

# THE BENCH & BEYOND

## Newsletter of San Diego BioMed

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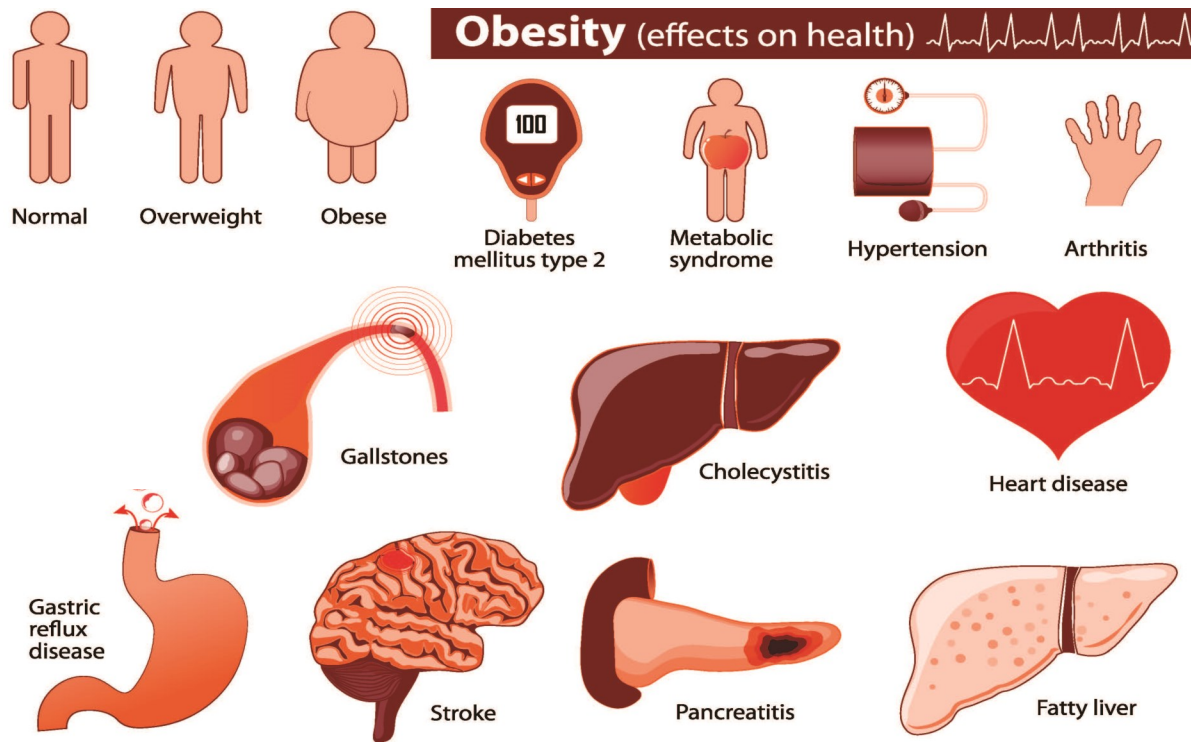
Scientists at San Diego BioMed have dedicated their careers to disease research with the goal of giving every patient the chance to fight diseases that have changed their lives. Our wide range of research topics and our belief in collaboration has enabled us to use every resource that we can to achieve this, giving patients the hope of a better quality of life.

One such disease that San Diego BioMed focuses on is obesity. Obesity, a disease that has become an increasing concern over the last few decades, has reached pandemic proportions with over 650 million adults and 340 million children considered obese. While obesity is a major contributor to many disorders including type 2 diabetes (T2D), heart disease, and cancer, treatment options remain limited due to challenges identifying suitable drug targets.

### **Research at San Diego BioMed—Obesity and Obesity Related Disorders**

Fat tissue is crucial for health. Its main function is to store excess energy in the form of fat molecules, otherwise known as lipids, and then release the energy in times of need. In addition, fat tissue produces various hormones vital to maintaining the body's energy balance, regulation of sugar levels, and cholesterol.

At the heart of obesity related diseases is that fat tissue can become dysfunctional during weight gain. During times of excess calorie intake, fat tissue begins to enlarge due to increased storage of existing and new fat cells. However, this system cannot be sustained indefinitely, and over time, fat tissue malfunctions causing excess fat to spill over into liver and muscle tissues. This negatively impacts the normal functioning of these tissues, leading to obesity related disorders.



While many think it is the amount of fat developed during weight gain that cause T2D, it has become increasingly clear that the dysfunction due to chronic inflammation and decreased production of new fat cells, is what creates health problems. Ultimately, these issues lead to insulin resistance, in which insulin is unable to maintain normal blood sugar levels, eventually leading to T2D.

San Diego BioMed scientist, Dr. Fahumiya Samad focuses on discovering pathways that cause fat cell dysfunction and inflammation during obesity, with the goal of identifying potential therapies. Recently, the Samad lab published two papers discussing drug targets for future pharmacological treatments.

