLINICS FOR AUTOIMMUNE AND CHRONIC DISEASES

Precision Medicine

Broader application occurred with the recent developments of large-scale biologic databases.

- Proteomics
- Metabolomics
- Genomics
- Diverse cellular assays
- Mobile health technology

A New Initiative on Precision Medicine. F Collins, H Varmus.
New England Journal of Medicine. 2015



METABOLOMIC MEDICINE®
HEALTH CLINICS FOR AUTOIMMUNE AND CHRONIC DISEASES

Precision Medicine



*“The **goal** of precision medicine is to target the right treatments to the right patients at the right time.”*

- US Food and Drug Administration, Medical Devices, Precision Medicine
- NIH All of Us Research Program



METABOLOMIC MEDICINE®
HEALTH CLINICS FOR AUTOIMMUNE AND CHRONIC DISEASES

Atopic diseases in childhood

- Atopic diseases are a group of diseases characterized by the development of an immunoglobulin (IgE) directed against allergens that are usually harmless.
- **Atopic diseases are the most common chronic conditions in childhood.**

1. Moreno MA. Atopic Diseases in Children. JAMA Pediatr. 2016;170(1):96.
2. Epidemiology and natural history of atopic diseases Simon F. Thomsen. Eur Clin Respir J. 2015

Atopic diseases in childhood

Childhood atopic diseases include:

- **Atopic dermatitis (*eczema*)**
- **Asthma**
- Allergic rhinitis
- Food allergy

Atopic dermatitis

- Atopic dermatitis (AD) is a chronic skin disorder with an immunologic basis.
- 10-20% of children in US and Western Europe have atopic dermatitis.



1. Williams H, Robertson C, Stewart A, Ait-Khaled N, Anabwani G, Anderson R, et al. Worldwide variations in the prevalence of symptoms of atopic eczema in the International Study of Asthma and Allergies in Childhood. *The Journal of allergy and clinical immunology*. 1999;103(1 Pt 1):125-38
2. Turner JD, Schwartz RA. Atopic dermatitis. A clinical challenge. *Acta Dermatovenereol Alp Panonica Adriat*. 2006 Jun.
3. Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: *Lancet* (2006)

Asthma

Asthma affects from 1-20% of the child population and includes:

- Airway obstruction that is reversible
- Lungs airway inflammation
- Bronchial hyper-responsiveness

1. Papadopoulos NG, Arakawa H, Carlsen KH, Custovic A, Gern J, Lemanske R, et al. International consensus on (ICON) pediatric asthma. *Allergy* 2012;67:976–97
2. GINA. GLOBAL STRATEGY FOR ASTHMA MANAGEMENT AND PREVENTION (2016 Update). <http://ginasthma.org/wp->

Challenges in asthma

Symptoms and pulmonary function measurements:

1. may not always reflect the underlying airway inflammation,
2. are insensitive to small variations in inflammatory status that might be of clinical significance.

1. Smith AD, Cowan JO, Brassett KP, Herbison GP, Taylor DR. Use of exhaled nitric oxide measurements to guide treatment in chronic asthma. *N Engl J Med* 2005;352:2163–73.

2. Katsardis ChV, Alexandraki S, Paraskakis E. Chapter 2: Spirometry in children from 6–16 years old. In: Katsardis Ch, Koumbourlis A, Anthracopoulos M, Paraskakis E, editors. *Paediatric Pulmonary Function Testing Indications and Interpretations*. New York, U.S.A: Nova Science Publishers; 2015. p. 15–42

Challenges in asthma

Exhaled nitric oxide analysis (eNO) is a non-invasive diagnostic test for monitoring eosinophilic airway inflammation.

Previous studies in children have reported a weak association among NO levels, asthma control and in predicting exacerbations.

1. Smith AD, Cowan JO, Brassett KP, Herbison GP, Taylor DR. Use of exhaled nitric oxide measurements to guide treatment in chronic asthma. N Engl J Med 2005;352:2163–73.
2. Katsardis ChV, Alexandraki S, Paraskakis E. Chapter 2: Spirometry in children from 6–16 years old. In: Katsardis Ch, Koumbourlis A, Anthracopoulos M, Paraskakis E, editors. Paediatric Pulmonary Function Testing Indications and Interpretations. New York, U.S.A: Nova Science Publishers; 2015. p. 15–42

Challenges in asthma

- Spirometry is not always available in medical clinics, is expensive, time-consuming and requires skilled technicians and is not executable for children younger than 5 years old.

1. Smith AD, Cowan JO, Brassett KP, Herbison GP, Taylor DR. Use of exhaled nitric oxide measurements to guide treatment in chronic asthma. *N Engl J Med* 2005;352:2163–73.

2. Katsardis ChV, Alexandraki S, Paraskakis E. Chapter 2: Spirometry in children from 6–16 years old. In: Katsardis Ch, Koumbourlis A, Anthracopoulos M, Paraskakis E, editors. *Paediatric Pulmonary Function Testing Indications and Interpretations*. New York, U.S.A: Nova Science Publishers; 2015. p. 15–42

Challenges in asthma

- Thus, the diagnosis of asthma can be difficult to confirm when no clear objective marker of asthma exists in a clinical setting.

1. Smith AD, Cowan JO, Brassett KP, Herbison GP, Taylor DR. Use of exhaled nitric oxide measurements to guide treatment in chronic asthma. *N Engl J Med* 2005;352:2163–73.

2. Katsardis ChV, Alexandraki S, Paraskakis E. Chapter 2: Spirometry in children from 6–16 years old. In: Katsardis Ch, Koumbourlis A, Anthracopoulos M, Paraskakis E, editors. *Paediatric Pulmonary Function Testing Indications and Interpretations*. New York, U.S.A: Nova Science Publishers; 2015. p. 15–42

Challenges in asthma

- From a clinical point of view, research focusing on asthma biomarkers would assist in the diagnosis, management and treatment of this disorder.

1. Smith AD, Cowan JO, Brassett KP, Herbison GP, Taylor DR. Use of exhaled nitric oxide measurements to guide treatment in chronic asthma. N Engl J Med 2005;352:2163–73.

