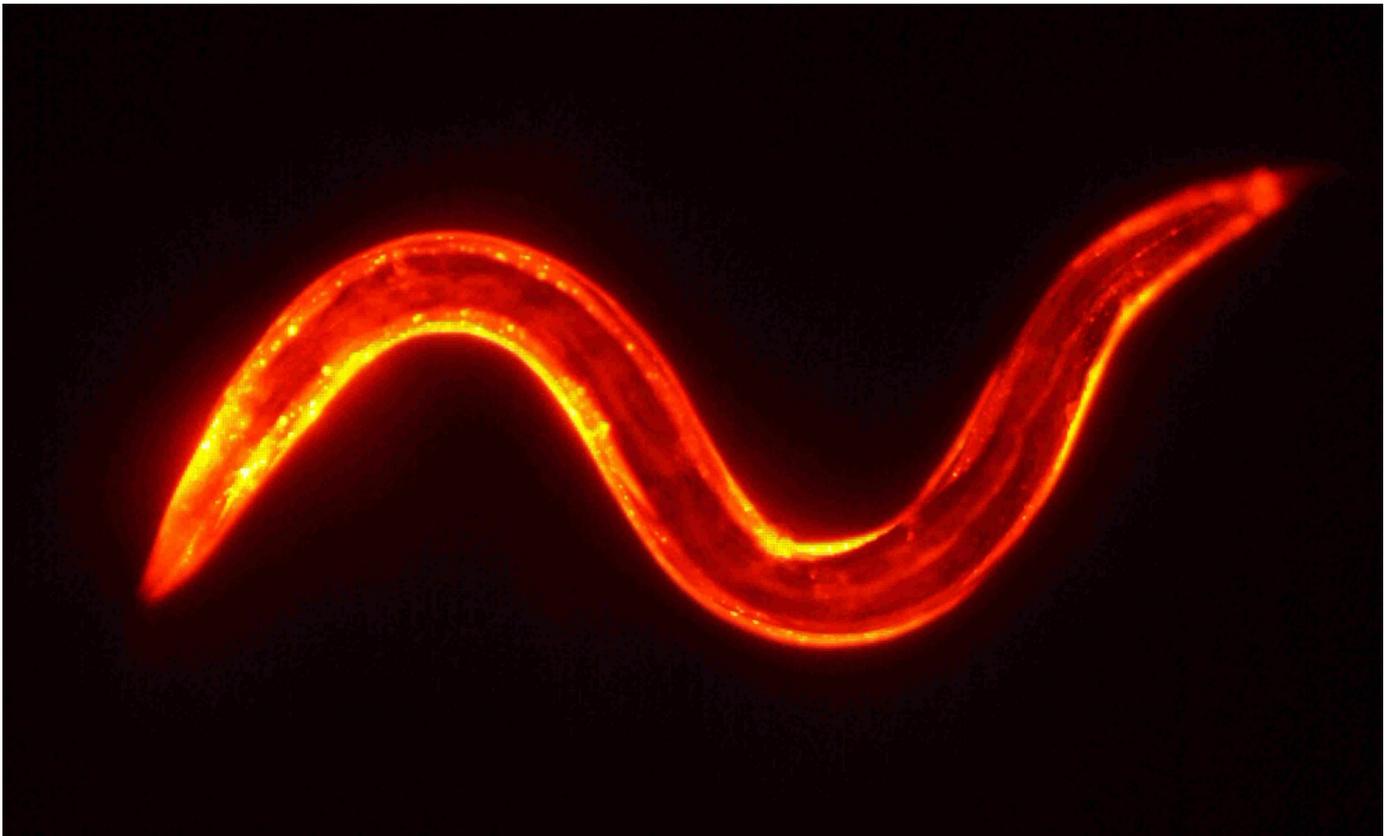


## Healthcare industry BW

# Freiburg researchers discover new effect of insulin

**Working with colleagues from the Harvard Medical School in Boston, USA, researchers from Freiburg University have discovered a previously unknown role of insulin in ageing and lifespan.**



Experiments in the digestive tract of *Caenorhabditis elegans* show that a previously unknown role of insulin can affect both ageing as well as lifespan. (Photo: Baumeister group)

The paper, which was published in the 21st March issue of *Cell*, reports that insulin inhibits a master stress regulator protein known as SKN-1. The researchers also found that increased SKN-1 activity increased lifespan. SKN-1 controls what is known as phase-2 detoxification pathway in medicine, a network of genes that protects cells and tissue against oxidative stress. This damage is caused by elevated levels of free radicals (by-products of metabolism) and by various environmental toxins. The new finding was demonstrated in experiments on the digestive system of *C. elegans*, a worm often used as model organism for human ageing-related diseases.

