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THE ROYAL (DICK) SCHOOL OF VETERINARY STUDIES

Microbial colonisation and canine atopic dermatitis

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Head of Dermatology

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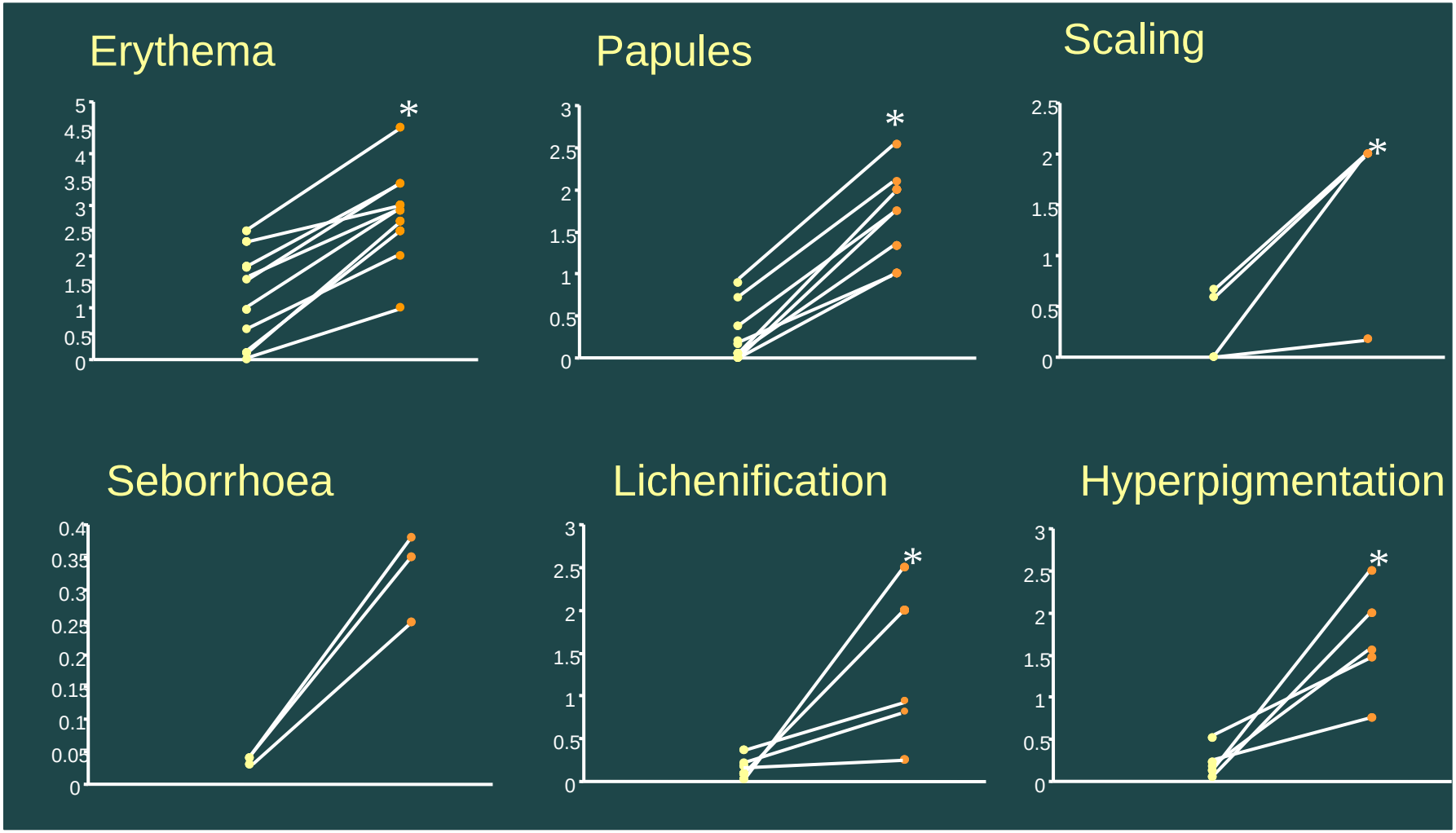
Staphylococcal colonisation exacerbates canine AD



