

# BiophysicalPre-D™

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Biomarker Report

# BiophysicalPre-D™

## Sample Report

BiophysicalPre-D is a comprehensive clinical laboratory assessment of relevant biomarkers to aid your physician in the diagnosis and monitoring for pre-diabetes.

Numerous studies have shown that, in addition to elevated glucose levels, there are other biomarkers that change as a person begins to develop pre-diabetes. Biophysical reviewed the results from numerous large, randomized, multicenter, double-blind, placebo controlled, peer-reviewed studies that looked for biomarker changes in pre-diabetic people. From these studies, Biophysical selected the biomarkers that best indicate pre-diabetes is developing in the body. We have grouped these biomarkers into the BiophysicalPre-D so that you and your physician can determine if you are starting to experience changes associated with pre-diabetes.

Pre-diabetes is especially prevalent in people over 45 years of age who are over-weight (as indicated by a body mass index over 25). This group of people has a higher risk of developing pre-diabetes and type 2 diabetes. However, not everyone in this group will develop these conditions. BiophysicalPre-D is especially useful for identifying people within this higher risk group who show signs of pre-diabetes and who, therefore, are most likely to benefit from early medical intervention.

BiophysicalPre-D is part of an overall health program that allows you and your physician to:

- Assess your risk for developing pre-diabetes;
- Evaluate the effect of body fat, especially around the abdominal area, on your health;
- Monitor the effect of lifestyle and treatment changes;
- Understand how your body is responding to glucose (also known as blood sugar) – this helps determine if you have diabetes, a pre-diabetic condition called insulin resistance or metabolic syndrome.

The results of your BiophysicalPre-D are based on the following assumptions:

- You are not currently taking diabetic medications or medications that may affect the test results (for example, glucocorticoids, insulin, beta-blockers, etc). Please consult with your physician or pharmacist to determine if your medications may alter lab results;
- You are not pregnant;
- You have been fasting for more than 8 hours.

If any of these assumptions are not true, your risk for pre-diabetes conditions may change.

**On the basis of your findings and with the assumptions made,  
your risk for developing a pre-diabetic condition is:**

**MODERATE**

## Diabetes and Insulin Resistance

Diabetes is a disease in which the body cannot make or respond to insulin, thereby allowing glucose to build up in the bloodstream. Insulin is a hormone produced by your pancreas that helps your body's cells take in glucose and convert it to energy, rather like an escort for glucose into the cells. When the pancreas does not make enough insulin or the body is resistant to the insulin that is present, excess glucose builds up in the bloodstream, setting the stage for diabetes. Diabetes is a growing health concern, affecting about 6% of the U.S. population. When poorly controlled, it plays a major role in strokes, cardiac and vascular disease and can cause injury to the kidneys, eyes, and other parts of the body.

Diabetes is generally divided into two types: Type 1 (also called juvenile or insulin-dependent diabetes) and type 2 (also called adult-onset or non-insulin dependent diabetes). In addition, there is a form of pre-diabetes called insulin resistance.

Insulin resistance is often observed in individuals with an elevated body mass index (BMI) and increases the risk of developing type 2 diabetes mellitus. Often a person is unaware they are insulin resistant. Some of the more common signs and symptoms of insulin resistance include: fatigue, inability to focus, weight gain, intestinal bloating, increased triglyceride level, increased blood pressure, depression and acanthosis nigricans (brown to blackish discolored patches of skin caused by chronically increased insulin levels). However, more often than not, there are no symptoms.

### *Diabetes and Insulin Resistance Biomarkers*

Physicians classically diagnose diabetes by measuring the fasting blood **glucose** level. A level from 65 – 100 mg/dL indicates normal glucose metabolism. A level from 101 – 125 mg/dL indicates insulin resistance, while a level above 125 mg/dL on two separate occasions indicates the presence of diabetes.

**Insulin** is the hormone released by your pancreas that helps take glucose out of your bloodstream and into your body's cells where it can be used. An insulin measurement may help determine whether a high blood glucose reading is the result of insufficient insulin production (as in type 1) or poor use of insulin (as in type 2). In type 2 diabetes and insulin resistance, both fasting blood glucose and insulin levels will be high, indicating the body's inability to use the available insulin effectively. Some people have high insulin levels and normal glucose levels indicating the need for a lot of insulin to maintain normal blood glucose levels. **Proinsulin** is a hormone precursor to insulin that is made in the beta cells of the pancreas. Pro-insulin splits apart to create insulin and **C-peptide**. C-peptide is a subunit of the insulin hormone and helps newly diagnosed diabetics to determine how much insulin is being produced in the body.

