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[How Are Sleep, Hunger and Thinness Connected?](#)

Orexin and HIF-1

Lazy bone individuals are slimmer. It is known that people sleeping less are prone to be overweight or obese. But a new research published in the journal *Genes and Development* has also revealed how orexin, a hormone controlling sleep and hunger, works: it activates a protein, named HIF-1, previously known for its role on activating cancerous tumor growth. "The study is among the first to show how HIF-1 operates in healthy tissues rather than in tumors", said senior author Dr. Thomas Kodadek, chief of translational research at UT Southwestern. Dr. Masashi Yanagisawa, professor of molecular genetics at UT Southwestern, had discovered that the lack of orexin induces the sleep disorder narcolepsy. The new study effectuated a massive gene-screening to detect genes activated or deactivated by orexin. The active form of HIF, HIF1-alpha, was among the most sensitive molecules to orexin. Orexin activated HIF1-alpha spurred the activity of an array of genes involved in burning sugar for getting energy, fact enforced by brain slices of mice with and without orexin receptors. "The findings help explain orexin's link to the metabolic system," wrote the authors. The body increases orexin release when blood sugar decreases, causing the hunger sensation. More orexin boosts HIF-1 synthesis, speeding up metabolism so the body uses the available sugar more effectively. "This action of HIF-1 when stimulated by orexin is different than how it acts in tumors," said Kodadek. In cases of patients suffering from cancer, HIF-1 enables cells to breakdown sugar for energy without oxygen, a low efficiency way which allows the cell to survive in conditions of low oxygen supply. Orexin makes HIF-1 force cells to burn sugar with oxygen, producing much more energy. "You need to be active and energetic, especially when you're hungry, so you can search for a meal", said lead author Dr. Devanjan Sikder, instructor of internal medicine. "This orexin pathway we found is basically an overdrive function. Even though blood sugar levels are low, you're not only awake, but you're also energetic because of the action of HIF-1. Not only was this orexin-HIF link unexpected, but it showed an entirely new way HIF-1 operates. There have been a few recent studies on its function in healthy tissues, but none involving mechanisms related to sleep", said Kodadek. "If anything, our findings may be a cautionary tale about whether HIF-related mechanisms are going to be appropriate targets for chemotherapy", he added.