

Doctoraat in Functional Genomics

Caenorhabditis elegans as a model for studying feeding behaviour

Promotor: *Liliane Schoofs*

Description: Functional elucidation of the cholecystokinin signaling pathway in nematodes.

A pandemic of metabolic diseases (atherosclerosis, diabetes mellitus, and obesity), unleashed by multiple social and economic factors beyond the control of most individuals, threatens to diminish human lifespan for the first time in the modern era. Given the redundancy and inherent complexity of processes regulating the uptake, transport, catabolism, and synthesis of nutrients, magic bullets to target these diseases will be hard to find. Recent studies using the worm *Caenorhabditis elegans*, indicate that this tiny nematode possesses unique attributes that could help in identifying, investigating, and even validating new pharmaceutical targets for these diseases (1-6). As in all living organisms, survival in nematodes requires adequate management of energy supplies. Core fat and sugar metabolic pathways are conserved between mammals, arthropods and nematodes (5; 7-10).

Members of the mammalian cholecystokinin (CCK) peptide family, including the arthropod sulfakinins, and their cognate receptors, play an important role in the regulation of feeding behavior and energy homeostasis. Our lab has now uncovered a CCK signaling system in nematodes with similar structure and function with respect to digestive enzyme secretion and fat storage (2-3). Recent quantitative real-time PCR and microarray experiments indicate that the *C. elegans* CCK system is likely to be involved in fat storage, survival responses during starvation and the initiation and/or maintenance of the dauer stage (longliving survival stage induced by starvation and crowding). As obesity and its alimentary diseases are rapidly becoming the industrial epidemic of the 21st century, the fundamental study of this signaling system in nematodes could open the door to a better understanding of the role of this system in mammalian feeding behavior, fat storage and satiety.

We now plan to study this system in more detail to identify the up- and downstream elements and unravel the entire CCK pathway in nematodes. To do this you will use a combinatorial approach including techniques of basic biochemistry, molecular biology, reverse and forward genetic screens, physiology, genomics and phenomics. As part of the phenotypic analysis of feeding behaviour you will develop new microfluidics experiments for *C. elegans* (11-12) together with Professor Jeroen Lammertyn (www.biosensors.be).

References

Promotor: Prof. Dr. Liliane Schoofs (<http://bio.kuleuven.be/df/LS/>)

Co-promotors: Prof Dr. Jeroen Lammertyn, Dr. Tom Janssen

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Functional Genomics and Proteomics