

Lab Bio Markers to evaluate Metaflammation and Inflammaging: Looking at Lab Biomarkers through the lens of trend analysis



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James LaValle is an internationally recognized clinical pharmacist, author, board-certified clinical nutritionist, and expert and educator in integrative and precision health. James is best known for his expertise in personalized integrative therapies uncovering the underlying metabolic issues that keep people from feeling healthy and vital.

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Jim LaValle, RPh, CCN, DHM, DHPh, N.D. (trad)

- Founder and CEO, Metabolic Code Enterprises
- Clinical Director Pro Football Hall of Fame Performance Health
- Academic Co-Chair A4M

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METABOLISM

The sum total of all the chemical reactions driving how you feel today and creating the chemistry moving you toward future health.



METABOLISM

Directly under the influence of Global Metabolic Inflammatory Signaling =

Metaflammation drives Metabolic Dysregulation



Metaflammation Constructs



Egger G, et al. Obesity Reviews. 2008;10(2):237-49.

Key Tenants of Aging, Performance and Vitality

Oxidative Stress / Inflammation

Hormonal Balance

- Stress Hormones
- Glucose / Insulin Regulation

GUT integrity and microbiome diversity

🐆 Immune Balance

Environmental Burden

Individuality



2017;2017:00316.

Metabolic Networks

Understanding the "disruptors" to your current metabolic performance leads to strategies to cut off excessive inflammatory signals and rejuvenate health on a cellular level.

Metaflammation Induces a Catabolic State



Ferruci L, et al. Inflammageing: chronic inflammation in ageing, cardiovascular disease and frailty. Nat Rev Cardiol. 2018;15(9):505-22.

Metaflammation

- Also know as "Inflammageing" and metabolism induced inflammation
- Chronic low-grade inflammatory sequelae
- Increases aging processes and metabolic signaling issues
- Increased peripheral and central inflammation

Prattichizzo F, et al. Inflammageing and metaflammation: the yin and yang of type 2 diabetes. Ageing Res Rev. 2018;41:1-17.

Systems Biology Approach to Metaflammation

• Optimizing Inter-relationship of organ systems important in treatment



Stress/Cortisol Gets the Metaflammation Ball Rolling

- Stress causes cravings, sleep disturbance and weight gain
- Cortisol DHEA ratio
- Insulin resistance follows
- Weight gain leads to adiponectin alterations and loss of AMPK in the cell

... the inflammatory cycle begins ...



Baylis D, et al. Understanding how we age: insights into inflammaging. Long Healthspan. 2013;2(8):1-8

Unlock Your Healthiest You™

Metabolic Code[®] is the complete solution to managing your health, lifestyle and metabolism.

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Ranking Order	1	fotal Predictiv	ve Risk	LAB SCORE	10546	TOTAL TRAD RSK PROFILE
	ADRENAL	CURRENT RANGE PREVIOUS ANNUE	85	115	200	LOWIES WOODANTIES HIGHE
1	THYROID	CURRENT RANGE PREVIOUS RANGE	60	145	245	
	PANCREAS	CURRENT RANGE PREVIOUS RANGE	300	235	405	
(NU)	CARDIO	CURRENT ANNUE PREVIOUS IMINGE	105	260	295	
(3)	PULMONARY	CURRENT MINIGE PREVIOUS MINIGE	165	25	190	
	NEURO-VASCULAR	CURRENT NUNCE PREVIOUS IMINGE	110	70	180	
715	GUT	CURRENT ARRIVE	125	1/10	295	
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····	TESTOSTERONE	PREVIOUS ANNUE OURIENT INNUE	305	135	160	
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	PROGESTERONE	PREVIOUS ARINGE	20	15	55	
0-Copyright 2020 Wetabolic C	ode. All rights manved.	3				MetabolicCod

How the Metabolic Code Works Metabotypes

DRENAL PARCENTERS	GUT BRANK	CARDIO NEUROUNPECULAR PUT	LIVER 4 HUMPS	TESTOSTERONKE BOGESHERONKE
Adrenal glands	GUT (<u>gastrointestinal</u> system or digestive tract)	Cardiovascular	Liver	Testosterone
Thyroid gland	Immune system	Pulmonary	Lymph	Estrogen
Pancreas	Brain (Central Nervous System)	Neurovascular	Kidneys	Progesterone

