Genetic Polymorphisms in the Cholesterol Transport Pathway of Parrots
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Hypothesis
Parrots predisposed to atherosclerosis will have functional polymorphisms in PCSK9, a gene related to low density lipoprotein (LDL) uptake from blood.

Atherosclerosis
Atherosclerosis is the hardening and narrowing of arteries due to plaques that affect both humans and parrots.\(^1\)

Key reasons parrots are a useful animal model for human atherosclerosis: \(^2\)
1) they can develop it spontaneously
2) it can be induced experimentally
3) lesions are histopathologically similar

Studies have shown that increased total cholesterol (TC) is highly correlated to the development of atherosclerosis in humans and parrots.\(^3\) We predict that genetic mechanisms leading to high TC in humans are the same in parrots.

Candidate Gene: PCSK9

The gene PCSK9 can lead to dyslipidemia if mutated. PCSK9 encodes a protein that binds to and degrades the LDL receptor (LDLR). Once degraded, LDLR can no longer remove LDL from the blood.\(^4\)

Methods

Whole blood samples obtained from:
13 Hispaniolan Amazons (HAP) = high risk pop.
16 Orange-Winged Amazons (OWA) = medium risk pop.
15 Cockatoos species (TOO) = low risk pop.

Isolated plasma for lipid profile analysis and biochemistry panels

Removal of unhealthy or reproductively active subjects

Lipid profile results were statistically compared between groups using Kruskal-Wallis Test

Isolated DNA from heparin blood pellets using 5' ArchivePure

Optimized and cleaned PCR products were submitted for Sanger sequencing to UCD Genomics Core

Sequences were aligned using DNA Star Genomics Suite to identify and catalogue frequency of polymorphisms

All polymorphisms were analyzed for functional significance (amino acid sequence, protein structure, correlation to lipid profile results)

Identified SNPs submitted to GenBank

Results

Figure 1. Amazon parrots have a higher prevalence of atherosclerosis compared to cockatoos suggesting a genetic etiology.\(^3\) Figure reproduced from Beaufrère, 2013.

Figure 3. Cholesterol values vs. Parrot species. According to a Kruskal-Wallis test median dLDL levels (A), median HDL levels (B), and median TC levels (C) were significantly different between all species with p values p=0.0014, p=0.0002, and p<0.0001 respectively.

Table 1. Mutations observed that change the protein sequence of PCSK9.
Het = Heterozygote. Ho = homozygous. HAP = Hispaniolan Amazon parrot. OWA = Orange-winged Amazon parrot. TOO = Cockatoo species.

Amazon parrots have significantly higher plasma TC, HDL, and dLDL levels compared to Cockatoos. This finding supports what was found in previous literature.\(^4\)

Discussion

Figure 4. The structure of processed PCSK9.

Confirming the long-suspected genetic influence of atherosclerosis in parrots is the first step to a deeper understanding of this condition.

References

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Figure 2. When PCSK9 is absent, LDL is removed from the blood (left). When PCSK9 is present, LDLR is degraded and LDL builds up in the blood (right).

Table 2. Median and interquartile range values for TC, dLDL and HDL for study groups.

<table>
<thead>
<tr>
<th>Lipid</th>
<th>Species</th>
<th>Median(mg/dL)</th>
<th>IQR</th>
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<tr>
<td>dLDL</td>
<td>HAP</td>
<td>142.3</td>
<td>85.1-167.0</td>
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<td>OWA</td>
<td>75.0</td>
<td>52.9-102.9</td>
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<td>TOO</td>
<td>65.7</td>
<td>55.9-76.2</td>
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<tr>
<td>HDL</td>
<td>HAP</td>
<td>171.0</td>
<td>141.3-190.5</td>
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<td>OWA</td>
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<td>122.6-200.3</td>
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Support

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