Candidates for a Causative Gene Mutation Causing an Atypical Hypothyroidism in a Feline Research Breeding Colony

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Objective:
The purpose of this study was to identify the gene mutation causing hypothyroidism within a sample population using a feline genetic disease model spanning multiple generations.

Background and Significance:
- Hypothyroidism: thyroid gland produces insufficient amounts of thyroid hormones.
- Thyroid hormone regulates basic metabolic functions such as heart rate, ventilation rate, cardiac output and basal metabolic rate.
- Approximately 5% of the adult human population is affected by hypothyroidism (NIH).
- Thyroid hormone plays a role in brain and skeletal system development. Symptoms can be caused due to thyroid gland dysgenesis or dyshormonogenesis.
- Identifying the cause of the abnormal thyroid function can lead to effective treatment of the hypothyroid symptoms and a better understanding of thyroid homeostasis.

Methods Overview:

Results:

<table>
<thead>
<tr>
<th>Gene</th>
<th>Samples from L to R: Vagus (A), Sputnik (A), Artemis (C), Hamm (N)</th>
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</thead>
<tbody>
<tr>
<td>TG</td>
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<tr>
<td>DUOX1</td>
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<td>SLC5A5</td>
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Discussion:
TG: The mutation at the TG locus was not consistent with the endocrine data of the control animals. Multiple families were genotyped and showed no concordance between mutations and endocrine data.
DUOX1: The mutation at the DUOX1 showed mutations in the control animals consistent with endocrine data. However, upon genotyping of multiple families, there was no concordance between at the DUOX1 locus and endocrine data.
SLC5A5: Upon genotyping the three control animals, it was seen that all animals produced within the feline colony were fixed for the mutation at the SLC5A5 locus. This was further confirmed by genotyping the colony’s founder animals, of which all were fixed at the SLC5A5 locus. The data suggests that mutations at the aforementioned loci are not predictive of the disease. In the case of SLC5A5, the status of this population as fixed for the mutation cannot be ruled out as being a permissive genotype for the condition in this population. Future studies will focus on further loci which show homozygous mutant alleles in the proband.

References:
1. NIH-https://www.niddk.nih.gov/health-information/endocrine/hypothyroidism/Pages/fact-sheet.aspx

Acknowledgements: Funding was provided by ISU Honors Program Foundation and Cecil R. and Phyllis Stewart Endowment Fund.