

Sirtris' review of sirtuin therapeutics for diseases of aging in *Nature Reviews Drug Discovery*

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Sirtris, a GSK company focused on discovering and developing small molecule drugs to treat diseases of aging such as Type 2 Diabetes, announced today that it published a new review article on the growing body of sirtuin research and its potential to treat diseases of aging such as Type 2 Diabetes, mitochondrial disorders, inflammation, cancer, and heart disease. Entitled "SIRTUINS – Novel Therapeutic Targets to Treat Age-Associated Diseases," the review appears in today's issue of the journal *Nature Reviews Drug Discovery*.

Sirtuins are a family of enzymes which target genes that control aging. There are a total of seven sirtuin enzymes that exist in mammals. SIRT1 is the founding member of this class of enzymes and is currently the most studied of the group. When activated, SIRT1 appears to mimic some of the positive health effects seen in calorie-restricted animals.

"We are excited to be at the forefront of this research, which continues to intensify as we see positive results from early human clinical studies," said Christoph Westphal, M.D., Ph.D., Chief Executive Officer of Sirtris, a GSK company. "The body of clinical data supporting the role of SIRT1 activation as a viable mechanism for treating a broad range of diseases of metabolism and aging is growing."

Peter Elliott, Ph.D., Senior Vice President of Development, said, "At Sirtris, we are targeting the genes which control the aging process with

the potential to treat diseases of aging such as diabetes, neurodegeneration, cancer, and inflammation."

This review highlights the molecular mechanism of action of sirtuins with a view towards diseases where SIRT1 activation shows therapeutic promise. Such diseases of aging include Type 2 Diabetes and mitochondrial disorders, cardiovascular disease, cancer, neurodegeneration and inflammatory diseases. One of the first small molecules discovered to exhibit the positive effects of calorie restriction is resveratrol, a natural ingredient found in red wine. Since then, Sirtris has developed its own proprietary formulation of resveratrol, SRT501. Early clinical studies in patients with Type 2 Diabetes indicate that SRT501 may lower glucose and improve insulin sensitivity. Sirtris also has new chemical entities (NCEs) which are structurally unrelated to and one-thousand times more potent than resveratrol. Sirtris' first new chemical entity is currently being evaluated for safety and tolerability in a Phase 1a study in humans.

"We are beginning to understand more about activation of other enzymes in the sirtuin family, SIRT2-7, and we're encouraged by early data that indicates a role for other sirtuins in multiple therapeutic areas," continued Dr. Westphal.

Source: Pure Communications Inc.

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