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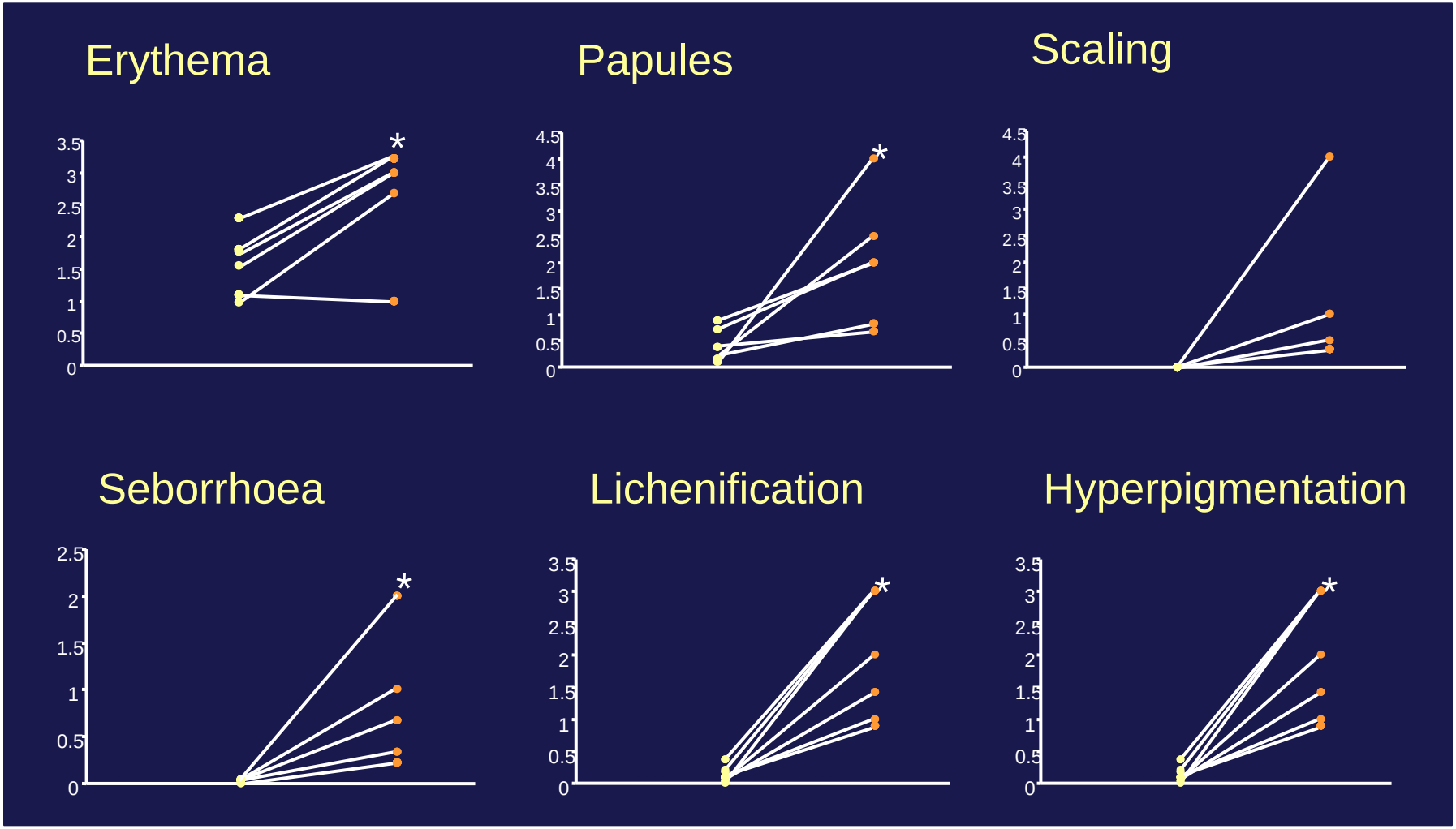
Malassezia colonisation exacerbates canine AD