In some cases the proinsulin is only partially processed resulting in derivatives of proinsulin, such as **split proinsulin**. Studies have shown that proinsulin and split proinsulin can be used to assess beta cell function and to predict insulin resistance. Increases in the levels of proinsulin and split proinsulin are an indication of pancreatic dysfunction.

Your results are:

Diabetes and Insulin Resistance Biomarkers			
Biomarker	Out of Range	In Range	Reference Range
Glucose		93	65-100 MG/DL
Insulin		1.0	<14 uIU/mL
Proinsulin, Total		<2.5	<42 pmol/L
C-Peptide	3.1		0.71 - 5.3 ng/mL
Split Proinsulin		<1.55	<32.2 pmol/L

**Note: Blood glucose is best measured after fasting for at least 8 hours. If you did not fast for at least 8 hours, your fasting glucose level most likely will not reflect your diabetes status.**

### Obesity and Weight Related Biomarkers

Obesity is strongly correlated with type 2 diabetes (accounting for about 80% of type 2 diabetes), insulin resistance and metabolic syndrome. Additionally, obesity can cause health problems in virtually every body system, either causing disease directly or increasing risk. Obesity-related diseases include diabetes, cancer, cardiovascular disease, non-alcoholic fatty liver disease, high blood pressure, problems with lipid metabolism, obstructive sleep apnea and osteoarthritis.

As a person gains weight, existing fat cells increase in size. Large fat cells behave differently than small fat cells; in particular, they change the amounts of hormones that they excrete – almost always in a manner that is detrimental to health.

Central obesity is a particular type of obesity in which fat accumulates around the abdominal area. Central obesity is defined as a high waist to hip ratio. Fat cells produce hormones and the fat cells associated with central obesity are particularly active. This explains why people with central obesity are particularly prone to type 2 diabetes, insulin resistance and metabolic syndrome.

### Biomarkers of Diabetes and Risk Factors of Obesity

**Leptin** is a hormone released by fat cells that helps to control body weight through its effect on the appetite centers in the brain. Increased calorie intake as well as increased body fat leads to high leptin levels which, correspondingly, causes a decrease in hunger. Decreased caloric intake and decreased body fat cause a decrease in leptin levels and, therefore, an increase in appetite. Leptin is released in a pulsatile fashion, with levels highest at night and lowest in the morning.

Because obese people have larger fat cells, they produce more leptin and levels, therefore, tend to run high. High leptin levels normally tell the body to stop eating, yet obese people continue to eat, despite having consumed enough calories. This paradox is caused by “leptin resistance”. In obese people, leptin levels are chronically high and after awhile the brain starts to ignore or become resistant to its effects. Without the effect of leptin, there is not the appetite controlling factor that tells the body that it is full and not hungry.

**Resistin** is a hormone released by fat cells. An increase in fat cells leads to an increase in resistin levels which directly leads to insulin resistance. Because the fat cells associated with central obesity are more active in terms of producing hormones, resistin levels may be higher for these people and account for why central obesity is closely associated with insulin resistance and type 2 diabetes. There is a direct correlation between high resistin levels and type 2 diabetes and resistin, like leptin, is associated with inflammation. Resistin levels decrease with weight loss.

**Adiponectin** is also a hormone produced by fat cells. Unlike leptin and resistin, adiponectin levels paradoxically decrease as body fat increases. Thus, adiponectin levels have been shown to be decreased in individuals who are overweight and normal or elevated in individuals who are lean. Adiponectin has anti-inflammatory effects, therefore, high levels help to decrease inflammation in the body and low levels may allow a state of inflammation to exist.

Low levels of adiponectin (i.e., <4.0 ug/mL) have been shown to be associated with increased levels of C-reactive protein, glucose, insulin, C-peptide, and body mass index (BMI). In fact, studies show that low adiponectin levels may be an independent risk factor for type 2 diabetes.

