Microbial colonisation and canine atopic dermatitis

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Staphylococcal colonisation exacerbates canine AD

Erythema

Papules

Scaling

Seborrhoea

Lichenification

Hyperpigmentation
Malassezia colonisation exacerbates canine AD

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Hyperpigmentation
**Staphylococcus pseudintermedius**

- Opportunistic pathogen
- 37.2% healthy dogs colonised
- 87.5% of atopic dogs colonised
  - Infections common
  - Worsen clinical lesions
Isolates from atopic and healthy dogs

- No association with healthy, atopic or infected status
Staphyloccocal adhesion in canine AD

- Adhere more readily to atopic skin

FIG 1: Box plot of the adherence indices shown by *S. intermedius* to canine keratinocytes.
Adhere to lesional and non-lesional skin
Staphylococcal adhesion in canine AD

- Isolates from healthy and atopic dogs adhere equally well to fibronectin, fibrinogen and cytokeratin 10
Staphylococcal colonisation in AD

- Associated with host factors
- Altered cutaneous microenvironment
- Bind to sites of TH2-inflammation
- Expression of adhesion molecules
**Malassezia colonisation in canine AD**

- *Malassezia* skin and ear infections common
- Most atopic dogs are colonised
  - Interdigital skin (70%) and ears (63%)
- Less population diversity on atopic skin?
Genotyping of *Malassezia* isolates

- Multiple isolates from healthy or affected dogs
- Most isolated from multiple sites
- Isolate E2 associated with canine AD
- Phospholipase is a virulence factor?
Malassezia colonisation in canine AD

- Most if not all dogs colonised with *Malassezia*
- Density and population heterogeneity important in infection
- Role of host factors likely
- Role of more virulent isolates?
Innate immunity and canine AD

- Antimicrobial peptides (AMPs)
  - β-defensins (BD), cathelicidins (Cath) and others
- Broad spectrum antimicrobial activity
- Modulate innate and adaptive responses
- Cell recruitment and activation
- Wound healing
- Coat colour in dogs
## Human beta-defensins

<table>
<thead>
<tr>
<th>Expression</th>
<th>hBD1</th>
<th>hBD2</th>
<th>hBD3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constitutive</td>
<td></td>
<td>Induced</td>
<td>Induced</td>
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</table>

<table>
<thead>
<tr>
<th>Inflammatory stimuli</th>
<th>hBD1</th>
<th>hBD2</th>
<th>hBD3</th>
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<tbody>
<tr>
<td>No</td>
<td></td>
<td>TNF(\alpha), IL-1(\beta), G-ve bacteria (also G+ve and yeasts)</td>
<td>TNF(\alpha), G+ve and G-ve bacteria</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Antimicrobial activity</th>
<th>hBD1</th>
<th>hBD2</th>
<th>hBD3</th>
</tr>
</thead>
<tbody>
<tr>
<td>G-ve</td>
<td></td>
<td>G-ve</td>
<td>G+ve (esp. S. aureus)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Yeast</td>
<td>G-ve Yeast</td>
</tr>
</tbody>
</table>
Innate immunity and human AD

- Complex pattern of relationships
- Down-regulation of hBD1
- Up-regulation of hBD2, hBD3, RNase7 and psoriasin in lesional skin
- Dermcidin expression decreased in lesional skin
- No changes in Cath (LL-37)
- No differences in non-lesional atopic and healthy skin
Antimicrobial peptides in canine AD

- hBD3 effective against *S. pseudintermedius*
Canine beta-defensins in AD

- Very variable and inconsistent findings for cBD1, cBD3, cBD103, cCath and others in atopic and healthy skin
cBDs in canine AD and inflammatory dermatoses
Staphylococcal exacerbation of AD

- Staphylococcal proteins can penetrate the stratum corneum following mast cell degranulation
- Toxins affect the skin barrier and immune system
  - Enterotoxins and exfoliative exotoxins
  - Staphylococcal enterotoxin B (SEB) induces T-cell production of IL-31 in *D. farinae*-sensitized dogs
Staphylococcal exacerbation of AD
Staphylococcal SAGs in AD

• Staphylococcal SAGs in humans
  – Induce CLA on T-cells
  – Induce MHCII, IL-1, IL-4, TNFα and IL-12
  – Up-regulate endothelial ICAM-1 and VCAM-1
• *S. pseudintermedius* SAGs stimulate canine PBMCs
Staphylococci and TSLP

- Langerhans cell activation and inflammation
- Increased expression with TLR3 and TLR4 ligands
Malassezia exacerbation of canine AD

- Intradermal test reactivity, specific IgE serology, passive transfer and PBMC proliferation studies
**Malassezia** major and minor allergens

Chen and others (2002) Veterinary Dermatology 13: 141-150
Microbial colonisation in chronic AD
Antimicrobial therapy in AD – can we do better?

- Routine use of topical antiseptics
  - May be drying
  - Incorporating anti-adhesives
- Manage the underlying inflammation
- Colonisation with less pathogenic species to modify the microbiome?