2. Katsardis ChV, Alexandraki S, Paraskakis E. Chapter 2: Spirometry in children from 6–16 years old. In: Katsardis Ch, Koumbourlis A, Anthracopoulos M, Paraskakis E, editors. Paediatric Pulmonary Function Testing Indications and Interpretations. New York, U.S.A: Nova Science Publishers; 2015. p. 15–42

Metabolomics

Metabolomics is the most reliable method to analyze the ultimate effect of epigenetic factors to the onset and development of disease.

1. German JB, Hammock BD, Watkins SM (2005) *Metabolomics*
2. *Fathoming Metabolism Harvard Mag.* 2011
3. Clish C. 2015 Metabolomics: an emerging but powerful tool for precision medicine. *Molecular Case Studies*



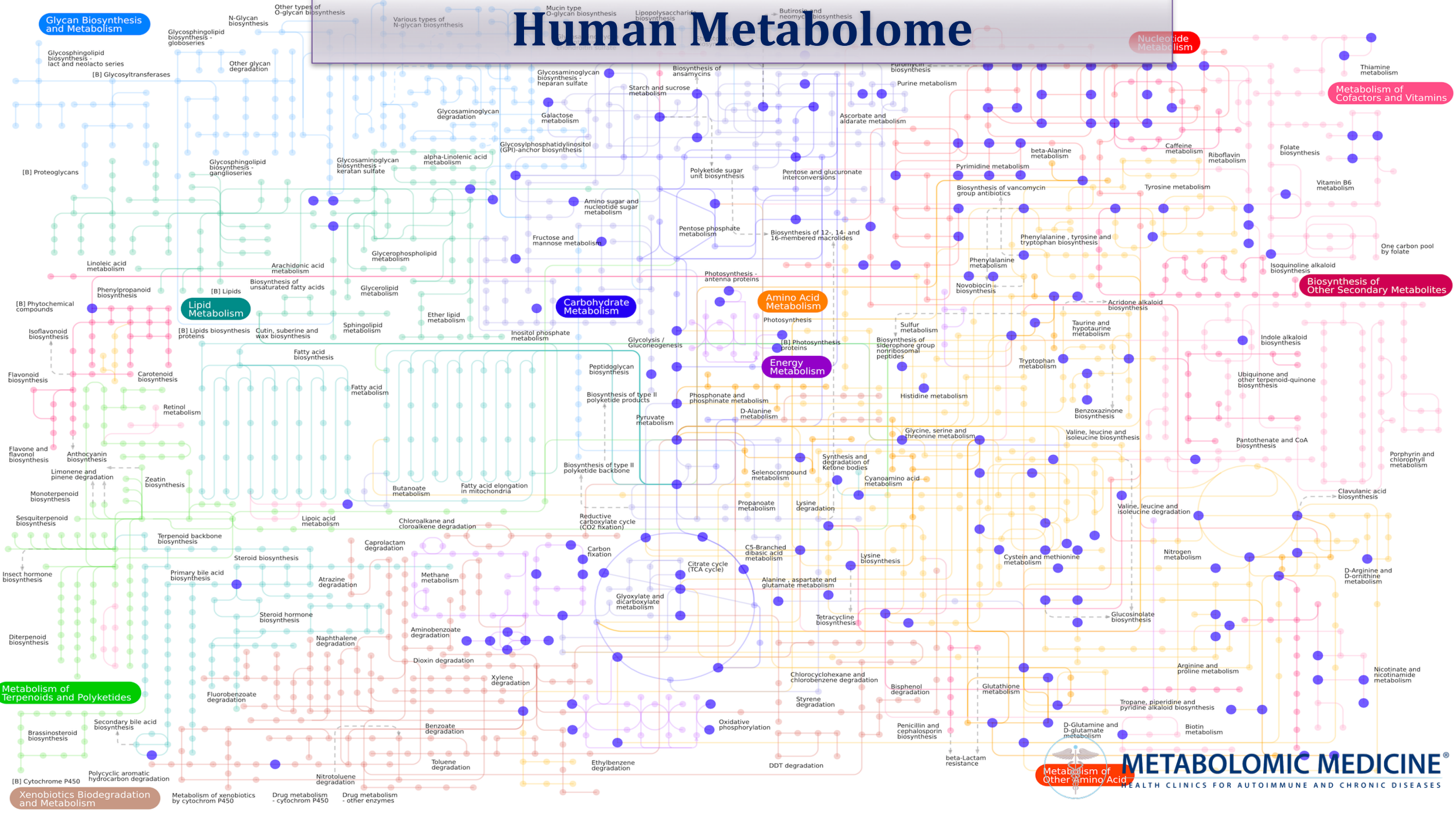
METABOLOMIC MEDICINE®
HEALTH CLINICS FOR AUTOIMMUNE AND CHRONIC DISEASES

Risk factors in atopic diseases

- Epigenetic risk factors related to nutrition, environmental exposure, lifestyle and lack of protective factors are considered to explain the observed increase of atopy in childhood.