Your results are:

Weight Related Biomarkers			
<u>Biomarker</u>	<u>Out of Range</u>	<u>In Range</u>	<u>Reference Range</u>
Leptin		5.3	<26 ng/mL
Resistin		3.5	0.54 - 5.8 ng/mL
Adiponectin		2.2	1.1 - 13 ug/mL

#### Sex Hormone Binding Globulin Biomarker

Sex hormone binding globulin (SHBG) is a protein that binds to hormones such as estradiol and testosterone and carries them in the bloodstream. Most of the estradiol and testosterone in the body is bound to SHBG, some is bound to albumin, and a small amount is free and able to enter cells for use. While testosterone and estradiol are bound to SHBG they are not biologically active, meaning, their function is inhibited. This is particularly important in the case of estradiol. Estrogens are produced by fat cells; therefore, obese people tend to have higher estrogen levels. High estrogen levels can have adverse health effects. Because SHBG helps to lower the amount of free estradiol, higher levels are more desirable. SHBG is mainly produced by the liver, and studies show that diets high in simple sugars cause the liver to produce less SHBG. Low levels of SHBG are seen in obesity, pre-diabetes, insulin resistance and type 2 diabetes. Low levels of

SHBG are also seen in polycystic ovarian disease, a condition that is associated with obesity, insulin resistance and type 2 diabetes.

Your result is:

Sex Hormone Binding Globulin Biomarker			
Biomarker	Out of Range	In Range	Reference Range
Sex Hormone Binding Globulin (SHBG)	15		18 - 114 nmol/L

### Inflammation Related Biomarkers

Central obesity, insulin resistance and type 2 diabetes are associated with a pro-inflammatory state. In other words, the body is producing higher than normal levels of biomarkers that are involved in the immune system's response to disease. Studies show that inflammation itself contributes and precedes the development of insulin resistance and type 2 diabetes.

**Interleukin-6 (IL-6)** is an inflammatory biomarker that normally stimulates the immune system to respond to conditions such as infection, trauma and tissue damage. Abdominal fat produces a significant amount of IL-6. IL-6, along with other types of pro-inflammatory biomarkers disrupts the normal action of insulin in the body. High IL-6 levels are also related to atherosclerosis, a common complication of diabetes.

**Interleukin-8 (IL-8)**, like IL-6 is released by adipose (fat) tissue and studies show that people with central obesity may have higher IL-8 levels than people without central obesity. IL-8 is a pro-inflammatory cytokine that is implicated in a number of diseases that cause damage to small blood vessels, including cardiovascular disease and retinopathy (a leading cause of blindness) that may occur as a complication of diabetes.

Studies show a link between **tumor necrosis factor alpha (TNF alpha)**, **tumor necrosis factor receptor-2 (TNFR2)** and the development of type 2 diabetes in insulin resistant people. TNF alpha is produced by a variety of cells including the fat cells associated with central (abdominal) obesity. Obesity causes an increase in overall TNF alpha levels. Studies have shown a correlation between high levels of TNF alpha and insulin resistance. Further, studies have shown an increase in cardiovascular abnormalities associated with insulin resistance when there are elevated levels of TNFR2.

**High sensitivity C-reactive protein (hs-CRP)** is also an inflammatory biomarker. Most CRP is produced by the liver with additional production coming from fat cells and the cells that line the insides of blood vessels. Production of CRP is increased in response to an increase in levels of IL-6. It is an excellent indicator of both acute and chronic inflammation in the body. Studies

show that people who are at highest risk for developing pre-diabetes have higher levels of hs-CRP.

Your results are:

<b>Inflammation Related Biomarkers</b>			
<u>Biomarker</u>	<u>Out of Range</u>	<u>In Range</u>	<u>Reference Range</u>
Interleukin-6 (IL-6)		<1.8	<12 pg/mL
Interleukin-8 (IL-8)		16	<119 pg/mL
Tumor Necrosis Factor Alpha (TNF Alpha)		8.6	<18 pg/mL
Tumor Necrosis Factor Receptor-2 (TNFR2)		2.8	<10 ng/mL
High Sensitivity C-Reactive Protein (hs-CRP)		1.4	<3 ug/mL

#### **Blood Clotting Biomarker**

**Plasminogen activator inhibitor type 1 (PAI-1)** is an enzyme that prevents the breakdown of blood clots; therefore, elevated levels are associated with increased blood clotting. PAI-1 is produced by the cells that line the inside of blood vessels and by fat tissue. PAI-1 levels are increased in obesity, insulin resistance and metabolic syndrome, and are associated with an increase in blood clotting in people with these conditions.

Your result is:

<b>bBlood Clotting Biomarker</b>			
<u>Biomarker</u>	<u>Out of Range</u>	<u>In Range</u>	<u>Reference Range</u>
Plasminogen Activator Inhibitor Type 1 (PAI-1)		190	109 - 389 ng/mL

Your results indicate your risk based on blood-based biomarkers. There are other risk factors for diabetes and pre-diabetes that you and your physician should consider. These additional risk factors include:

- Age over 45 years;
- Ethnicity (increased risk for black/African American, Hispanic, native American and Hispanic people);
- Obesity, defined as a high body mass index;
- Family history of diabetes;
- High blood pressure;
- History of gestational diabetes (diabetes while you were pregnant); and
- Decreased physical activity.