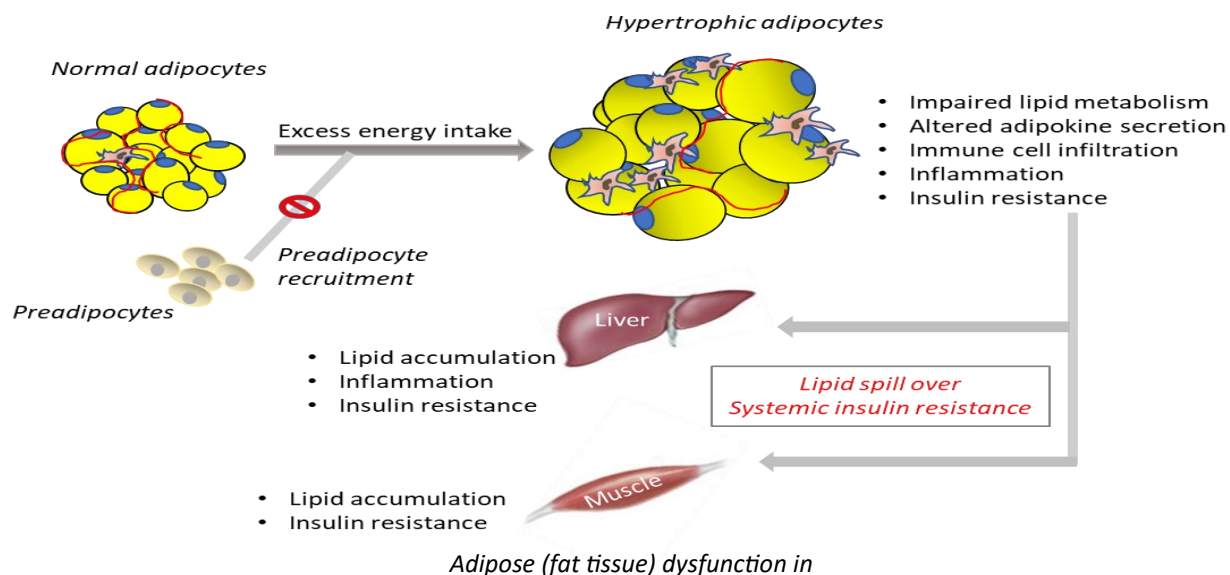
### The Fight Against Obesity and Related Disorders

In the first of the two papers, the Samad group looked at a unique protein called Plg-R<sub>KT</sub>. This protein is located on the surface of various cell types and plays an important role in dissolving blood clots, thereby preventing the clogging of blood vessels and fibrosis in the organs. The Samad group found this protein was unexpectedly located on the surface of fat cells and began to investigate its role in the function of those

In a series of studies, Dr. Samad and her lab demonstrated that the Plg-R<sub>KT</sub> protein is a crucial regulator of weight gain and fat cell development as well as fat cell inflammation, fatty liver, and insulin resistance. This provides evidence that the protein plays a key role in promoting healthy fat cell function and has the potential to be a target for future therapies.



*Dr. Fahumiya Samad*



A common obesity related disorder is T2D which is characterized by the body not responding appropriately to insulin. The drug family thiazolidinediones (TZDs) are potent insulin sensitizers that have proven to be effective against T2D. The Samad group wanted to determine if the effects of TZDs are associated with something called S1P levels. S1Ps are a specific class of fat molecules that help to regulate several biological functions and are known to have great potential as therapeutic drug targets for a spectrum of diseases.

The lab tested this by measuring S1P levels in subjects after four months on TZD and found that levels were significantly increased in response to the drug, suggesting that S1P may contribute to the anti-diabetic outcome of TZDs.

To further determine the impact of S1P, the Samad lab then examined a receptor of S1P (i.e. S1PR3) on fat cells. After comparing obese subjects that had an excess of the receptor, normal levels of the receptor, and did not have the receptor, they found that those without the receptor had more insulin resistance and blood sugar intolerance among other health issues. These results reveal an anti-diabetic role for S1P through actions of the S1PR3 and provide evidence that pharmacological therapies have the potential to be developed to prevent and/or treat obesity associated metabolic disease.

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### San Diego BioMed Donor Spotlight

Mr. Richard Woltman, a long-time resident of La Jolla, California, and an entrepreneur in business and finance, has recently donated \$200,000 to San Diego BioMed! Mr. Woltman and his family have played a major role in San Diego philanthropy and fundraising over several decades with an emphasis on health and science. Mr. Woltman has been a great supporter of San Diego BioMed and our research programs. "The progress and growth of San Diego BioMed is excellent, and I believe in and support its leadership and CEO, Joanna Davies and its world class scientists."

San Diego BioMed would like to extend our gratitude to Richard Woltman and his family for their advice, effort, and donation to the institute.



Mr. Richard Woltman