Human Metabolome

Glycan Biosynthesis and Metabolism



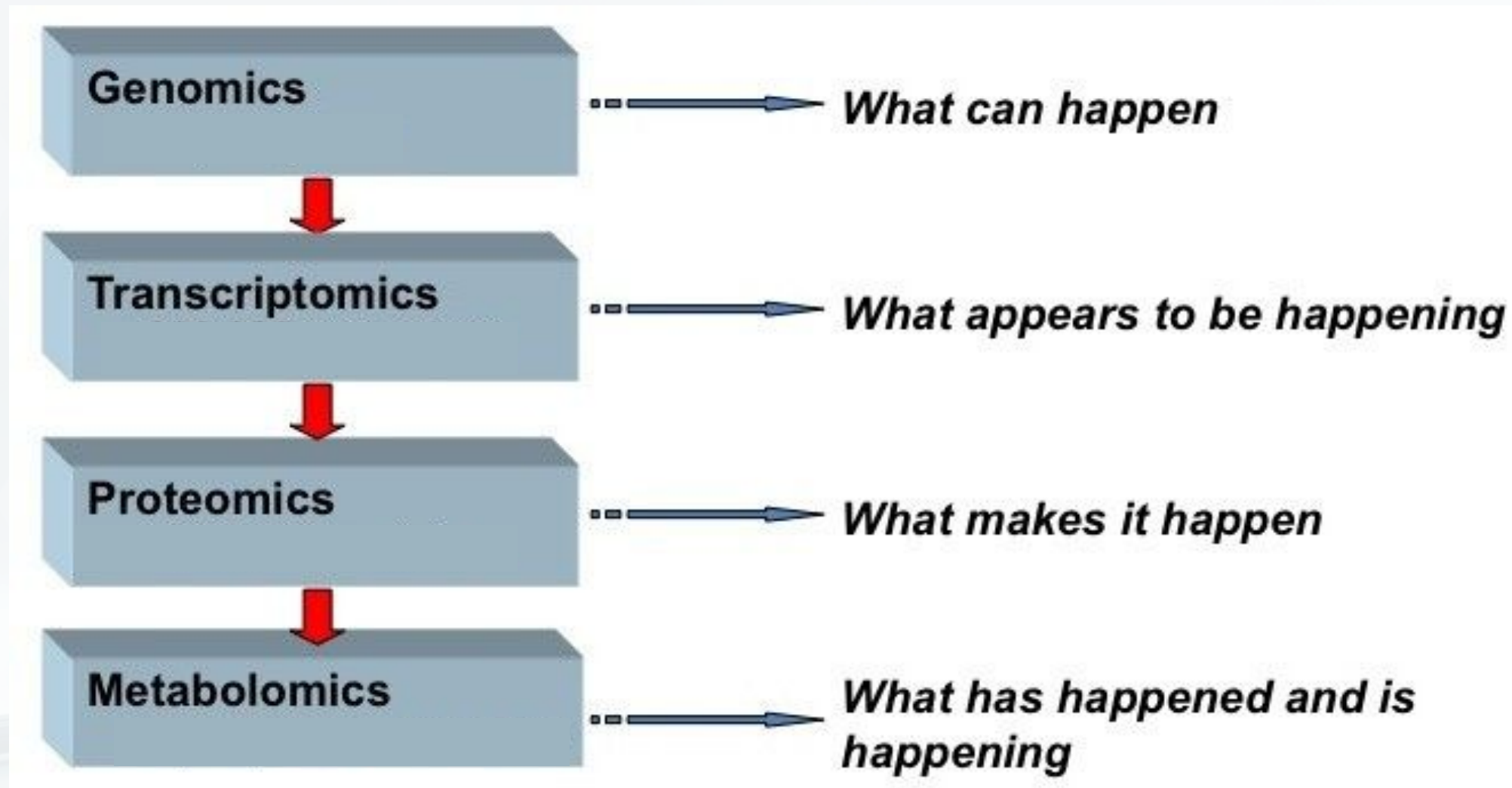
Metabolomics

With metabolomics, we look into the phenotype as this is expressed at a molecular level.

German JB, Hammock BD, Watkins SM (2005) *Metabolomics*



METABOLOMIC MEDICINE®
HEALTH CLINICS FOR AUTOIMMUNE AND CHRONIC DISEASES



Application of Metabolomics in pediatric asthma (I)



Nutrition Research
Volume 61, January 2019, Pages 31-40



Urinary organic acids as biomarkers in the assessment of pulmonary function in children with asthma

Maria Michelle Papamichael ^a ✉, Charis Katsardis ^c ✉, Bircan Erbas ^b ✉, Catherine Itsiopoulos ^a  ✉, Dimitris Tsoukalas ^d ✉



METABOLOMIC MEDICINE®
HEALTH CLINICS FOR AUTOIMMUNE AND CHRONIC DISEASES

Application of Metabolomics in pediatric asthma (I)

The aim

The purpose of this study was to investigate correlations between urinary organic acids, pulmonary diagnostic tests and asthma control in Greek asthmatic children.

[Urinary organic acids as biomarkers in the assessment of pulmonary function in children with asthma](#) Maria Michelle Papamichael, Chris Katsardis, Bircan Erbas, Catherine Itsiopoulos, Dimitris Tsoukalas. Nutrition Research, Elsevier. October 2018.



Application of Metabolomics in pediatric asthma (I)

We hypothesized that urinary organic acids are positively associated with poor pulmonary function in children with asthma.

Urinary organic acids as biomarkers in the assessment of pulmonary function in children with asthma Maria Michelle Papamichael, Chris Katsardis, Bircan Erbas, Catherine Itsiopoulos, Dimitris Tsoukalas. Nutrition Research, Elsevier. October 2018.



METABOLOMIC MEDICINE®
HEALTH CLINICS FOR AUTOIMMUNE AND CHRONIC DISEASES

Application of Metabolomics in pediatric asthma (I)

Methods

72 children 5–12 years old [54% M/ 46% F) with “mild” asthma, according to Global Initiative for Asthma (GINA) criteria.

Readouts:

- 34 targeted urinary Organic Acids using GC-MS
- Pulmonary function test
- Asthma control questionnaire.

[Urinary organic acids as biomarkers in the assessment of pulmonary function in children with asthma](#) Maria Michelle Papamichael, Chris Katsardis, Bircan Erbas, Catherine Itsiopoulos, Dimitris Tsoukalas. Nutrition Research, Elsevier. October 2018.



METABOLOMIC MEDICINE®
HEALTH CLINICS FOR AUTOIMMUNE AND CHRONIC DISEASES

Application of Metabolomics in pediatric asthma (I)

Key findings

Negative associations metabolites and spirometry parameters FVC, FEV1, eNO and PEF (p<0.05):

- lactic acid – FVC, FEV1
- 4-hydroxyphenylacetic acid – FVC, FEV1
- 5- hydroxyindoleacetic acid – eNO
- glycolic acid - PEF

FEV1- Forced Expiratory Volume in 1 second; **FVC**- Forced Vital Capacity; **FEV1/FVC**- ratio of Forced Expiratory Volume in 1 second and Forced Vital Capacity, **PEF**- Peak Expiratory Flow, **FEF 25–75%** -Forced Expiratory Flow at 25–75% of the pulmonary volume, **eNO**- exhaled Nitric Oxide Analysis.