MC Laboratory Testing – The Basics







- Properly functioning metabolic pathways depend on balancing all aspects of body chemistry
- Can be done through MC Questionnaire and adding laboratory testing parameters including blood, urine and saliva
- MC has 3 panels + additional add-on labs which adds more weight to the MC report
- Uses "trends" not just "high" or "low" in an accelerated model
- Thousands of algorithms calculations to target where to start with a person to target a quick "win" as well as roadmap

YOUR HEALTH & WHAT YOU CAN DO ABOUT IT YOUR HEALTH & WHAT YOU CAN DO ABOUT IT YOUR HEALTH & WHAT YOU CAN DO ABOUT IT YOUR HEALTH & WHAT YOU CAN DO ABOUT IT YOUR HEALTH & WHAT YOU CAN DO ABOUT IT YOUR HEALTH & WHAT YOU CAN DO ABOUT IT YOUR HEALTH & WHAT YOU CAN DO ABOUT IT YOUR HEALTH & WHAT YOU CAN DO ABOUT IT YOUR HEALTH & WHAT YOU CAN DO ABOUT IT YOUR HEALTH & WHAT YOU CAN DO ABOUT IT YOUR HEALTH & WHAT YOU CAN DO ABOUT IT YOUR HEALTH & WHAT YOU CAN DO ABOUT IT YOUR HEALTH & WHAT YOU CAN DO ABOUT IT YOUR HEALTH & WHAT YOU CAN DO ABOUT IT YOUR HEALTH & WHAT YOU CAN DO ABOUT IT YOUR HEALTH & WHAT YOU CAN DO ABOUT IT YOUR HEALTH & WHAT YOU CAN DO ABOUT IT H

Initial Lab Testing

- Biometrics
 - BP, UpH, BMI, % body fat
- CBC and CMP
 - Includes MEB %
- Fasting glucose
- Hemoglobin A1c
- Insulin
- Thyroid panel TPO/ThyAb, free T3, free T4, TSH, rT3
- Homocysteine
- Hs-CRP
- Estradiol, estrone, progesterone, DHT,SHGB
- Urinary estrogen metabolites optional

- Cortisol serum(urinary,salivary optional)
- DHEA-s
- Comprehensive Vitamin D Test
- Testosterone free and total
- CRP
- Vitamin B12
- RBC Magnesium
- Iron/Ferritin/% sat/TIBC
- PSA and %free PSA

Initial Lab Testing – Add-Ons

- 8-OHdG
- F2 isoprostanes
- Glutathione total and reduced
- Adiponectin/Leptin
- TNF alpha / IL-6
- Lpa
- Lp-PLA2
- АроВ
- LDP-P
- oxLDL

- VEGF vascular endothelial growth factor
- Vitamin B12
- MMA methylmalonic acid
- MSH melanocyte stimulating hormone
- MMP9 matrix metalloproteinase-9
- MPO Myeloperoxidase
- RBC Zinc
- Zonulin/histamine/LPS

Metaflammation Labs

Group labs based on systems biology effects

• Which "TRIAD" based on labs/biometrics and symptoms has greatest effect on disrupting metabolic homeostasis.

Metaflammation

- Overt hsCRP, homocysteine, ox LDL, RBC Mag, MPV, IRON/TIBC/Ferritin Also consider
- T1 Cortisol/Cortisone, thyroid and blood glucose/insulin
- T2 Gut/Immune/Brain. %MEB's Neutrophils, Lymphocytes
- T3 lipids, fibrinogen, Lpa, ApoB, LDLP, Lp-PLA2, Trigs
- T4 Liver/Lymph/Kidney. AS, ALT, Alk Phos., RDW H&H RDW, MPV
- T5 hormonal axis Testosterone/Estrogens/Progesterone/DHT



PRACTICE

Date: 8/29/2019



B: 10/06/1972

Metabolic Code Enterprise Practitioner: Andrew Heyman

Total Predictive Risk

Ranking Order			SYMPTOM SCORE	LAB SCORE	TOTAL	TOTAL TRIAD RISK PROFILE
						LOW RISK MODERATE RISK HIGH RISK
1	ADRENAL	CURRENT RANGE	110	45	155	
	ADRENAL	PREVIOUS RANGE				
	THYROID	CURRENT RANGE	95	185	280	
		PREVIOUS RANGE				
	PANCREAS	CURRENT RANGE	215	345	560	
	PANCREAS	PREVIOUS RANGE				

