GENETICS OF THE TEMPERATURE-SIZE RULE IN C. ELEGANS

Jan Kammenga [1], Agnieszka Doroszuk [2], Joost Riksen [2], Esther Hazendonk [3], Laurentiu Spiridon [4], Andrei-Jose Petrescu [4], Marcel Tijsterman [3], Ronald Plasterk [3], Jaap Bakker [2]

[1] *Wageningen University, Nematology, Binnenhaven 5, 6709PD, Wageningen, The Netherlands*
[2] *Wageningen University, Laboratory of Nematology, Binnenhaven 5, 6709PD, Wageningen, The Netherlands*
[3] *Hubrecht Laboratory, Netherlands Institute of Developmental Biology, Uppsalalaan 8, 3584CT, Utrecht, The Netherlands*
[4] *Institute of Biochemistry of the Romanian Academy, Bucharest, Romania*

Jan.Kammenga@wur.nl

Ectotherms rely for their body heat on surrounding temperatures. A key question in biology is why most ectotherms mature at a larger size at lower temperatures, a phenomenon known as the temperature–size rule. Since temperature affects virtually all processes in a living organism, current theories to explain this phenomenon are diverse and complex and assert often from opposing assumptions. Although widely studied, the molecular genetic control of the temperature–size rule is unknown. We found that the *Caenorhabditis elegans* wild-type N2 complied with the temperature–size rule, whereas wild-type CB4856 defied it. Using a candidate gene approach based on an N2 x CB4856 recombinant inbred panel in combination with mutant analysis, complementation, and transgenic studies, we show that a single nucleotide polymorphism in *tra-3* leads to mutation F96L in the encoded calpain-like protease. This mutation attenuates the ability of CB4856 to grow larger at low temperature. Homology modelling predicts that F96L reduces TRA-3 activity by destabilizing the DII-A domain. The data show that size adaptation of ectotherms to temperature changes may be less complex than previously thought because a subtle wild-type polymorphism modulates the temperature responsiveness of body size. These findings provide a novel step toward the molecular understanding of the temperature–size rule, which has puzzled biologists for decades.