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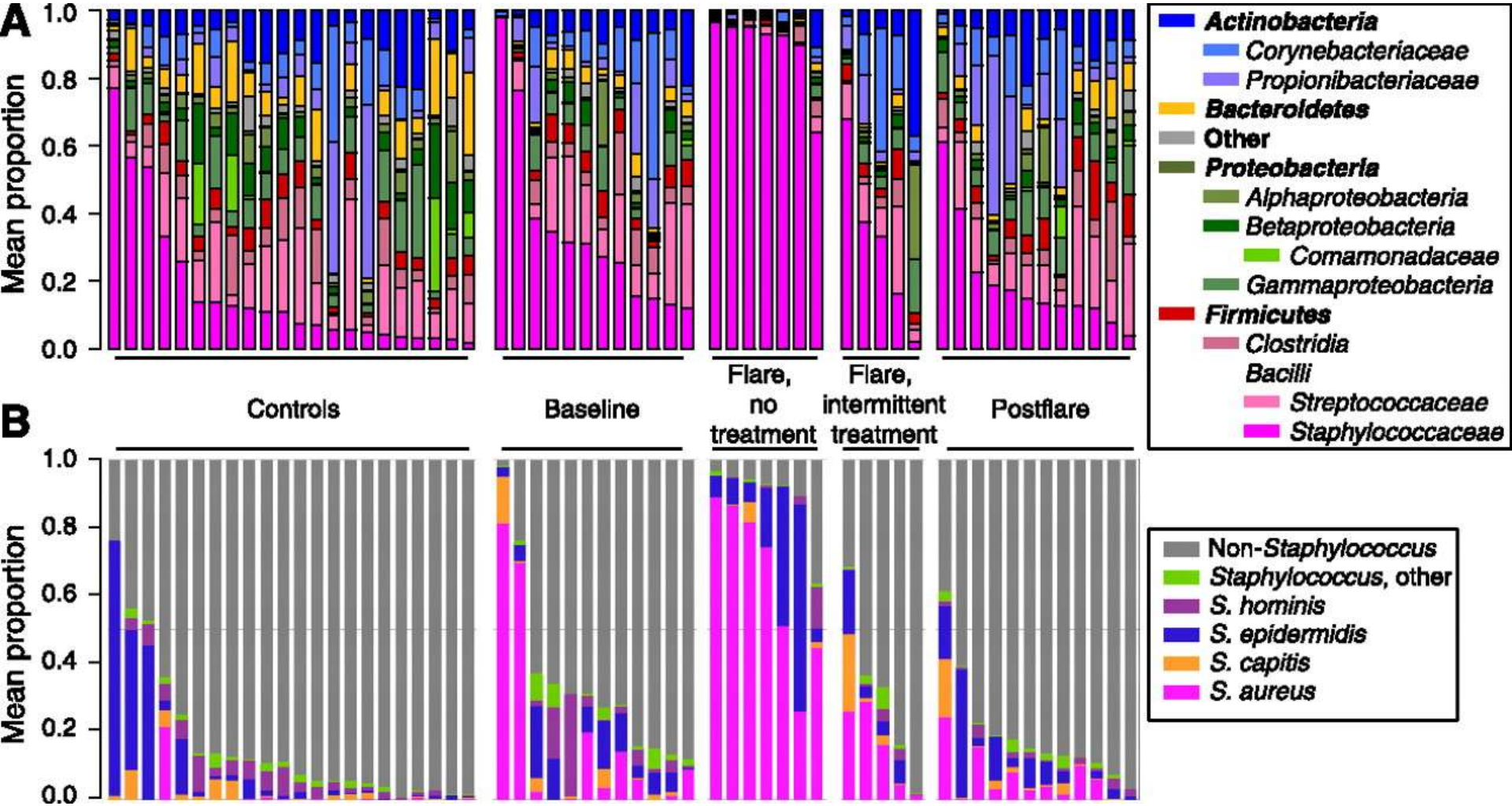