690

TESTOSTERONE	CURRENT RANGE	215	260	475	
ESTROGEN	CURRENT RANGE	125	80	205	
PROGESTERONE	CURRENT RANGE PREVIOUS RANGE	10	0	10	

645

GUT	CURRENT RANGE PREVIOUS RANGE	105	110	215	
IMMUNE	CURRENT RANGE PREVIOUS RANGE	85	170	255	
BRAIN	CURRENT RANGE	70	105	175	

Total Predictive Risk



ALL	CARDIO	CURRENT RANGE	70	445	515	
3	PULMONARY	CURRENT RANGE	50	25	75	
a stall	NEURO-VASCULAR	CURRENT RANGE	25	25	50	



LIVER	CURRENT RANGE PREVIOUS RANGE	80	150	230	
LYMPH	CURRENT RANGE PREVIOUS RANGE	50	20	70	
KIDNEY	CURRENT RANGE	95	100	195	

T1: Adrenal Thyroid Lab Results



A.M. Cortisol is normal but given Thyroid numbers & history and report result suggest Salivary or Urinary Cortisol



Thyroid					T1 LAB VALUES
T3 Free	2.0-4.4	3.2		\land	
T4 Free	0.93-1.7	0.99			
T3 Total	80-200	112			
T4 Total	4.5-11.7	5.8			
Reverse T3	8-24	9			
Thyroid Antibodies	<30	< 10		\bigtriangleup	
Thyroid Peroxidase	<34	< 10		\bigtriangleup	
тѕн	0.27-4.2	3.54			

T1: Pancreas

Lab Results

MY PREVIOUS



BG 95= 60% risk of being diabetic in the next decade

Risk is accelerating through related numbers

	NORMAL RANGE	MY LAB VALUES	LAB VALUES	MY CURRENT LAB VALUES				
				ALERT LOW	LOW NORMAL	OPTIMAL NORMAL	HIGH NORMAL	ALERT HIGH
Pancreas							T1 LAI	B VALUES
ВМІ	18-35	33.47						
Adiponectin	>16	10						
Ferritin	30-400	285						
Glucose (fasting)	65-99	95						
Hemoglobin A1c	<5.6	5.5						
HDL	>39	38						
Insulin	3-9	19						
Leptin	< 43	14						
Potassium	3.5-5.3	3.9						
RBC Magnesium	4.2-6.8	5.3						

T2: GUT IMMUNE BRAINLab Results



%MEB=16 Vitamin D low Insulin resistance influencing Triad 2 (stacking)

ApoE3,4 low sat fat MC Phase 1 diet Homocysteine= metaflammation

Consider Food Allergy testing







T3: Cardio Pulmonary NeuroVascular



Insulin resistance + ApoE status loading into Triad 3

Dyslipidemia from metaflammation: Fibrinogen, LPA, Myeloper. OxLDL

Check Toxic Metals in future

	NORMAL RANGE	MY LAB VALUES	MY PREVIOUS LAB VALUES	MY CURRENT LAB VALUES				
				ALERT LOW	LOW NORMAL	OPTIMAL NORMAL	HIGH NORMAL	ALERT HIGH
Cardio							T3 LA	B VALUES
АроВ	<80	97						
Calcium	8.8-10.5	9.8				\sim		
Cholesterol (total)	125-200	196						
CoQ10	< 2	1.06						
Fibrinogen	126-437	466						
Galectin-3	< 25.9	11.1				\sim		
oxLDL	< 70	74						
LDL	<130	125						
Lpa	<75	284						
Lp-PLA2	<383	229				\frown		
Myeloperoxidase	<254.9	253						

Lab Results

Pulmonary			T3 LAB VALUES
Carbon Dioxide	19-31	27	

Neuro-Vascu	ular	T3 LAB VALUES
BP (diastolic)	40-100	
BP (systolic)	80-145	
Pulse	40-80	