We hope that you have found this report helpful. We encourage you to work with your physician, especially if you have out of range results or if you are experiencing symptoms. BiophysicalPre-D can be used on a routine basis to proactively monitor for pre-diabetic changes to your health or to evaluate the effect of treatment and lifestyle changes that you and your physician make.

To learn more about biomarkers, please visit our website at [www.biophysicalcorp.com](http://www.biophysicalcorp.com) or call us at 800.532.7092.

Biophysical reports are intended to be used for health information only. Reports are not diagnostic of any disease or condition and should not be used to self-diagnose or self treat. Biophysical encourages every individual to share their results with their personal physician. Only a physician can interpret laboratory results, recommend additional testing, treatment and lifestyle changes or use the information as a baseline from which future test results can be compared.

No employee of The Biophysical Corporation (Biophysical) will provide individuals who purchase a Biophysical test with a diagnosis of any disease or health condition or any advice regarding follow-up. Biophysical will not recommend any specific follow-up, further evaluation, therapy or treatment based on Biophysical health assessment results.

Communication with medical professionals employed by Biophysical about a Biophysical test or the results of the test does not establish a physician-patient relationship.

Out-of-range results do not necessarily indicate a health problem, just as in-range results do not indicate the absence of disease. Biophysical clients should consult with their personal physician if they are experiencing any symptoms or have any health concerns.

Biophysical test results are the personal property of each individual client and their physician where required by law. Results will not be shared with any other party unless required by law. Clients who reside in a state where a physician is required by law to receive the results, will be notified accordingly. Biophysical products may be purchased by third party payors, such as though a corporate program, however, results will remain the property of the client and will not be shared with the payor, including a corporate payor. Biophysical clients are not required to share their Biophysical results with their employer.

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# BiophysicalPre-D™

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Laboratory Report

# BiophysicalPre-D™

Client Initials: SMP	Age: 45	Gender: Female	Sample ID:
Test Requested: BiophysicalPre-D	Blood Draw Date: 10/02/2009	Time: 8:35AM	
Blood Received Date: 10/03/2009	Time: 11:50AM	Reported Date: 10/07/2009	Time: 11:40AM

Test		Results		
Rules-Based Medicine, Inc.		3300 Duval Road, Austin, TX 78759		CLIA # 45D1037483
	Out-of-Range	Within Range	Units	Expected Range
Insulin*		1.0	uIU/mL	<14
Proinsulin, Total*		<2.5	pmol/L	<42
C-Peptide*	3.1		ng/mL	0.71 - 5.3
Split Proinsulin (Calculated)		<1.55	pmol/L	<32.2
Leptin*		5.3	ng/mL	<26
Resistin*		3.5	ng/mL	0.54 - 5.8
Adiponectin*		2.2	ug/mL	1.1 - 13
Sex Hormone-Binding Globulin (SHBG)*	15		nmol/L	18 - 114
Interleukin-6 (IL-6)*		<1.8	pg/mL	<12
Interleukin-8 (IL-8)*		16	pg/mL	<119
Tumor Necrosis Factor Alpha (TNF Alpha)*		8.6	pg/mL	<18
Tumor Necrosis Factor Receptor-2 (TNFR2)*		2.8	ng/mL	<10
High Sensitivity C-Reactive Protein (hsCRP)*		1.4	ug/mL	<3
Plasminogen Activator Inhibitor Type 1 (PAI-1)*		190	ng/mL	109 - 389

Test		Results		
Clinical Pathologies Laboratories, Inc.		9200 Wall Street, Austin, TX 78754		CLIA # 45D0505003
	Out-of-Range	Within Range	Units	Expected Range
Glucose		93	MG/DL	65-100

Disclaimer: Biophysical tests are designed to identify early signs of potential health risk. Biophysical tests do not look for all diseases or health conditions. Biophysical tests are not a substitute for a full medical examination by your physician, and do not incorporate medical history, family history, or other information that is part of a full medical assessment. Biophysical test results do not constitute a medical opinion or advice. These test results are not medical care, treatment, a treatment recommendation, or a diagnosis. Biophysical tests results within normal range do not mean that a disease or health condition is not present. Test results outside the normal range do not mean that a disease or health condition is present. Test results may vary if repeated, or change over time. These tests as a whole have not been approved by the Food and Drug Administration for diagnostic or clinical use.

\* Denotes a test that is "For Research Use Only. Not for use in diagnostic procedures."