SAA Transcription and Expression in Island Foxes (Urocyon littoralis) with AA Amyloidosis

Mackenzie Ruehl1 2  , Patricia M. Gaffney1 2 , Christina J. Sigurdson1 2

1 School of Veterinary Medicine, UC Davis, Davis, CA 95616, USA
2 Department of Pathology and Medicine, UC San Diego, La Jolla, CA 92093, USA

Introduction

- AA amyloidosis is a misfolded protein disease caused by aggregation of serum amyloid A (SAA) which deposits in tissue causing organ dysfunction.
- Amyloid A (AA) amyloidosis is highly prevalent (34%) in the endangered island fox (Urocyon littoralis) and poses a threat to island fox recovery.
- SAA transcription is initiated by the binding of transcription factors nuclear factor- kappa B (NF-κB) and cis enhancing binding protein (CEBP) at the SAA promoter.
- SAA transcription is upregulated in hepatocytes in response to pro-inflammatory cytokines IL-1, IL-6, and TNF-α.
- Persistent elevation of serum SAA concentrations predisposes to AA amyloidosis.

Background: Histology and protein sequence of AA amyloid

The interstitum of the renal medulla is expanded by extracellular deposits of amyloid (Figure A). Island fox amyloid is congophilic, apple-green birefringent under polarized light (Figure B) and immunoreactive to anti-canine AA antibody (Figure C).

Island fox SAA is a 111 amino acid protein with 8 polymorphic residues (*). Among canids, there are isoforms found only in island fox, shared with arctic fox, and shared with domestic dog.

Hypothesis: SAA, CEBP and NF-κB are elevated in island foxes with AA Amyloidosis

IL-1, IL-6, and TNF-α promote SAA transcription in hepatocytes through activation of a transcription complex including CEBP and NF-κB.

Experimental Approach

Liver

RNA Extraction cDNA RT-qPCR

Quantify and Compare Transcripts

Liver

SAA

IL-1

NF-κB

CEBP

TNF-α

Spleen

Future Directions

- We will measure transcription of pro-inflammatory cytokines IL-1, IL-6 and TNF-α and investigate possible correlations between these cytokines and their related transcription factors.
- Using the island fox exome, we will explore sequence differences in the genes of the SAA transcription pathway.

Acknowledgements

NIH grant, T35 #5T35OD010956-15  STAR Program  UC Davis School of Veterinary Medicine