T4: Liver Lymph

Lab Results



Insulin Resistance loading into liver function

	NORMAL RANGE	MY LAB VALUES	MY PREVIOUS LAB VALUES		мүс	URRENT LAB V	ALUES	
				ALERT LOW	LOW NORMAL	OPTIMAL NORMAL	HIGH NORMAL	ALERT HIGH
Liver							T4 LAE	B VALUES
Albumin	3.7-5.1	4.3				\sim		
ALP	45-129	87				\sim		
ALT	<42	25				\frown		
AST	<41	15				\sim		
Hematocrit	36-50	45				\frown		
Hemoglobin	12.5-17	15.2				\frown		
Iron	59-158	95				\frown		
мсн	27-34	30				\frown		
мснс	32-36	34						
мсч	80-98	88				\sim		
Platelets	140-415	257				\sim		
RBC	4.1-5.6	5.1				\frown		
RDW	11.7-15	13.6				\sim		
Triglycerides	<150	327						

Lymph			T4 LAB VALUES
GGT	8-61	27	
WBC	4-10.5	8.1	



T5 Hormonal Axis

Lab Results



MY PREVIOUS **MY CURRENT LAB VALUES** NORMAL RANGE MY LAB VALUES LAB VALUES ALERT HIGH ALERT LOW LOW NORMAL **OPTIMAL NORMAL** HIGH NORMAL Testosterone **T5 LAB VALUES** DHT serum 30-85 31 4.04-15.2 Prolactin 18.10 PSA (total) 2.09 <4

SHBG	10-80	37		\land	
Testosterone (free) serum	4.7-24.4	6.21			
Testosterone (total) serum	348-1197	332			

Estrogen

T5 LAB VALUES

Estradiol serum	25.8-60.7	26.90		\bigtriangleup	
Estrone serum	13-58	27.99		\land	
LH serum	1.7-8.6	3.7		\land	



Lab Analysis

Ranking Order

ALERT RELATIONSHIP RISK-LABS

LOW RISK MODERATE RISK HIGH RISK



TRIAD1: ADRENAL - THYROID - PANCREAS



Triad 1 encompasses the relationship between 3 important hormones - cortisol, insulin and thyroid hormones. These hormones reflect the state of stress, sugar metabolism and total efficiency of your metabolism. In their most basic function, each is responsible for the production of energy in the body. More generally, when these hormones are in balance, the individual feels vital and healthy.

Lab Analysis

Ranking Order

ALERT RELATIONSHIP RISK-LABS

HIGH RISK

MODERATE RISK

LOW RISK



TRIAD3: CARDIOVASCULAR - PULMONARY - NEUROVASCULAR	
--	--

ApoB个个个	Cholesterol (total) 🛧 🛧	Carbon Dioxide 🛧	CRP-hs 个 个
Fibrinogen 个 个 个	Homocysteine 🛧 🛧	LDL 🛧	Lpa个个个
Potassium 🕁 🗸	RBC Magnesium $\Psi \Psi \Psi$	T4 Free 🕹	T3 Total ↓
T4 Total ∳	Testosterone (free) serum ↓	Testosterone (total) serum ↓↓↓	Vitamin D 🌵 🌵 🖖

Triad3 includes the cardiopulmonary unit, autonomic and central nervous system and vascular tree. This triad reflects the relationship of cardiovascular health, cognition and mood, and stress. When in balance, the individual has plenty of metabolic resilency and strength to meet life's challenges.



TRIAD2: GUT - IMMUNE - BRAIN

Adiponectin 🕁 🕁	CRP-hs∱	Eosinophils %个个个	Ferritin 🛧 🛧
Homocysteine 🛧 🛧 🛧	Monocytes % 🛧 🛧 🛧	RBC Magnesium Ψ	T4 Free 🖌
T3 Total 🕹	T4 Total ↓	Vitamin D 🕁 🕁 🕁 🕁	

Triad2 is comprised of three important body systems - digestive tract, immune system and central nervous system. Together, these intelligent body functions make moment to moment decisions with regard to absorption and assimilation, self/non-self, and setting key boundaries physically immunologically and emotionally. When working well, the individual is safe and secure themselves and the world around them.