M.M. Papamichael et al 2018 Nutr Res



METABOLOMIC MEDICINE®
HEALTH CLINICS FOR AUTOIMMUNE AND CHRONIC DISEASES

Application of Metabolomics in pediatric asthma (I)

Key findings

Positive associations between ($p < 0.05$):

- Malic acid – asthma control scores
- 5-hydroxyindoleacetic acid - FEV1/FVC

FEV1- Forced Expiratory Volume in 1 second; **FVC**- Forced Vital Capacity; **FEV1/FVC**- ratio of Forced Expiratory Volume in 1 second and Forced Vital Capacity, **PEF**- Peak Expiratory Flow, **FEF 25–75%** -Forced Expiratory Flow at 25–75% of the pulmonary volume, **eNO**- exhaled Nitric Oxide Analysis.

Application of Metabolomics in pediatric asthma (I)

Key findings

Negative associations between ($p < 0.05$):

lactic acid – FVC, FEV1

FEV1 - Forced Expiratory Volume in 1 second;
FVC - Forced Vital Capacity

Lactic acid, is produced during cellular respiration under conditions of hypoxia or thiamine (Vitamin B1) deficiency, thus this association would indicate the inflammatory state of asthma.

M.M. Papamichael et al 2018 Nutr Res

1. Gunnerson K. Lactic Acidosis. USA: Medscape; 2017 <https://emedicine.medscape.com/article/167027-overview>.
2. Moskowitz et al 2014 J. Cr Care The relationship between lactate and thiamine levels in patients with diabetic ketoacidosis★



METABOLOMIC MEDICINE®
HEALTH CLINICS FOR AUTOIMMUNE AND CHRONIC DISEASES

Application of Metabolomics in pediatric asthma (I)

Key findings

Negative associations between ($p < 0.05$):

4-hydroxyphenylacetic acid – FVC, FEV1

FEV1- Forced Expiratory Volume in 1 second; *FVC*- Forced Vital Capacity;

4-hydroxyphenylacetate is a marker of bacterial overgrowth. Dysbiosis has been linked to airway inflammation.

M.M. Papamichael et al 2018 Nutr Res

1. Liu Z, Xi R, Zhang Z, Li W, Liu Y, Jin F, et al. 4- hydroxyphenylacetic acid attenuated inflammation and edema via suppressing HIF-1 alpha in seawater aspiration- induced lung injury in rats. Int J Mol Sci 2014;15:12861–84.
2. Chalmers RA, Valman HB, Liberman MM. Measurement of 4- hydroxyphenylacetic aciduria as a screening test for small- bowel



METABOLOMIC MEDICINE®
HEALTH CLINICS FOR AUTOIMMUNE AND CHRONIC DISEASES

Application of Metabolomics in pediatric asthma (I)

Key findings

Negative associations between ($p < 0.05$)

5- hydroxyindoleacetic acid – eNO

eNO- exhaled Nitric Oxide Analysis,

Positive associations between ($p < 0.05$)

5-hydroxyindoleacetic acid-FEV1/FVC

FEV1/FVC- ratio of Forced Expiratory Volume in 1 second and Forced Vital Capacity

Hydroxyindoleacetate is the main product of serotonin (5-HT) metabolism. Serotonin is important player of immune response signaling.

M.M. Papamichael et al 2018 Nutr Res

1. Arreola R, Becerril-Villanueva E, et al. J Immunol Res 2015;2015:354957.2. Nau Jr F, Miller J, Saravia J, Ahlert T, Yu B, Happel KI, et al. Am J Physiol Lung Cell Mol Physiol 2015;308:L191–8. 6. 3. Szelenyi J, Vizi ES. Ann N Y Acad Sci 2007;1113:311–24.



METABOLOMIC MEDICINE®
HEALTH CLINICS FOR AUTOIMMUNE AND CHRONIC DISEASES

Application of Metabolomics in pediatric asthma (I)

Key findings

Negative associations between ($p < 0.05$):

5- hydroxyindoleacetic acid – eNO

eNO- exhaled Nitric Oxide Analysis,

Positive associations between ($p < 0.05$)

5-hydroxyindoleacetic acid-FEV1/FVC

FEV1/FVC- ratio of Forced Expiratory Volume in 1 second and Forced Vital Capacity

The anti-inflammatory properties of serotonin might explain the associations observed between hydroxyindoleacetate and normal spirometry measurements for FEV1/FVC and absence of bronchial inflammation as indicated by eNO.

M.M. Papamichael et al 2018 Nutr Res

1. Arreola R, Becerril-Villanueva E, et al. J Immunol Res 2015;2015:354957.2. Nau Jr F, Miller J, Saravia J, Ahlert T, Yu B, Happel KI, et al. Am J Physiol Lung Cell Mol Physiol 2015;308:L191–8. 6. 3. Szelenyi J, Vizi ES. Ann N Y Acad Sci 2007;1113:311–24.



METABOLOMIC MEDICINE®
HEALTH CLINICS FOR AUTOIMMUNE AND CHRONIC DISEASES

Application of Metabolomics in pediatric asthma (I)

Key findings

Negative associations between ($p < 0.05$):

glycolic acid - PEF *PEF- Peak Expiratory Flow*

Glycolic acid is involved in the metabolism of catecholamines that are released under conditions of stress and are involved in the regulation of the immune system.

Children in the study did not have asthma attacks which explains the inverse PEF correlation.

Application of Metabolomics in pediatric asthma (I)

Key findings

Positive associations between ($p < 0.05$):

Malic acid – asthma control scores

The presence of urinary malic acid in our study might be a marker for chronic inflammation and oxidative stress in airways that contribute to asthma exacerbations and consequently poor asthma control.

M.M. Papamichael et al 2018 Nutr Res

1. Rosanna DP, Salvatore C. Reactive oxygen species, inflammation, and lung diseases. Curr Pharm Des 2012;18: 3889–900.



METABOLOMIC MEDICINE®
HEALTH CLINICS FOR AUTOIMMUNE AND CHRONIC DISEASES

Application of Metabolomics in pediatric asthma (I)

Conclusions

Metabolomics could be a promising approach for asthma research for the detection of novel biomarkers in asthma monitoring and therapeutic targets for childhood asthma.

