

CANINE SINO-NASAL ASPERGILLOSIS: PARALLELS WITH HUMAN DISEASE

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CANINE ASPERGILLOSIS

SINO-NASAL DISSEMINATED

HUMAN *ASPERGILLUS* SINUSITIS

INVASIVE

- Acute necrotizing
- Chronic
- Granulomatous

IMMUNO-
COMPROMISED

NON-INVASIVE

- Fungal ball
- Allergic
- Chronic-erosive

IMMUNO-
COMPETENT

*Canine sino-nasal aspergillosis
most closely approximates
human chronic-erosive, non-invasive,
fungal sinusitis*

*CANINE SINO-NASAL
ASPERGILLOSIS*

SIGNALMENT

- Medium to large breed
- Dolichocephalic or
mestaticcephalic
- Young to middle-aged
- Not immuno-compromised
- No underlying disease

AETIOLOGY

A. fumigatus

RARELY

Penicillium

A. niger

A. nidulans

A. flavus

CLINICAL

- Relatively uncommon
- Chronic, serous to mucopurulent or sanguinopurulent nasal discharge
- Unilateral becoming bilateral
- Episodic epistaxis
- Regional pain

CLINICAL

- Stertor, stridor or open-mouth breathing
- Depigmentation, ulceration or hyperkeratosis of nasal planum
- Facial deformity
- Ocular involvement/epiphora

*DIAGNOSIS REQUIRES
A COMBINATION
OF METHODS*

DIAGNOSIS

IMAGING

- Radiology

- CT

- MRI

DIAGNOSIS

RHINOSCOPY

- Visualize fungal plaque
- Assess tissue damage

DIAGNOSIS

NASAL CYTOLOGY

- Lavage
- Brush
- Squash of biopsy

DIAGNOSIS

BIOPSY

Culture from biopsy

DIAGNOSIS

SEROLOGY

- AGD
- CIEP
- ELISA
- Serum galactomannan

DIAGNOSTIC CRITERIA

1. Characteristic imaging changes
2. Serum antibody
3. Positive culture

THERAPY

SYSTEMIC MEDICAL

- Rarely used
 - Ketoconazole
 - Itraconazole
 - Fluconazole
-
- Success rate up to 70%

THERAPY

INDWELLING CATHETER

- Repeated enilconazole
- Prolonged single clotrimazole

THERAPY

Follow-up with
clotrimazole cream
instilled via
trephine holes to
frontal sinus

OUTCOME

Successful cure
in 90%

10% may recur

May develop
secondary
bacterial rhinitis

IMMUNOPATHOGENESIS

*DETECTION OF FUNGAL DNA
IN TISSUE BY REAL-TIME PCR*

METHODOLOGY

- Rhinoscopy 'gold standard'
- Tissue biopsy from standard site and EDTA blood
- Enzymatic and mechanical disruption
- Ribosomal RNA gene
- Taqman probes
- Normalized to G3PDH

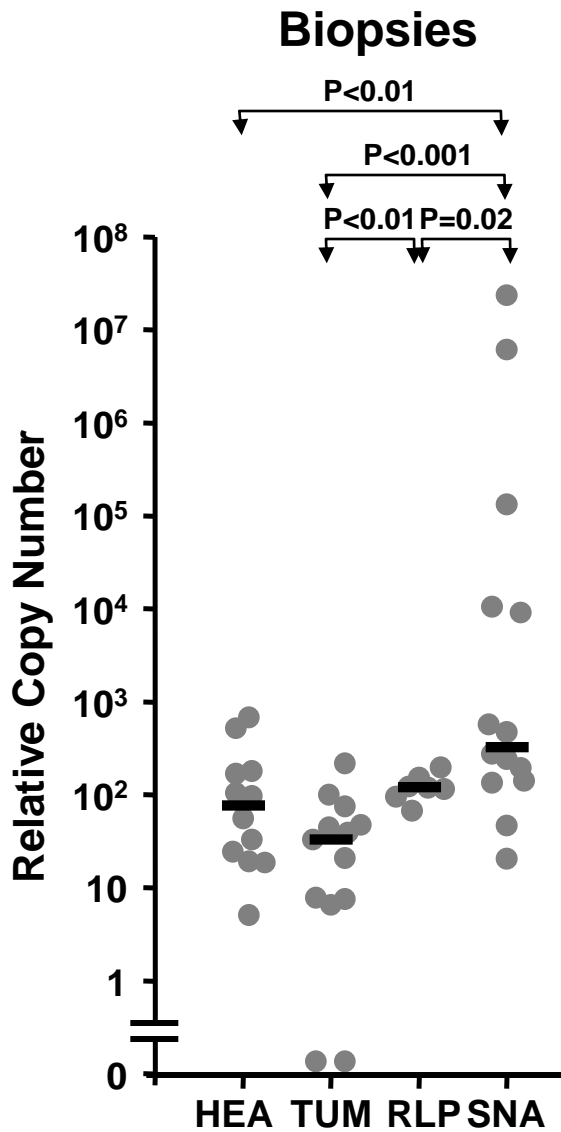
DETECTION OF FUNGAL DNA IN TISSUE BY REAL-TIME PCR