Lab Analysis

TRIAD5: TESTOSTERONE - ESTROGEN - PROGESTERONE

TRIAD4: LIVER - LYMPH - KIDNEY



Adiponectin 🗸	DHEA-S serum ↓	Prolactin 🕈	RBC Magnesium Ψ Ψ
Testosterone (free) serum ↓↓	Testosterone (total) serum ↓↓↓		

Triad 5 includes the sex hormones estrogen, progesterone and testosterone that play a central role in the human life cycle. These hormones play an important role in either metabolic or global health. More fundamentally, they confer a sense of potency and power to the individual when in balance for both women and men

ALERT RELATIONSHIP RISK-LABS

MODERATE RISK

LOW RISK

270 14 15

Adiponectin 🕹 🕹	Chloride 🕇	Cholesterol (total) 🕈	CRP-hs 个 个
Ferritin 🕆 🕇	Homocysteine 🛧 🛧	LDL↑	Monocytes % 个 个
Potassium ↓	RBC Magnesium 🕹	Triglycerides 🛧 🛧	Uric Acid 🛧 🛧

Triad4 contains the detoxification systems of the liver, lymph and kidney. These form a functional unit to ensure adequate metabolism, shuttling removal of both internally derived and external toxins. Detoxification is an ongoing process that requires efficiency in order to maintain health.

Ranking Order

Sex Hormones Kidneys

- Gonadal dysfunction is a common occurrence in patients with CKD
- Estrogens play a role in the reducing progression of some chronic renal diseases
- Testosterone
 - Low T linked to increased risk of death in CKD
 - Males have higher predominance of CKD

Gluhovschi GH, et al. Chronic kidney disease and the involvement of estrogen hormones in its pathogenesis and progression. Rom J Intern Med. 2012;50(2):135-44, Yeo JK, et al. Effects of testosterone treatment on quality of life in patients with Chronic kidney disease. Am J Mens Health. 2020;14(3):1557988320917258.

Exogenous Testosterone Effects

- 2017 cohort study analysis
- 2 groups veterans diagnosed with Low T
 - 38,708 men treated w/ test. and resulting normalized T
 - 9755 men not treated and with low T
- Follow up was 6.1 and 5.1 years respectively
- Treated group showed significant delay in progression of CKD
- Treated men had a 24% decreased risk of ESRD and 25% decreased risk of death when compared w/ untreated men

Goel A, et al. Testosterone replacement therapy (TRT) delays progression of CKD and ESRD. Poster presented at the National Kidney Foundation's 2017 Spring Clinical Meetings in Orlando, Florida. Poster 239.

Testosterone Deficiency

 2008 Endocrine Society report studied 2000 German men aged 20 to 79 and found that those with low testosterone had a 2.5 times greater risk of dying over the next 10 years - all cause mortality

Schneider HJ, et al. Prevalence of low male testosterone levels in primary care in Germany: cross-sectional results from the DETECT study. Clin Endocrinol (Oxf). 2009;70(3):446-54.

 2006 study reported in JAMA showed that of 858 men over the age of 40, followed for 4 to 8 years, those with low testosterone had 88% increased risk of death in that time frame.

Shores MM, et al. Low serum testosterone and mortality in male veterans. Arch Intern Med. 2006;166(15):1660-5.

Testosterone Deficiency

2014 meta-analysis of 20 observational studies

 Men with low total testosterone, low SHBG OR low free testosterone significantly more likely to have MetS

Brand JS, et al. Testosterone, sex-hormone binding globulin and the metabolic syndrome in men: an indvidual participant data meta-analysis of observational studies. PLoS One. 2014;9(7):e100409.

Estrogen Effects Kidneys

- Both estrogen alpha and beta receptors present in the nephron more alpha
- Estrogen hormones act upon the nephron component cells
- Estrogens regulate several processes
 - Nephroprotective
 - Attenuate glomerulosclerosis and tubulo-interstitial fibrosis
 - Estradiol reverses TGF-beta-1 induced mesangial cell apoptosis
 - Estrogens play an important part in disturbances of the phosphorus-calcium metabolism - exert favorable effects on renal osteodystrophy

Gluhovschi GH, et al. Chronic kidney disease and the involvement of estrogen hormones in its pathogenesis and progression. Rom J Intern Med. 2012;50(2):135-44.

RBC Magnesium

- RBC Mg more important clinically than serum Mg
- Low mag levels directly correlated with increased HOMA-IR
- Higher risk for cardiovascular diseases
- RBC mag Ranges: (4-6.4 mg/dL)
 - Alert Low = <4
 - Trending Low = 4-5.6
 - OPTIMAL = 5.7-6.2
 - Trending high = 6.3-6.4
 - Alert High = >6.2

Laires MJ, et al. Magnesium insulin resistance and body composition in healthy postmenopausal women. J A coll Nutr. 2004;23(5):510S-513S.