M.M. Papamichael et al 2018 Nutr Res

1. Rosanna DP, Salvatore C. Reactive oxygen species, inflammation, and lung diseases. Curr Pharm Des 2012;18: 3889–900.



METABOLOMIC MEDICINE®
HEALTH CLINICS FOR AUTOIMMUNE AND CHRONIC DISEASES

Application of Metabolomics in pediatric asthma (II)



Allergy and Atopy

Efficacy of a Mediterranean diet supplemented with fatty fish in ameliorating inflammation in paediatric asthma: a randomised controlled trial

M. M. Papamichael✉, Ch. Katsardis, K. Lambert, D. Tsoukalas, M. Koutsilieris, B. Erbas, C. Itsiopoulos

First published: 30 October 2018 | <https://doi.org/10.1111/jhn.12609> |



METABOLOMIC MEDICINE®
HEALTH CLINICS FOR AUTOIMMUNE AND CHRONIC DISEASES

Application of Metabolomics in pediatric asthma (II)

The aim

To investigate the efficacy of a Mediterranean diet supplemented with high omega-3 'fatty' fish intake in Greek asthmatic children.

We hypothesized that a dietary modification could reduce asthma burden and improve the quality of life in children suffering with asthma.

Methods

6-month parallel randomised controlled trial (RCT) using CONSORT recommendations.

Interventional group: Intake of two fatty fish meals per week (at least 150 g of cooked fish) as part of the Greek Mediterranean diet for 6 months.

Control group: Consumption of their usual diet.

Adherence to the Mediterranean dietary pattern was measured using the KIDMED Index

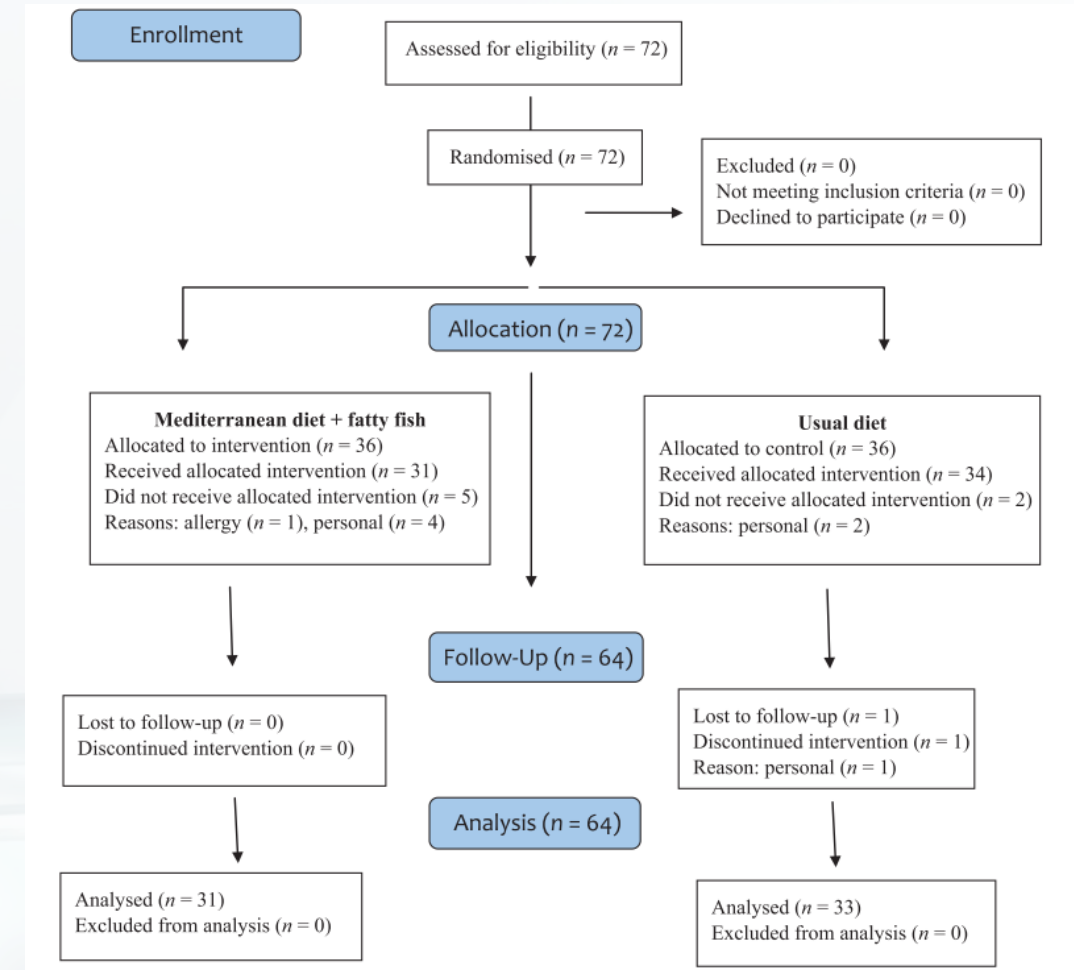


Figure 1 Consort flow diagram of study design

Readouts:

