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Sirtuins are a family of NAD<sup>+</sup>-dependent enzymes that was proposed to control organismal life span about a decade ago. While such role of sirtuins is now debated, mounting evidence involves these enzymes in numerous physiological processes and disease conditions, including metabolism, nutritional behavior, circadian rhythm, but also inflammation and cancer. SIRT1, SIRT2, SIRT3, SIRT6, and SIRT7 have all been linked to carcinogenesis either as tumor suppressor or as cancer promoting proteins. Here, we review the biological rationale for the search of sirtuin inhibitors and activators for treating cancer and the experimental approaches to their identification.

**Keywords:** Sirtuin modulators, cancer, drug design, epigenetics, drug discovery.