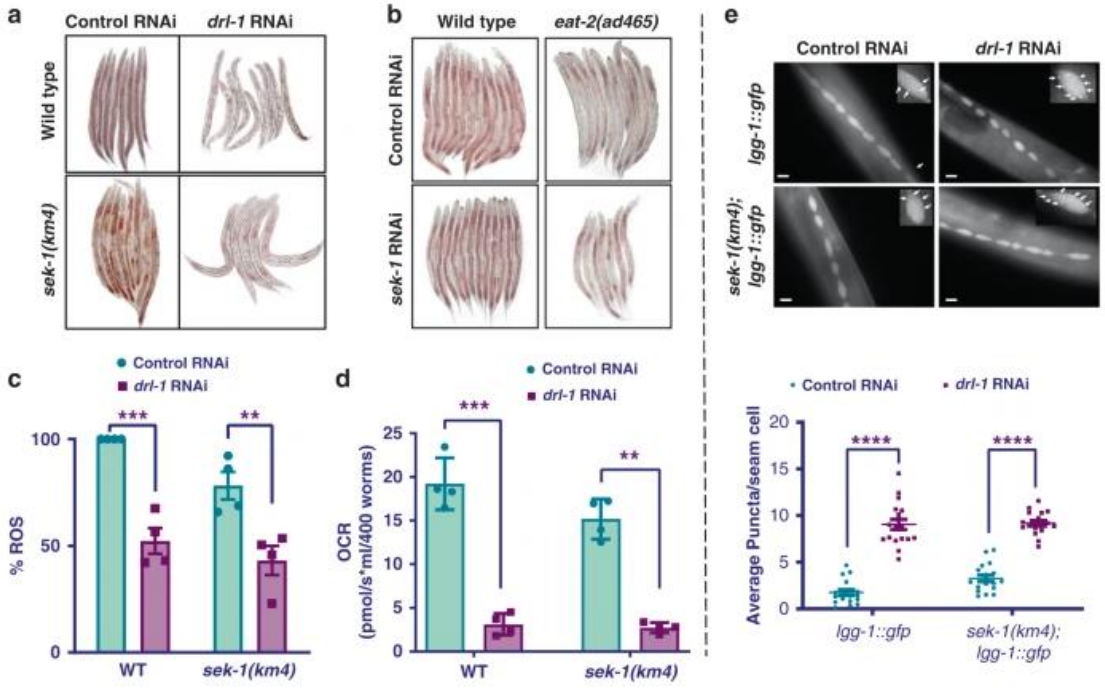
Polyunsaturated fatty acids and p38-MAPK link metabolic reprogramming to cytoprotective gene expression during dietary restriction

Scientists at DBT's National Institute of Immunology (NII), New Delhi, have shown in multiple model systems that restricting the amount of food or nutrition can delay many age-onset diseases and increase life span. This process is called calorie restriction (CR) or dietary restriction (DR). Their lab is interested in understanding how DR works at the molecular level and finding out how cells communicate metabolic states to regulate genes that code for proteins beneficial for health and longevity.



In this direction, previously team had shown that at the onset of DR, organisms shift their metabolism to an energy efficient one, producing lower quantities of harmful reactive oxygen species (ROS) and molecules that attack important cellular machineries. This reprogramming of metabolism also activates cell-protective genes and together, they support the increased health and life span in organisms undergoing DR. In this current study, we have discovered how cells communicate information of changes in metabolism to activate cell-protective genes. We show that certain types of fatty acids (called polyunsaturated fatty acids or PUFA) are produced by the organism undergoing DR. These fatty acids can then stimulate a stress-responsive, signal transduction protein cascade that helps in activating the cell-protective events.

For deciphering these complex molecular events, we employed *Caenorhabditis elegans*, a small worm that has been a workhorse for aging biology researchers for over 30 years. This worm recapitulates many of the attributes of human aging and important biological phenomenon discovered in the worms has been found to be conserved in mammals. Our study is important because it shows for the first time how cells communicate internal metabolic parameters to control gene expression required for extended longevity and health span on DR. It will contribute to the growing body of literature on understanding the mechanisms of longevity assurance on DR that will eventually lead to pharmaceutical interventions to delay aging and age-related diseases.

Research over the last few decades has unequivocally proven that aging is controlled by our genes as well as the environment. One of the major environmental inputs that control the plasticity of aging is food or nutrients. To this effect, we have learnt that over nutrition is killing more people in today's world in forms of various life style diseases, compared to undernourishment. Over nutrition-induced obesity is a leading cause of debilitating diseases like type II diabetes, cardiovascular diseases, hypertension, cancer etc. Such diseases have immense economic and societal costs that hinder progress of a nation.

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