- Pulmonary function test
- Fatty acids using GC-MS
- Asthma control

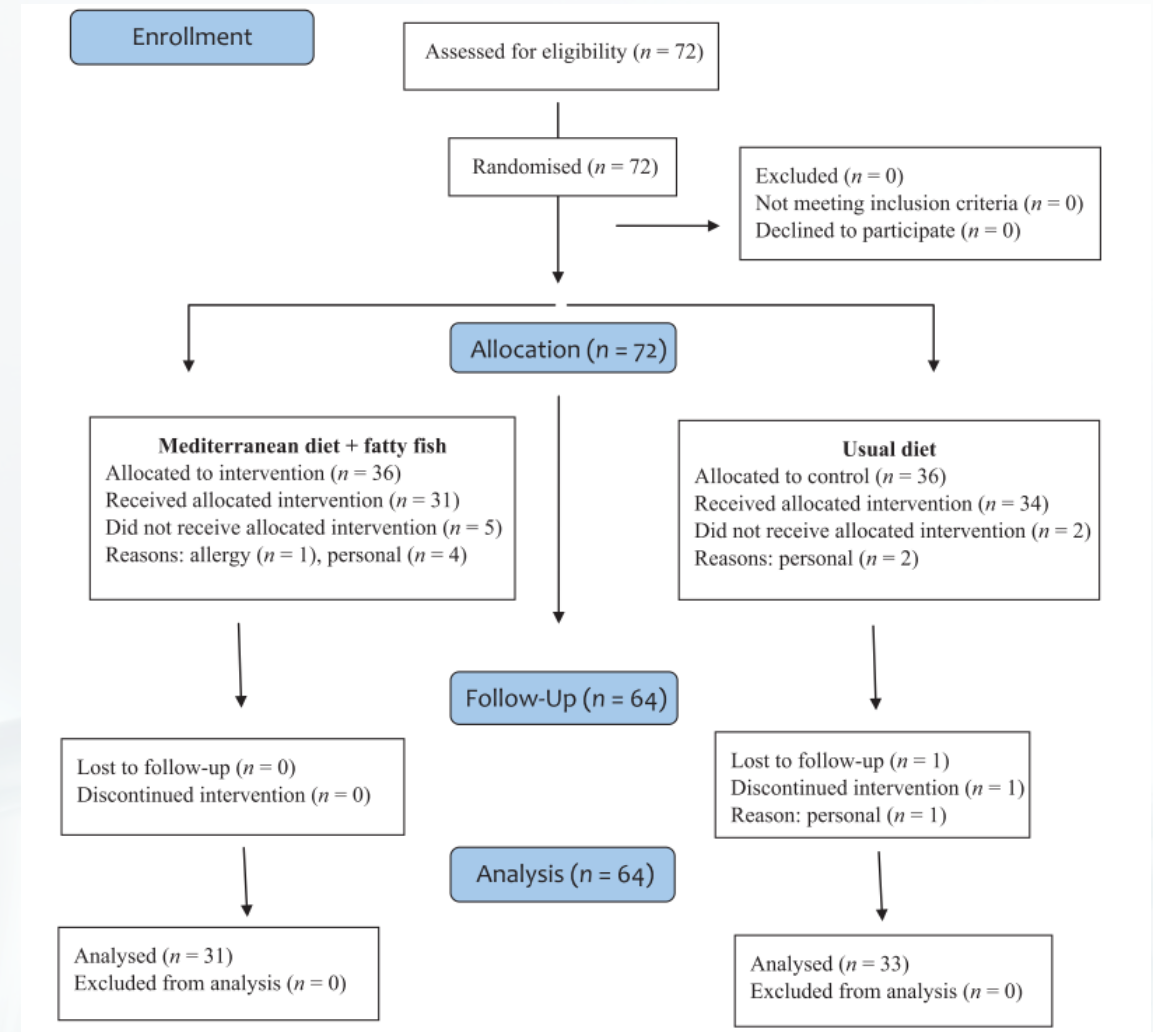


Figure 1 Consort flow diagram of study design

DHA and total omega-3 significantly increased

Table 4 Plasma fatty acid composition of children at baseline and 6 months per group

Plasma fatty acids composition										
Plasma fatty acid (μmol L ^{−1})	Baseline group					Six-month Group				
	Intervention		Control			Intervention		Control		
	Mean	(SD)	Mean	(SD)	<i>P</i> [†]	Mean	(SD)	Mean	(SD)	<i>P</i> [†]
Omega-3 fatty acids										
alpha-Linolenic acid	10.81	(5.0)	12.33	(4.94)	0.38	14.72	(5.23)	14.40	(4.20)	0.91
EPA	30.22	(13.53)	33.01	(21.57)	0.54	29.99	(15.78)	25.08	(8.10)	0.33
DHA	54.54	(30.94)	50.07	(33.67)	0.33	119.88	(41.43)	71.80	(26.36)	0.00
Omega-6 fatty acids										
gamma- Linolenic acid	10.15	(6.92)	11.67	(6.35)	0.25	25.80	(16.01)	28.37	(19.86)	0.79
Linoleic acid	1124.29	(443.25)	1147.32	(428.68)	0.87	1724.34	(546.64)	1602.04	(433.88)	0.34
Arachidonic acid	446.55	(643.37)	362.12	(85.64)	0.24	381.54	(84.42)	411.59	(122.76)	0.33
Total plasma fatty acids	4939.01	(1084.76)	5118.12	(1175.32)	0.64	5973.66	(1391.99)	5678.64	(1229.67)	0.62
Total plasma Ω3 fatty acids	99.17	(46.61)	99.45	(57.31)	0.35	168.20	(56.40)	115.82	(34.61)	0.00
Total plasma Ω6 fatty acids	1557.90	(443.45)	1618.86	(479.28)	0.79	2254.36	(607.29)	2167.93	(547.56)	0.62
Ratio Ω6 : Ω3	24.24	(26.48)	23.21	(25.81)	0.13	14.48	(4.92)	19.44	(4.64)	0.00

Bold characters represent statistical significant P -values.

$^\dagger P$ -values estimated using Mann–Whitney test.

PUFA, polyunsaturated fatty acids; $\Omega 3$, omega-3 fatty acids; $\Omega 6$, omega-6 fatty acids.

Papamichael M.M., Katsardis Ch., Lambert K., Tsoukalas D., Koutsilieris M., Erbas B., Itsiopoulos C. (2018) Efficacy of a Mediterranean diet supplemented with fatty fish in ameliorating inflammation in paediatric asthma: a randomised controlled trial. J Hum Nutr Diet. <https://doi.org/10.1111/jhn.12609>



After adjusting for age, sex, BMI and regular physical activity, FeNO was significantly improved after 6m of fatty fish intake

Table 5 Univariate and multivariate analysis showing mean change in asthma control, quality of life and pulmonary function parameter estimates from baseline to follow-up in the intervention and control groups

Mean change	Group		Difference		<i>p</i> *	<i>p</i> †
	Intervention	Control	Mean	95% CI		
ACQ score	−0.13	−0.16	0.03	−0.19; 0.24	0.80	0.66
PAQLQ score	0.05	0.19	−0.14	−0.34; 0.05	0.15	0.23
FVC (% predicted)	2.45	−0.12	2.57	−1.81; 6.96	0.24	0.33
FEV ₁ (% predicted)	2.84	0.61	2.23	−1.87; 6.34	0.28	0.38
FEV ₁ /FVC (%predicted)	0.58	0.79	−0.21	−2.54; 2.12	0.86	0.86
PEF % (%predicted)	6.06	7.06	−0.99	−11.18; 9.18	0.85	0.71
FEF _{25–75} (% predicted)	2.35	−1.24	3.60	−3.09; 10.28	0.29	0.44
FeNO (ppb)	−3.84	8.09	−11.93	−24.32; 0.46	0.06	0.04

Bold characters represent statistical significant *P*-values.