MPV – Mean Platelet Volume

- Platelet size demonstrated to reflect platelet activity
- METAFLAMMATION marker
- Useful predictive and prognostic biomarker of cardiovascular events
- Associated with prothrombotic and proinflammatory events
- Changes in MPV reported to be important biomarker for inflammatory processes
- Also neoplastic diseases

Korniluk A, et al. Mean platelet volume (MPV): New perspectives for an old marker in the course and prognosis of inflammatory conditions. Mediat Inflamm. 2019;2019:9213074/

Adiponectin

- Increases insulin receptor sensitivity low levels associated with IR
- Elevates AMP kinase which 个 glucose transport into skeletal muscle and burning of fat (fatty acid oxidation)
- Current top target for glucose control along with incretins (GIP, GLP-1).
- Antiathrogenic properties
- IL-6, TNF α inhibit adiponectin release
- High levels adiponectin \downarrow risk of MI

Achari AE, et al. Adiponectin, a therapeutic target for obesity, diabetes, and endothelial dysfunction. Int J Mol Sci. 2017;18(6):1321.

Adiponectin

- Ranges based on gender and BMI (kg/m²)
- Female BMI <25
 - Range 5-37 mcg/ml
- Female BMI 25-30
 - Range 5-28
- Female BMI >30
 - Range 4-22

• Male BMI <25

- Range 4-26 mcg/ml
- Male BMI 25-30
 - Range 4-20
- Male BMI >30
 - Range 2-20

oxLDL

- Proinflammatory
- More important than LDL alone
- Transforms macrophages into foam cells
 - Major constituent of arterial plaque
- Increased levels correlate with increased risk of coronary artery disease (CAD)
- MetS risk increased 4x w/ increase LDLox
- Levels increase as CAD severity increases
- Range < 60 U/L

Holvoet P, et al. Association between circulating oxidezed low-density lipoprotein and incidence of the metabolic syndrome. JAMA. 2008;299:2287-93.



LDL-P

LDL-Particle number - nmol/L

• Lower the value, less risk for cardiovascular disease

Stronger correlation to CVD than LDL-C

Reference Values

LDL Particle Number

LDL-P <1000 nmol/L

Low:	<1000 nmol/L
Moderate:	1000 - 1299
Borderline-High:	1300 - 1599
High:	1600 - 2000
Very High:	>2000

Urinary and Saliva pH

- pH critical in determining biochemical balance
- Optimal pH salivary = 7 7.2

(trending low 6.1-6.9, trending hi 7.3-7.8)

- Optimal pH urinary = 6.5-7 (trending low 6-6.49, trending hi <7.1)
- The more acidic (lower pH) = more inflammation
- More lactic acid produced at lower pH
- Mitochondria less efficient
- Joints and tissues stressed





- A trending high or high pH means body too alkaline
 - Digestive issues (hypochlorhydria)
 - Detoxification and drainage problems (liver , lymph, kidney)
- Use digestive enzymes (with HCL if no problems with gastric pain), 2 tabs with each meal

- Probiotics, anti-candida (cat's claw + berberine)
- Kidney, lymph drainage support

CIRS Panel through Wellavate Labs

METABOLIC CODE COMPREHENSIVE BIOTOXIN

Test Code	Test Name
004440	Adrenocorticotropic Hormone (ACTH), Plasma
161950	Anticardiolipin Antibodies (ACA), IgA, IgG, IgM, Quantitative
010447	Antidiuretic Hormone (ADH), Plasma
004051	Cortisol
115188	D-Dimer
163402	Deaminated Gliadin Antibodies, IgA and IgG
167120	HLA DR1/3/4/5, DQ Intermediate Resolution
821342	Human Transforming Growth Factor beta 1 (TGF-b1)
146712	Leptin, Serum or Plasma
010421	Melanocyte-stimulating Hormone (MSH) (010421)
500124	MMP-9 (Matrix Metalloproteinase-9)
002071	Osmolality
117006	Vascular Endothelial Growth Factor (VEGF), Plasma
164509	von Willebrand Factor (vWF) Activity (Ristocetin Cofactor)

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