## Does insulin make the body sensitive to oxidative stress?

Four years ago, the Freiburg researchers led by Professor Dr. Ralf Baumeister discovered a gene that codes for an important cellular enzyme known as SGK-1 and that controls the cellular ageing programme in the insulin pathway. "At the same time, our colleagues at the Joslin Diabetes Centre at Harvard Medical School found that the stress regulator SKN-1 also had an impact on lifespan," said Baumeister, one of the authors of the recently published paper. "It was clear that we had to compare our data and work together on this topic. We discovered that we had approached the same phenomenon from two sides."

This new role of insulin should be taken into account when looking at the various functions of insulin in the human body. The publication suggests that insulin, under certain circumstances, might reduce the cellular defence against oxidative stress more than previously anticipated.

## New understanding of ageing

The researchers are now hoping that fine-tuning the activity of SKN-1 may lead to increased resistance to chronic diseases and influence longevity. The work could therefore be important for the understanding of diabetes and the many problems associated with the disease, particularly vascular (atherosclerosis) and renal complications.

"However, the major implication of our research is that we have found something new that effects lifespan and ageing," said Baumeister adding that, "although it has been known since the 1990s that the insulin pathway plays an important role in cellular ageing in many organisms, the majority of the details are still unknown." The researchers previously assumed that insulin inhibited a gene regulator protein known as FOXO. FOXO is important in diabetes metabolism, tumour suppression and stem cell maintenance. In addition, FOXO also controls genes that are involved in stress resistance. Studies in *C. elegans* showed that reduced insulin signalling, for example through the manipulation of SGK-1, boosted the activity of a FOXO protein known as DAF-16, leading to greater resistance to stress and a longer lifespan.

## Like archaeologists who discover a secret treasure chamber

The new finding shows that SKN-1 is a second master gene regulator that is also inhibited by insulin. The paper also suggests that SKN-1 controls a distinct genetic programme of stress defence and anti-ageing. "We felt like archaeologists discovering a secret treasure chamber. The activation of SKN-1 was all that was needed to increase longevity of the worm!" said Baumeister, the director of the Freiburg Centre for Biosystems Analysis ZBSA. His objective is to further investigate the complex regulatory network of the genes involved in ageing.

The experiments will have to be repeated in mammals, where insulin and insulin-like growth factor-1 (IGF-1) have a complex array of effects, of which the relation still needs to be clarified. However, according to the authors, in the past other findings in the *C. elegans* model have generally turned out to be applicable to mice and humans.

## *C. elegans* again an excellent model for human disease



The worm *C. elegans*, which is only 1 mm long, is one of the most important model organisms for insulin and ageing research. (Photo: Baumeister group)

The Freiburg researchers are using *C. elegans* as a model for a number of human diseases associated with ageing. In the past, the work of the researchers has contributed to gaining a better understanding of the processes involved in Alzheimer's, Parkinson's and muscular dystrophy. The research at the University of Freiburg is funded through the BMBF, the Landesstiftung Baden-Württemberg foundation, the German Chemical Industry Fund, DFG and the European Community.

### **Centre for Biosystems Analysis ZBSA**

The ZBSA is an interdisciplinary research centre supported with funds from the state of Baden-Württemberg and the University of Freiburg. Experimental scientists from biology and medicine are working together with theoretical scientists from physics and mathematics, computer scientists and robotics specialists for a better understanding of the complex interplay of genes and proteins in the organism and in the development of disease. The ZBSA is the central facility for the scientific projects that are funded by the German Excellence Initiative.

Source: Press Office - University of Freiburg - 20.04.2008

Further information:  
ZBSA - Centre for Biosystems Analysis

ZBMZ (Medical Faculty), Bioinformatics & Molecular Genetics (Biological Faculty)  
Prof. Dr. Ralf Baumeister  
Schänzlestr. 1  
D-79104 Freiburg i.Brsgr.  
Tel.: +49-761-203 8350  
Fax: +49-761-203 8351  
Mobile: +49-1520-986 3097  
E-mail: [baumeister@celegans.de](mailto:baumeister@celegans.de)

---

## Article

29-Mar-2008  
BioRegion Freiburg

 [More information](#)