**P*-value calculated using *t*-test.

†*P*-value from multiple linear regression analysis adjusted for confounders age, sex, body mass index and regular physical activity.

ACQ, asthma control questionnaire; CI, confidence interval; FEF_{25–75%}, mid expiratory flow 25–75% vital capacity; FeNO, fractional exhaled nitric oxide analysis; FEV₁, forced expiratory volume in 1 s; FEV₁/FVC, ratio of forced expiratory volume and forced vital capacity; FVC, forced vital capacity; PAQLQ, paediatric asthma quality of life questionnaire; PEF, peak expiratory flow.

Conclusion

150 g of fatty fish intake, twice weekly in the context of a Mediterranean diet, resulted in a decrease in bronchial inflammation (FeNO) by 14 units in the intervention group.

Table 6 Multiple linear regression analysis showing mean change in bronchial inflammation (FeNO) for intervention and control groups from baseline to follow-up

Mean score change	Variable	Difference		<i>P</i> *
		β	95% CI	
FeNO (ppb)	Group	−14.15	−27.39; −0.91	0.04
	Age	−1.69	−4.97; 1.59	0.31
	Sex	6.89	−6.23; 20.10	0.30
	Regular physical activity	1.69	−11.51; 14.89	0.80
	BMI	0.22	−1.64; 2.09	0.81

Bold characters represent statistical significant *P*-values.
 β , unstandardised beta; BMI, body mass index; CI, confidence interval; FeNO, fractional exhaled nitric oxide analysis.
**P*-value evaluated applying multiple linear regression model adjusted for confounders age, sex, BMI and regular physical activity.



Application of Metabolomics in Atopic Dermatitis.

The aim

To analyze metabolites that participate in central biological pathways of the cell organic acids and fatty acids that provide information on :

- 1. Nutrient deficiency**
- 2. Oxidation status**
- 3. Response to xenobiotics or Pharmaceutical treatment.**

Application of Metabolomics in Atopic Dermatitis.

Methods

Targeted Metabolomics was performed in over 100 Korean children with atopic dermatitis that did not respond to standard treatment.

Readouts: Organic acids and fatty acids using GC-MS, medical and nutritional history, clinical symptoms.

1. Application of metabolomics: Focus on the quantification of organic acids in healthy adults. Int. J. Mol. Med. Tsoukalas, D. et al. (2017), 2. Application of metabolomics part II: Focus on fatty acids and their metabolites in healthy adults. Int. J. Mol. Med. Tsoukalas, D. et al. (2019), 3. The emerging field of lipidomics. Wenk, M. R. Nature Reviews Drug Discov. (2005)



Application of Metabolomics in Atopic Dermatitis.

Key findings

1. Significant disruption in Citric Acid Cycle compatible with mitochondrial dysfunction due to xenobiotics toxicity, lack of the amino-acid glutamine and ubiquinol.
2. Cytochrome C dysfunction.
3. Imbalances in fatty acids markers omega 6 / omega 3 ratio, arachidonic / EPA ratio, Homo-g-linolenic acid levels.

Application of Metabolomics in Atopic Dermatitis.

Intervention:

Children were given personalized treatment that addressed nutrient deficiencies and nutritional regimens based on the metabolomic profile.

1. A review of the alleged health hazards of monosodium glutamate, Comprehensive Reviews in Food Science and Food Safety, 2019 Accepted subject to minor revisions
2. Food and food additives in severe atopic dermatitis, Allergy, 1989, 44, 588-594



Application of Metabolomics in Atopic Dermatitis.

Outcome:

1. Metabolic imbalances of the Krebs cycle were restored
2. The ratio of omega 6/omega 3 was improved
3. Significant improvement of skin lesions within a few weeks of treatment in 85% of the cases.



1. A review of the alleged health hazards of monosodium glutamate, Comprehensive Reviews in Food Science and Food Safety, 2019 Accepted subject to minor revisions 2. Food and food additives in severe atopic dermatitis, Allergy, 1989, 44, 588-594