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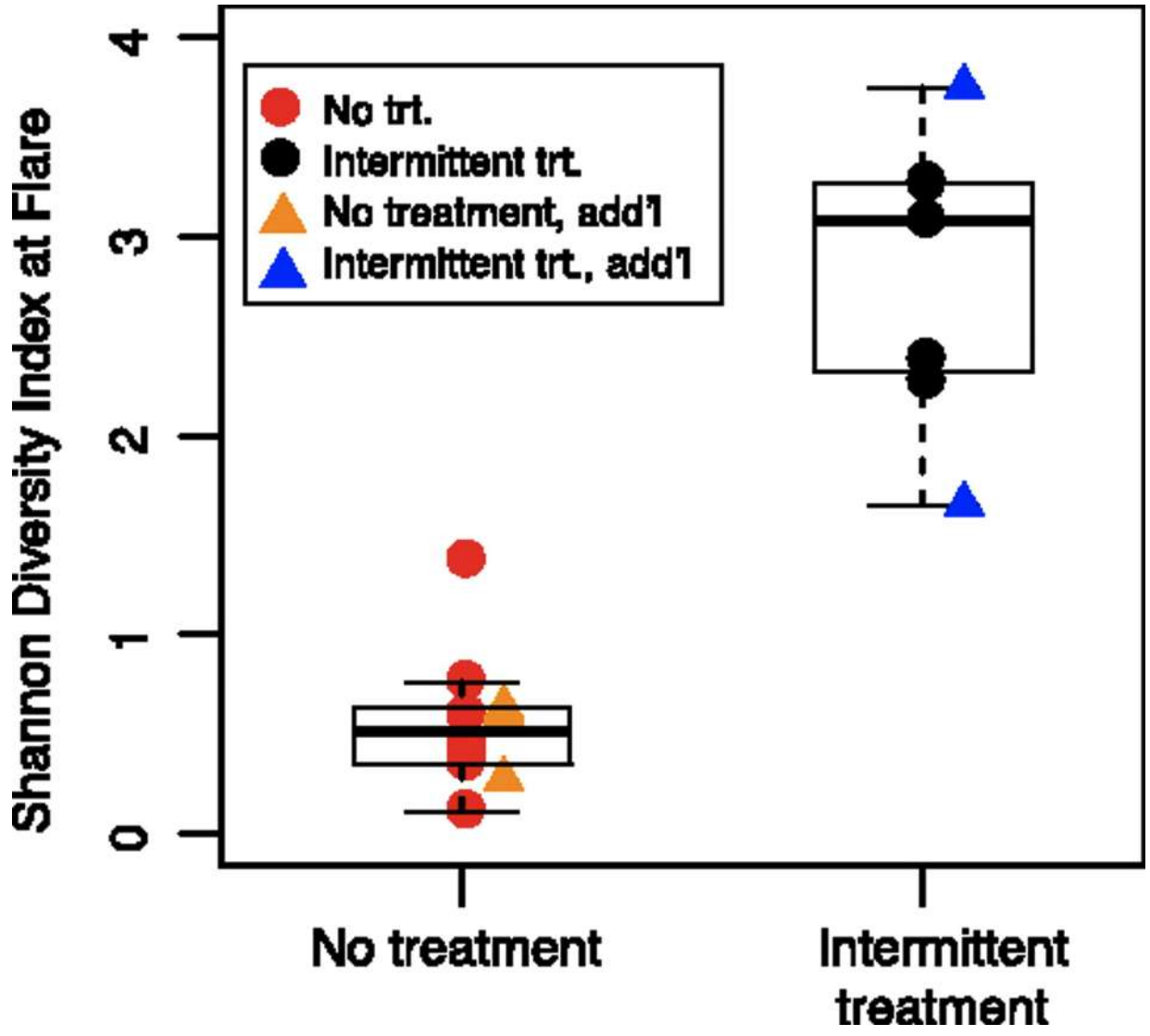

