INTERMITTENT KETOGENIC DIETS EXTEND LIFESPAN AND ATTENUATE INFLAMMAGING IN MALE MICE

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A ketogenic diet (KD) has been shown to increase functional lifespan in male mice when fed isocalorically to a control diet (CD). However, it is not clear if intermittent ketogenic diets (IKD) that induce brief and recurring periods of ketosis would be as effective at prolonging lifespan. In the present study, 12-month-old C57BL/6J male mice were fed an intermittent single day KD (KD fed on Mon, Wed and Fri each week, IK1) or 2-day KD (KD fed on 2 consecutive days each week, IK2). These two IKD regimes were selected to mimic the widely used alternate-day or 5:2 intermittent fasting approaches, without the caloric deficit. Our results showed that lifespan was significantly increased in both IK1 and IK2 groups, with IK1 showing a 13.6% and IK2 showing a 7.9% increase in median lifespan compared to the CD (p < 0.01). At 27 months of age, levels of circulating proinflammatory cytokines were significantly decreased in IK1 and IK2 mice compared to control mice. Also, levels of proinflammatory cytokines were significantly elevated in 27-month-old control mice compared to 12-month-old mice, while levels in IK1 and IK2 mice were not significantly altered with aging, and these effects were still persistent during days the animals were fed the CD. Unlike the continuous KD, health span measures were not altered in IK1 or IK2 mice at 26 months of age. In summary, IKDs that produce shorts episodes of ketosis can be effective at extending longevity in mice, possibly by attenuating systemic inflammation with aging.

SIGNIFICANT CHANGES IN TRANSCRIPTOME DURING AGING HAVE BEEN OBSERVED IN VARIOUS TISSUES AND CELL TYPES, EVEN AT THE SINGLE-CELL LEVEL. HOWEVER, THE MOLECULAR MECHANISMS THAT UNDERLY THESE CHANGES REMAIN POORLY UNDERSTOOD. USING AN EX VIVO MESENCHYMAL STEM CELLS (MSC) REPLICATIVE AGING MODEL AND HI-C TECHNOLOGY, WE DISCOVERED THAT, RATHER THAN LARGE-SCALE CHANGES IN CHROMOSOME CONFORMATION, ALTERATIONS TO SUPER ENHANCER – PROMOTER LOOPING INTERACTIONS HAD THE BEST POSITIVE CORRELATION WITH AGE-ASSOCIATED TRANSCRIPTOME. FURTHERMORE, WE FOUND EVIDENCE THAT THESE AGED-INDUCED TRANSCRIPTOMIC CHANGES ARE MEDIATED BY YY1, A KEY REGULATOR OF PROMOTER-ENHANCER LOOPING. THIS WORK, FOR THE FIRST TIME, UNVEILED A MOLECULAR MECHANISM ELUCIDATING THE CHANGES IN TRANSCRIPTION DURING AGING.

REGENERATION OF AGING LUNG TISSUE: A NOVEL WAY OF REOPENING THE PLASTICITY WINDOW OF POSTNATAL ALVEOLAR TYPE II CELLS

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Prevalence of chronic lung diseases, such as pulmonary fibrosis and chronic obstructive pulmonary disease, have been found to increase with age. Pulmonary disease can occur from failure to maintain alveolar type (AT) 1 and alveolar type 2 cells located in the epithelium of the lung. It is currently known that AT2 cells are the facultative stem cells of the lung, and can transform into AT1 cells which make up the structure of the alveoli. This process happens throughout embryonic development, but AT2 cells can also replenish AT1 cell populations post lung injury. This research investigates whether this process that normally occurs during development can also occur in mature AT2 cells, and studies