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# Human V-ATPase a2 P405L Mutation Results in Cutis Laxa by Affecting V-ATPase Assembly and/or Stability

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## MEDABSTRACTS

## Assessing the Effects of High Sugar and Protein Diets on Reproduction and Longevity in Crickets

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Studies on longevity are becoming increasingly important due to the aging population. The house cricket, Acheta domesticus, is an effective model for longevity studies due to its short lifespan of 120 days. This study explored the effects of diet on reproduction and longevity in A. domesticus. There were four treatment groups: 1) control diet with reproduction, 2) control diet with reproductive isolation, 3) high protein diet with reproduction, and 4) high sugar diet with reproduction. We began monitoring the crickets following maturity to allow for reproductive analysis. Death counts were conducted daily, followed by replenishment of food and water supplies. Egg counts and weight measurements were conducted weekly. Results showed that crickets on the high sugar diet had significantly longer lifespan than other treatments. The lowest lifespan was seen in crickets on the high protein diet. Conversely, the highest reproductive output was seen in the high protein diet and the lowest was in the high sugar diet. The reproductively isolated control group had a significantly greater longevity than the reproductive control group. Taken together, the research shows an inverse relationship between reproduction and longevity as modulated by dietary consumption of proteins and carbohydrates.

## Human V-ATPase a2 P405L Mutation Results in Cutis Laxa by Affecting V-ATPase Assembly and/or Stability

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Cutis Laxa is a genetic disorder in which a patient's skin becomes loose and inelastic. The autosomal recessive variant of this disorder has been linked to a genetic mutation in vacuolar-type H+-ATPase (V-ATPase). This enzyme contains a cytosolic domain, responsible for hydrolyzing ATP, and a membrane-bound domain that actively transports protons across intracellular and plasma membranes. Proton pumping regulates housekeeping functions inside the cell, resorption of bone, and acidification of urine. A human missense mutation in one of the V-ATPase subunits (a2 P405L) that causes Cutis Laxa was recreated in the yeast V-ATPase to elucidate why a single amino acid change could affect enzyme activity. The mutation recreated in the yeast V-ATPase disrupted activity based on the inability of yeast to acidify their vacuoles. The membrane domain of the mutant V-ATPase was correctly assembled and targeted to the yeast vacuole but the cytosolic domain was not attached explaining why the vacuoles were not acidic. These results suggest that the loss-of-function mutation present in cutis laxa leads to decreased V-ATPase stability and/or assembly. Further experiments will be designed to assess if the mutation results in a conformational defect, and if so, therapeutics assisting in protein folding can be explored. Such therapeutics not only hold promise for cutis laxa, but also for other V-ATPase genetic diseases such as osteopetrosis, distal renal tubular acidosis and male sterility.

# The Impact of HIV/AIDS Criminalization on Awareness, Preventiuon and Stigma in the GTA

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In Canada, the exposure and/or transmission of HIV is punishable by criminal law. Deficiencies in Canadian-focused research about the implications of criminalizing HIV exposure demonstrate a need for locally applicable research evidence. This study aims to investigate the impact of HIV/AIDS criminalization on awareness, prevention, and stigma in the Greater Toronto Area through a scoping review and stakeholder interviews. Eleven databases were searched and the results were reviewed for relevance. Search yielded 1301 results, 148 relevant articles. Primary research is limited to 12 articles, while the remainder is comprised of case reports, editorials, commentaries and essays (n=136). Literature highlights confusion regarding behaviours constituting "significant risk", resulting in difficulties in the application of legal precedent and uncertainty regarding HIV knowledge in the general public. Some evidence suggests that criminalization contributes to disincentives for testing and disclosure, strained therapeutic relationships, HIV related stigma, and barriers to promoting shared responsibility for safer sex. Stakeholders (policy/content experts, executive directors and front-line workers from community-based HIV/AIDS organizations) were identified, and a purposive sample invited to participate in one-on-one, semi-structured interviews. Interviews depict the negative impact of criminalization on prevention efforts, heightened community awareness of prosecutions, and increased stigmatization of people living with HIV/AIDS. Participants recommend guideline development to optimize the use of criminal law pertaining to HIV/AIDS non-disclosure. These findings will significantly contribute to increasing primary research on the impact of HIV/AIDS criminalization in the Greater Toronto Area. Further research is necessary to characterize the impact from the perspective of people living with HIV/AIDS.