METABOLOMIC MEDICINE®
HEALTH CLINICS FOR AUTOIMMUNE AND CHRONIC DISEASES

Before treatment

Child 1



After treatment

Child 1



Dr. Dimitris Tsoukalas, MD



METABOLOMIC MEDICINE®
HEALTH CLINICS FOR AUTOIMMUNE AND CHRONIC DISEASES

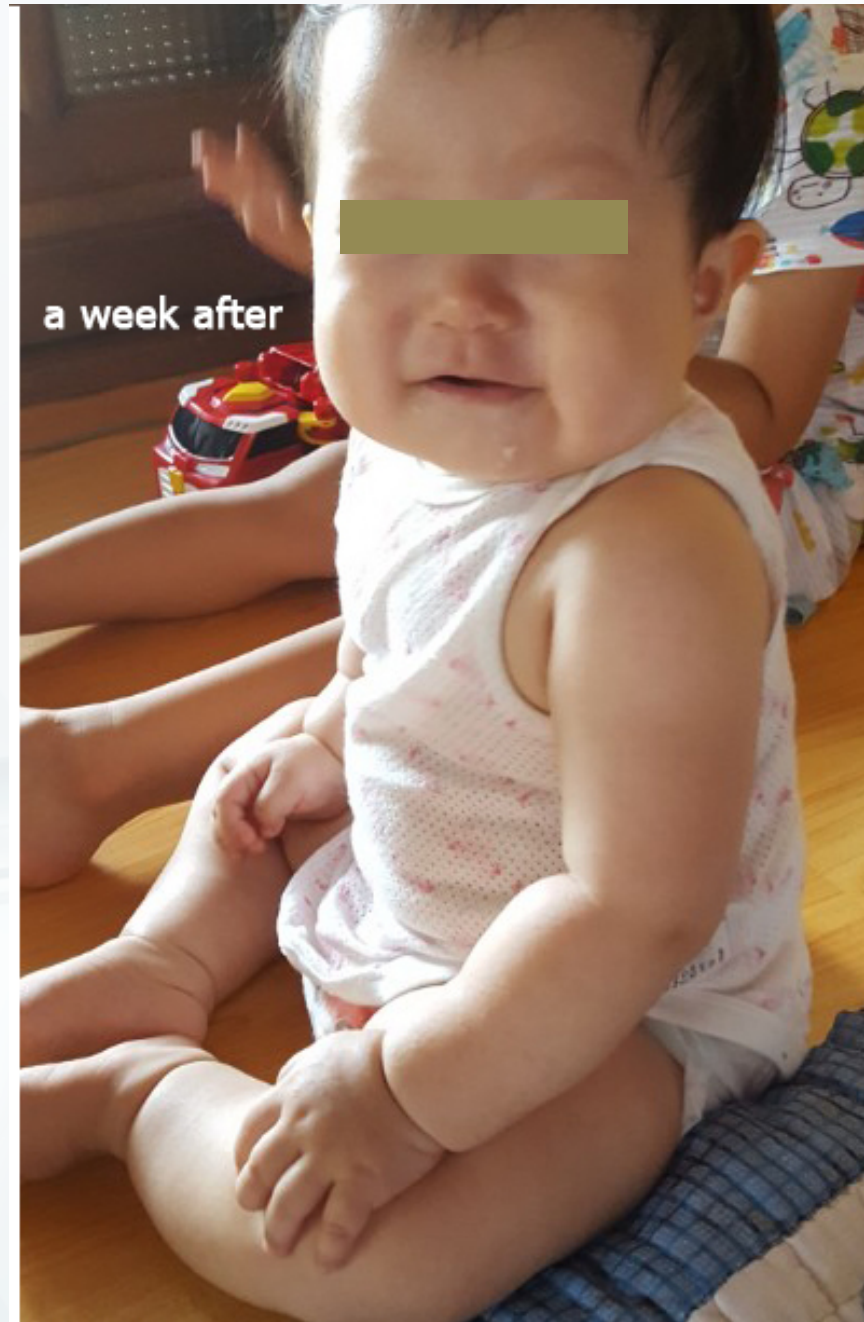
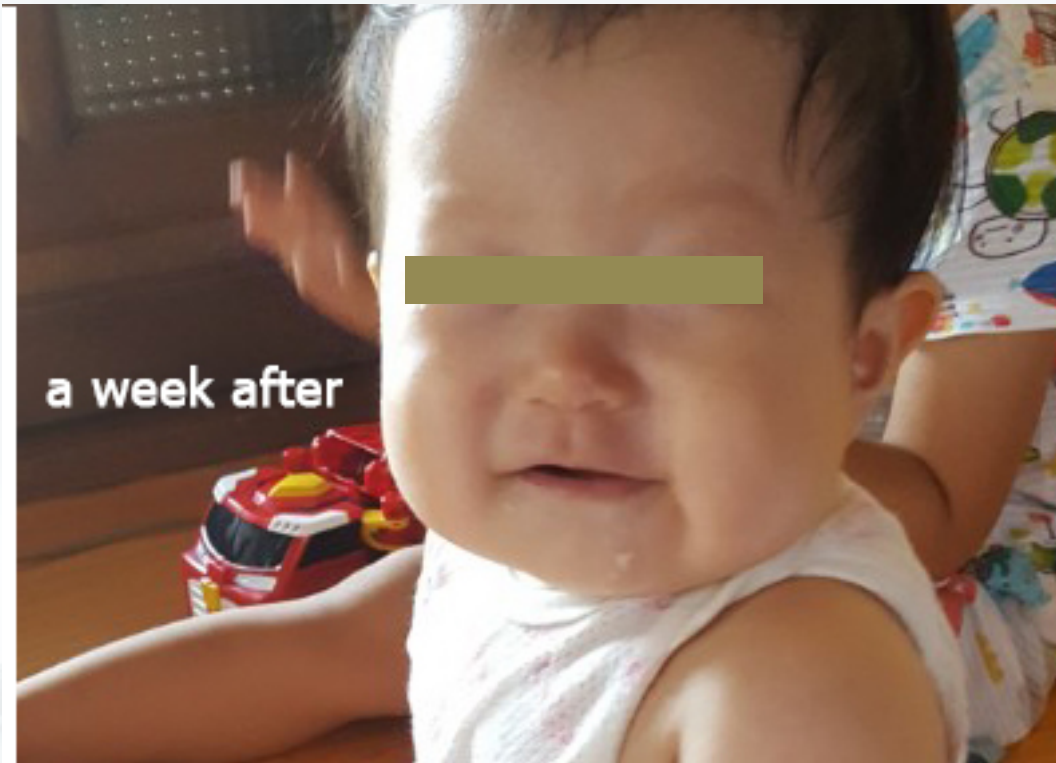
Before treatment

Child 2



After treatment

Child 2



Child 3



Before treatment



Child 4

After treatment



Child 4



Before treatment



Child 5

After treatment

Child 5



Before treatment

Child 6



After treatment

Child 6



Clinical application of Metabolomics: Treating children with atopic dermatitis.

Conclusion

- Metabolomics can be a useful tool for the application of precision nutrition in children suffering from atopic dermatitis.



Take home message

Metabolomics can be a promising tool for the application of precision medicine and precision nutrition in monitoring and addressing childhood asthma and atopic dermatitis.



METABOLOMIC MEDICINE®
HEALTH CLINICS FOR AUTOIMMUNE AND CHRONIC DISEASES

Thank you!



METABOLOMIC MEDICINE®
HEALTH CLINICS FOR AUTOIMMUNE AND CHRONIC DISEASES

www.metabolomicmedicine.com