SNA (n=14)	LPR (n=7)	Neoplasia (n=13)	Normal (n=9)
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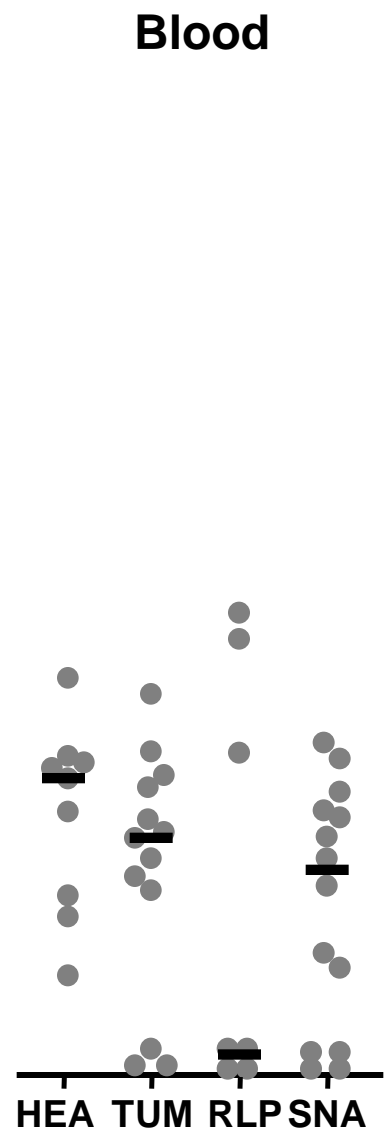
Pen-Asp