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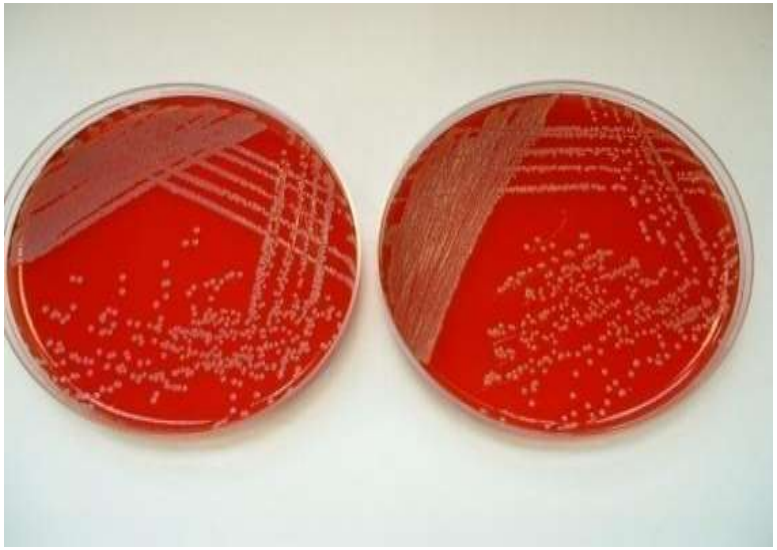
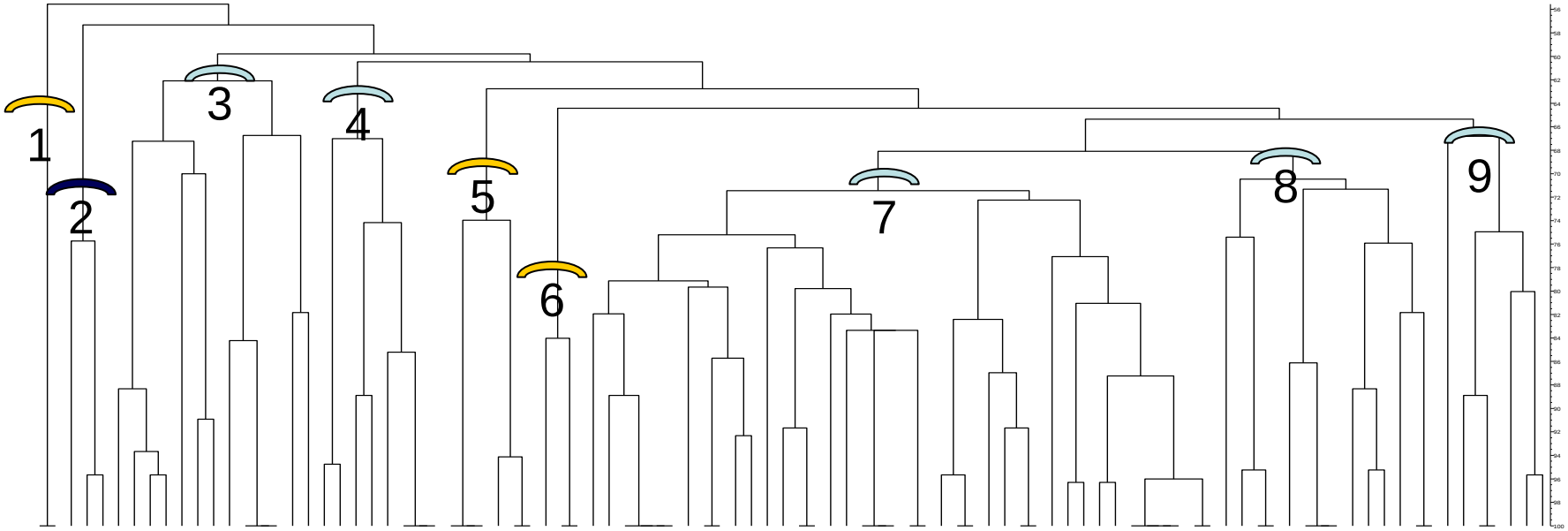
Staphylococcus pseudintermedius

