In the 1920s, Nobel Prize Winner Dr. Otto Warburg proposed that cancer was a metabolic disease. He was unable to discover a mechanism to prove his theory, so it fell to the sidelines of cancer research.

In recent years, however, there has been a resurgence of interest in the metabolism of cancer, evidenced by the growing number of publications on the subject. Among the active researchers in this emerging area is Xiaoyong Yang, PhD, Associate Professor of Comparative Medicine and of Cellular and Molecular Physiology.

“The question,” Dr. Yang explained, “has always been, how does a normal cell become a cancer cell? It’s becoming more and more clear from large-scale genomic studies that the mutations that lead to cancer are often relevant to cellular metabolism. Many groups in the world are starting to look at the difference between cancer cells and normal cells in terms of metabolic features.”

In the metabolism of normal cells, chemical processes convert nutrients into energy, allowing the cells to sustain themselves and maintain routine growth. In cancer cells, this orderly process breaks down. Cancer cells are not content to sustain themselves. They want to proliferate and colonize. To do so, Dr. Yang explained, they “reprogram” cell metabolism and send signals that cause the cell to grow wildly. Dr. Yang believes that metabolic changes drive most, perhaps all, of cancer cell growth.

This cellular proliferation requires an abnormal amount of fuel. “A tumor is like a manufacturing plant,” Dr. Yang said. “It needs machines to allow mass production of building blocks to constantly produce new cells. For that to happen, the cancer cell absolutely must reprogram the metabolic pathways of normal cells by upregulating a lot of biosynthetic enzymes.”

In the metabolism of normal cells, Dr. Yang and his lab are working to understand how this reprogramming occurs — the signals that change a cell’s metabolism. They are focused on a unique sugar (and metabolic fuel) called O-GlcNAc modification that attaches to many proteins. “Cancer cells are addicted to glucose,” Dr. Yang said. “They eat and eat and grow and grow.”

Dr. Yang has found that O-GlcNAc acts as a molecular switch, sending signals that regulate cell function. He and his colleagues have also found that O-GlcNAc can attach to a certain metabolic enzyme, which seems to cause reprogramming of the metabolic pathway. This enzyme is also found in many types of cancer. As 2013 ended, specifics about this research remained confidential, but Dr. Yang and his colleagues expect to publish a paper detailing this breakthrough in 2014.

“We think this will be useful for the diagnosis and treatment of cancer,” he said. “With a better understanding of how metabolic reprogramming occurs, we have a good chance of finding a molecular target for treatment of many different cancers, without causing harm to normal tissues.” Or, he added, it might be possible to develop pharmacological approaches that hinder the reprogramming of normal cells or that starve cancer cells by stopping the abnormal metabolism that is prone to produce the building blocks.

Because the metabolic approach to cancer shows such broad promise, many researchers and institutions are plunging into it. Dr. Yang hopes to keep Yale in the forefront. To that end, he and two colleagues began an initiative last December called the Cancer Metabolism Interest Group. Previously, the scientists at Yale studying metabolism and those studying cancer didn’t have much contact. Now they meet monthly to share research, listen to presentations, and review the growing volume of new publications.

“We hope to take advantage of Yale’s strengths in both areas,” Dr. Yang said, “and to use and share the cutting-edge tools available here that are related to cancer metabolism, such as epigenomics, proteomics, and metabolomics. Hopefully we can develop a new way to approach questions related to cancer metabolism.”