



Medical Education and Research Grant Outcome Report

Name: Linking Aging, Resveratrol and Sirtuins

Principal Investigator: John M. Denu, PhD

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Department: Biomolecular Chemistry

Program: Collaborative Health Sciences Program

Grant Duration: 07-01-2007 to 6-30-2009 (24 months)

Expenditures: \$300,000 (100%)

Use of Funds (Taxonomy): Basic Research

Research Keywords: metabolism, caloric restriction, sirtuins, regulation, aging

► **Description:** This project explored the molecular basis for the health benefits of caloric restriction and resveratrol, a plant compound found at high levels in wine and known to harbor a variety of cardiovascular and neurological health benefits, by performing a detailed metabolic analysis of mice subjected to these treatments. The hypothesis was that sirtuin enzymes, a novel group of conserved proteins, mediate the cellular effects of both caloric restriction and resveratrol.

► **Contributions/Results:** The initial results have provided new insight into the molecular basis of healthy aging and the role played by the sirtuin family of enzymes in that process.

The investigators discovered that several metabolites, which control the body's adaptive response to low fuel, are affected in the sirtuin 3 (SIRT3) knockout strain of mice. Nuclear magnetic resonance and mass spectrometer analysis have shown that the metabolite levels differed considerably in calorie restricted mice compared to control mice. Resveratrol treated mice, however, showed little change from the control. The investigators found support for the theory that sirtuins are involved in metabolic regulation, although the specific mechanisms and potential uses of sirtuin will require further study.

The investigators have also looked at several enzymes in metabolic pathways to assess changes in their activities to caloric restriction and resveratrol.

► **Met Objectives:** Project completed

► **Timeline for Application of Results:** Between 3-5 years

► **New Partnerships or Collaborations:** The results have suggested that specific metabolic pathways are controlled by sirtuin enzymes. Denu will continue to work with Tom Prolla, Department of Medical Genetics at UW School of Medicine and Public Health and Rick Weindruch, UW Institute on Aging, to explore these avenues.

► **Matched Dollars (cash or in-kind):** None

► **Dissemination:** This work has led to publications in the journals *Analytical Biochemistry* and *Cell*. Additional publications from this work are expected. Information about the efforts of the lab in regard to this project have appeared in *American Society of Biochemistry and Molecular Biology Today*.

► **Additional Funding:** The investigators will be pursuing funding from the National Institutes for Health.