- 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



Healthy only =

Atopic only =

Healthy & Atopic =

Staphylococcal adhesion in canine AD

- Adhere more readily to atopic skin

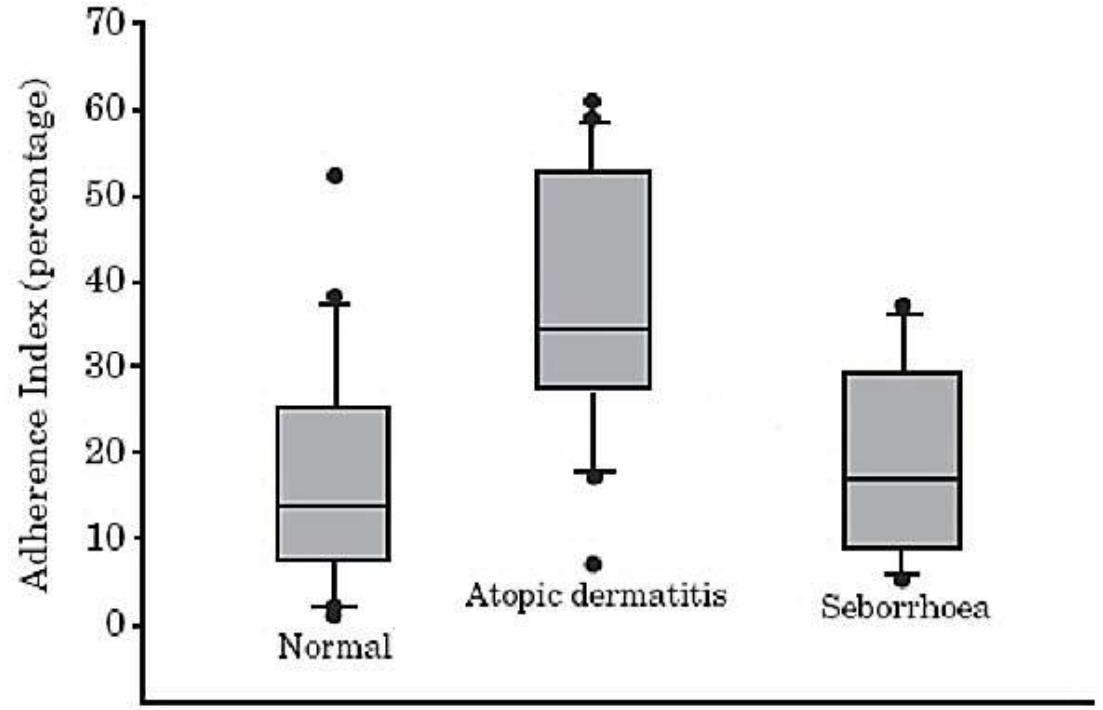
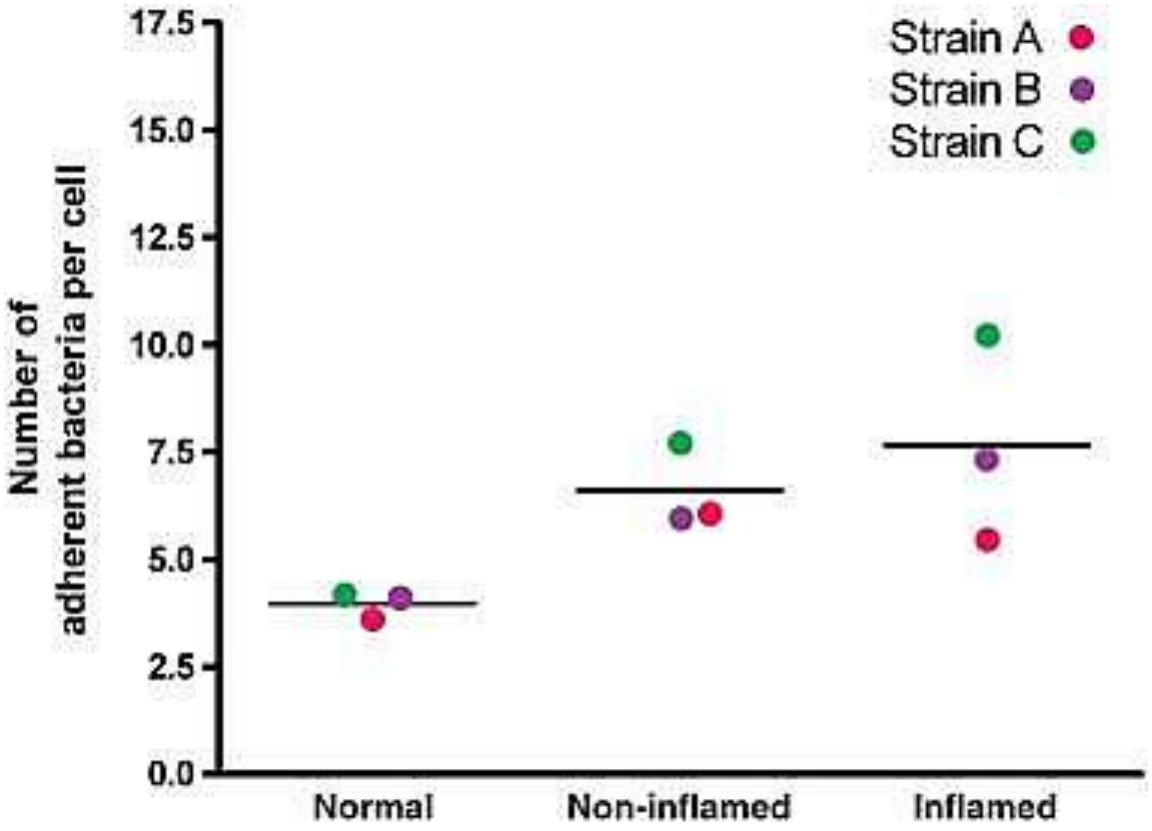