All dogs positive but > copy
number in dogs with SNA

A. fumigatus	7	0	1	0
A. terreus	0	0	0	0
A. flavus	0	0	0	0
A. niger	0	0	0	0

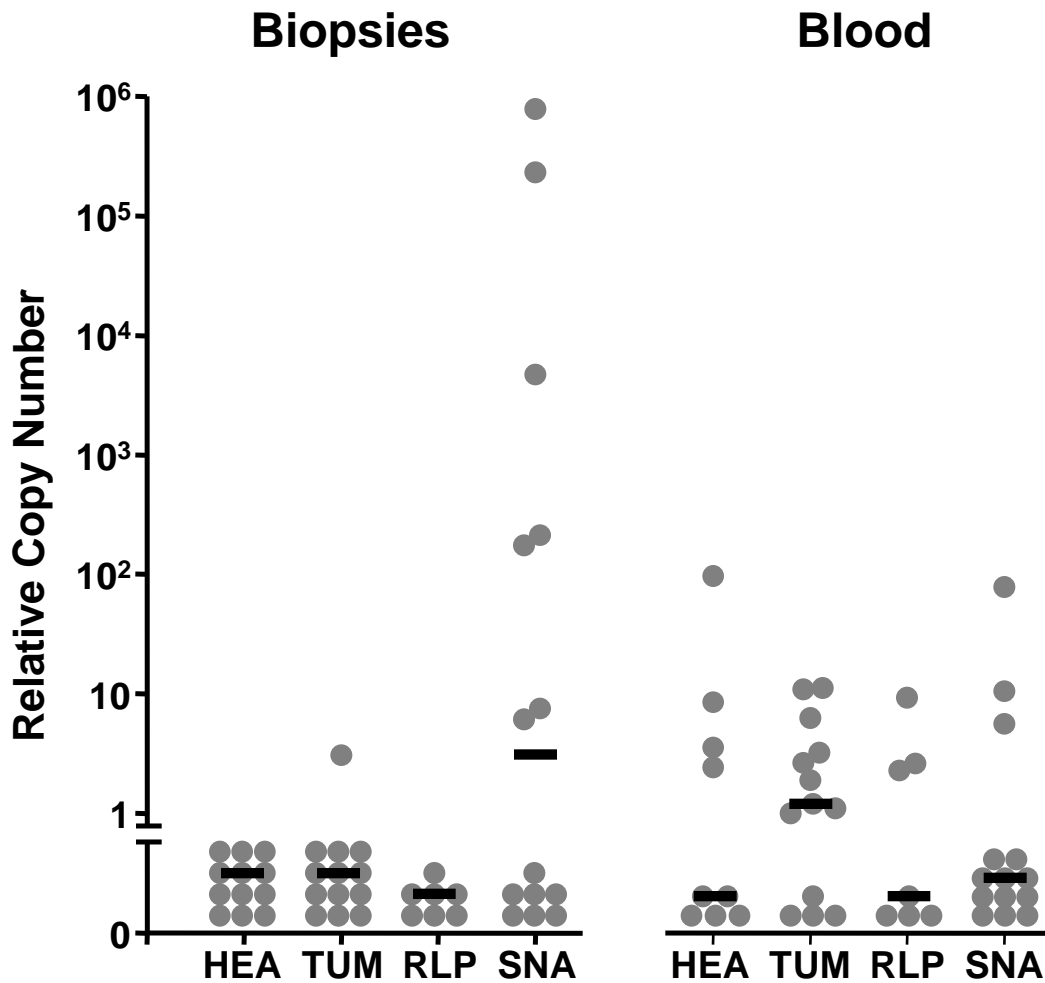


Sensitivity 1.00
Specificity 0.06



Sensitivity 0.71
Specificity 0.24

PEN-ASP



A. fumigatus

Sensitivity 0.50
Specificity 0.97

Sensitivity 0.21
Specificity 0.45

HISTOPATHOLOGY

Superficial
plaque

No invasion of
deeper tissue

- Ulceration
- Necrosis
- Haemorrhage
- Chronic-active
inflammation
- Granulation
- Bony destruction

IMMUNOHISTOCHEMISTRY

CD4⁺ & CD8⁺

T cells

(either dominates)

TCR $\alpha\beta$ > TCR $\gamma\delta$

IgG⁺ > IgA⁺ PC

CD1⁺ MHCII⁺
dendritic cells

MHCII⁺

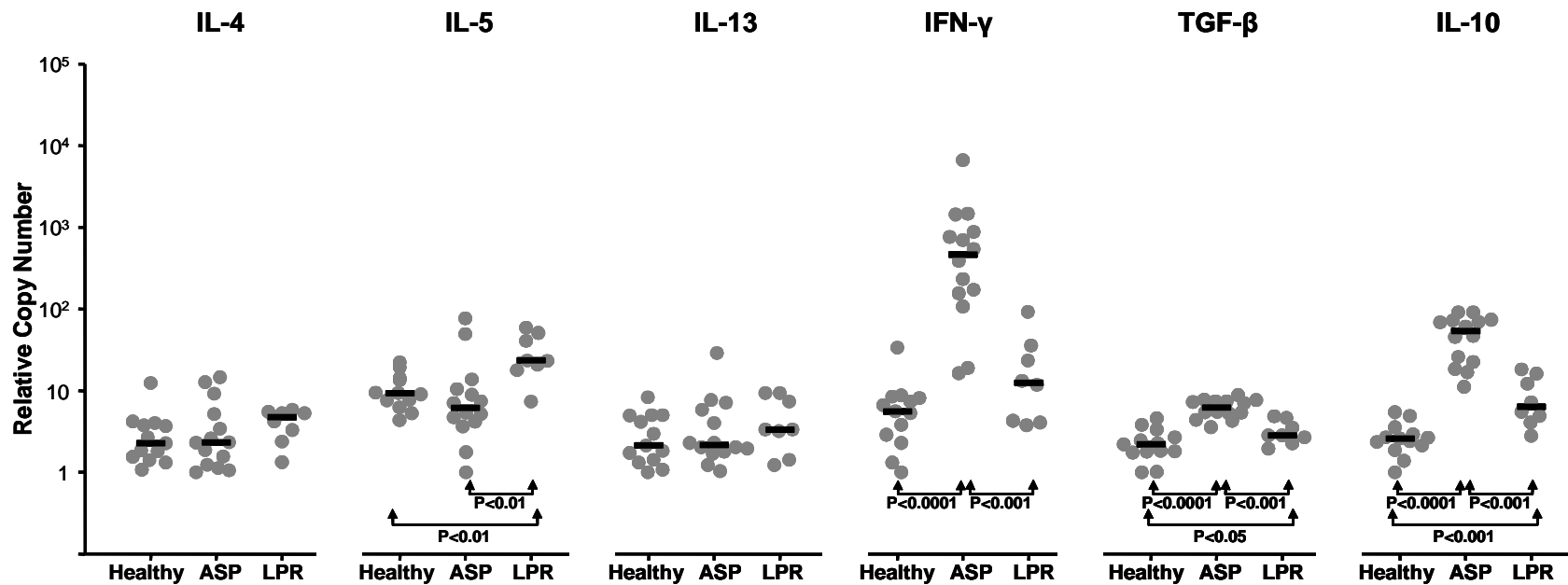
macrophages

MAC387⁺

macrophages &
neutrophils

IMMUNE FUNCTION

Real-time, RT-PCR normalized to multiple housekeeper genes for determination of expression of key cytokine and chemokine mRNA



LPR

SNA

IL-5

IL-8

IL-10

IL-12p19

IL-12p40

IL-18

TNF α

TGF β

MCP-2

MCP-3

IL-6

IL-8

IL-10

IL-12p19

IL-12p35

IL-12p40

IL-18

IFN γ

TNF α

TGF β

Eotax-2

MCP-1 to 4

MAIN FEATURES

- Th1 profile in SNA vs Th2-like in LPR
- IL-12 and IL-23 in SNA vs IL-23 in LPR; suggests role for Th17 cells in both
- IL-10 & TGF β expression suggests Treg [or Th1 differentiation] element and may explain chronicity of infection

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