

**The Calorie Restriction Society**

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**For immediate Release**

The CALORIE RESTRICTION SOCIETY to discover secrets of aging

Would you like to live an extraordinarily long and healthful life – perhaps starting a different career at 70 and pursuing your new ambition with the same zeal you had when you were young?

Or would you like to function at your peak without the significant decline that most experience as they age?

The Members of the Calorie Restriction Society give a resounding yes! to these and related questions. Inspired by hundreds of scientific studies, showing that calorie restriction slows aging in everything from yeast to monkeys, many have joined the calorie restriction movement in hopes of living long and healthfully. And for some it has worked wonders. Consider Ralph – who, going on 104, is the eldest member of the Society. Having only just retired from his real estate agency at the youthful age of 101, still dating, and going to his high school's football games – he is positive, spirited, and happy about having limited his calories for the past half century.

But others are not so lucky. Some do not experience the robustness and superb health that many devoted calorie restrictors enjoy. Unlike the scientific studies where calorie-restricted animals follow a controlled dietary and exercise regimen, some calorie-restricted humans – zealous to achieve optimal health – may actually go astray because of their lifestyle choices.

Consider dietary supplements, for example. In contrast to calorie restriction, which in certain cellular pathways slows apoptosis, some favorite supplements actually increase apoptosis. Or consider the effect of calorie restriction on p53 – the vital regulator of mutant cells that are on their way to becoming cancer. Normally, down-regulation of p53 by CR is logical: the CR'd body produces fewer mutant cells, so p53 is not needed so much. But what about the calorie restrictor who decides to supplement with estrogen, testosterone or other hormones that promote cell proliferation? Is that individual at more risk for developing cancer?

**People need answers!** It is vital to utilize newly available analytical methods to determine what's happening at the genetic and cell-signaling levels in human calorie restrictors. Serious longevists need scientifically verified ways to evaluate lifestyle choices.

That's why the Calorie Restriction Society has initiated a milestone study that will begin to establish genetic and cell-signaling profiles of human calorie restrictors and show how these regulators correspond to clinical markers that can easily be tested in most labs.

Three world-renowned scientists will implement this project.

### **Luigi Fontana, M.D., Ph.D.**

Luigi Fontana brings expertise from his years as a celebrated physician, as well as a researcher in Metabolism. His passion is aging science. Departing from experiments on animals, Dr. Fontana made medical history with studies, showing that calorie restriction has definite age-slowng effects in humans:

1) **Long-term calorie restriction is highly effective in reducing the risk for atherosclerosis in humans.**

*Proceedings of the National Academy of Sciences of the U. S. A.* 2004 Apr 7;101(17):6659-63. Fontana L, Meyer TE, Klein S, Holloszy JO. PMID: 15096581

2) **Long-term caloric restriction ameliorates the decline in diastolic function in humans.**

*Journal of the American College of Cardiology.* 2006 Jan 17;47(2):398-402. Meyer TE, Kovacs SJ, Ehsani AA, Klein S, Holloszy JO, Fontana L. PMID: 16412867

A key aspect of this new CR study will be to build on the CR study reported by Dr. Fontana in 2004, thus establishing a longitudinal aspect to the evaluation and adding many further tests. The major objective of the proposed research is to determine whether long-term CR with adequate nutrition results in some of the same metabolic, hormonal and gene expression changes in humans that have been shown to be made by CR in rodents.

This study may also help to characterize in humans new markers of aging and longevity that can help physicians contribute to the prediction of mortality and morbidity of the general population.

Dr. Fontana says, "It is the hope of those of us studying CR that, once its mechanisms of action are understood, it will be possible to mimic the effects of CR on aging using less drastic interventions."

### **Stephen Spindler, Ph.D.**

Stephen Spindler, distinguished professor of biochemistry at UCLA, researches the molecular basis of aging. One of his great contributions to aging science is the genetic profiling of calorie restriction effects on animals. Dr. Spindler in one of his famous CR studies ("Use of microarray biomarkers to identify longevity Therapeutics," *Aging Cell*, 2006. PMID: 16441842) writes, "CR acts rapidly, even in late adulthood, to begin to extend life- and health-span in mice. We have linked these effects with rapid changes in the levels of specific gene transcripts in the liver and the heart. Our results are consistent with the rapid effects of caloric intake on the lifespan and/or biochemistry and physiology of *Drosophila*, rodents, rhesus macaques and humans."

Building on years of work on animals, Dr. Spindler and his lab will provide insights into how calorie restriction affects genetic expression in calorie-restricted humans.

Two of his research papers that bear particularly strongly on this project:

1) **Temporal linkage between the phenotypic and genomic responses to caloric restriction.**

*Proceedings of the National Academy of Sciences of the U. S. A.* 2004 Apr 3;101(15):5524-9.

Dhahbi JM, Kim HJ, Mote PL, Beaver RJ, Spindler SR. PMID: 15044709

2) **Gene expression and physiologic responses of the heart to the initiation and withdrawal of caloric restriction.**

*The journals of gerontology. Series A, Biological sciences and medical sciences.* 2006 Mar;61(3):218-31.

Dhahbi JM, Tsuchiya T, Kim HJ, Mote PL, Spindler SR. PMID: 16567370

**Shin-Ichiro Imai, M.D., Ph.D.**

Shin Imai joins the study to focus on the function of mammalian Sir2 NAD-dependent deacetylase. Dr. Imai writes: Sir2 has been demonstrated to play key roles in regulating aging and longevity in lower eukaryotes and also implicated as a mediator for caloric restriction, which retards aging and extends life in variety of organisms.\*

\* <http://dbbs.wustl.edu/DBBS/website.nsf/RIB/107B3F3826243E9B86256D4E005B2D3A>, accessed July 24, 2006

The concentration of his lab at Washington University is on the molecular mechanisms of mammalian aging and longevity:

1) **Increased dosage of mammalian Sir2 in pancreatic beta cells enhances glucose-stimulated insulin secretion in mice.**

*Cell metabolism.* 2005 Aug;2(2):80-2.

Moynihan KA, Grimm AA, Plueger MM, Bernal-Mizrachi E, Ford E, Cras-Meneur C, Permutt MA, Imai S. PMID: 16098828

2) **The NAD biosynthesis pathway mediated by nicotinamide phosphoribosyltransferase regulates Sir2 activity in mammalian cells.**

*The Journal of biological chemistry.* 2004 Dec 3;279(49):50754-63.

Revollo JR, Grimm AA, Imai S. PMID: 15381699

As a physician, Dr. Imai is very eager to study the genetic and cell-signaling effects of CR on humans, as compared to those effects found on mice and other laboratory animals by his lab and others.

## **This study will happen only with your help.**

The Calorie Restriction Society needs to raise \$230,000 to move forward with this important work. The research will study three groups of volunteers, 40-70 years old:

- 1) 30 individuals who have practiced long-term (>3 yrs) intentional CR;
- 2) 30 endurance athletes matched with the CR individuals in terms of body fat content, age, gender, education, and socioeconomic status; and
- 3) 30 healthy lean sex- and age-matched controls.

The study protocol is well worked out to be very informative: An academic clinical nutrition center will evaluate the diets of the subjects. DXA (Dual-energy X-ray Absorptiometry) will be used to measure fat mass and fat free mass. The researchers will assess cardiovascular and lung function, growth factors, inflammation and oxidative stress markers.

## **This study will happen only if you help.**

Since the Calorie Restriction Society needs to raise \$230,000 for this important work, we need contributions large and small. Make an investment that is priceless and learn more about slowing aging – what works and what doesn't.

Please send your donation directly to our Treasurer  
David R. Stern, 7223 S Rt. 83 #142, Willowbrook, IL 60527

Or to

Bob Cavanaugh at the Calorie Restriction Society, 187 Ocean Drive, Newport, NC 28570

The Calorie Restriction Society is a tax-exempt organization under Section 501(c)3 of the IRS Code. Contributions are fully tax deductible.

Questions? Please be in touch with our Vice President for Research, Paul McGlothin ([research@calorierestriction.org](mailto:research@calorierestriction.org) or toll free: 866-894-1812). Want to know more about the Calorie Restriction Society? Ask Paul or contact Brian Delaney ([president@calorierestriction.org](mailto:president@calorierestriction.org)) or Meredith Averill ([boardchair@calorierestriction.org](mailto:boardchair@calorierestriction.org)).

Please hurry! We must raise the funds in time for testing to begin this fall at Washington University Medical School.

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