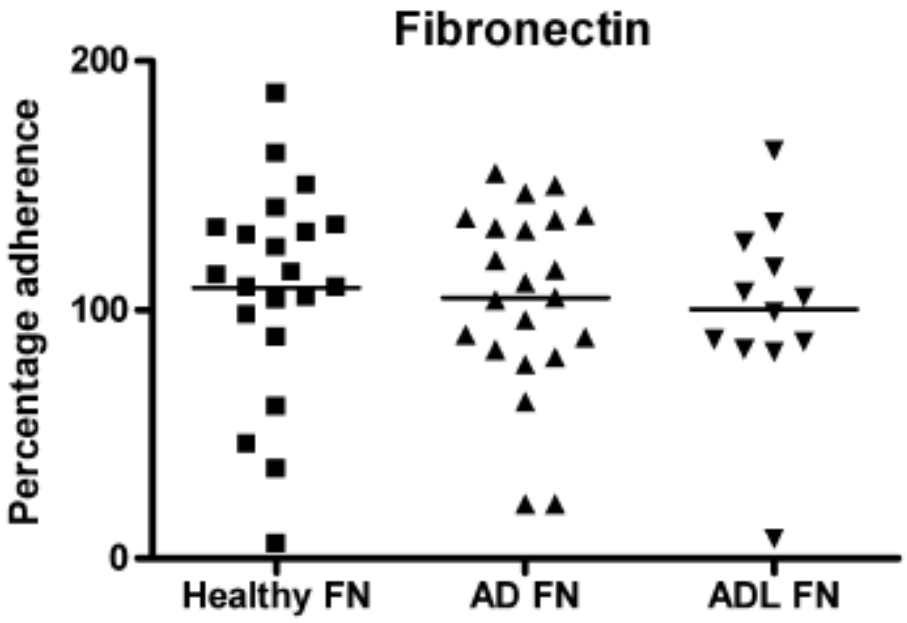
FIG 1: Box plot of the adherence indices shown by *S. intermedius* to canine keratinocytes.

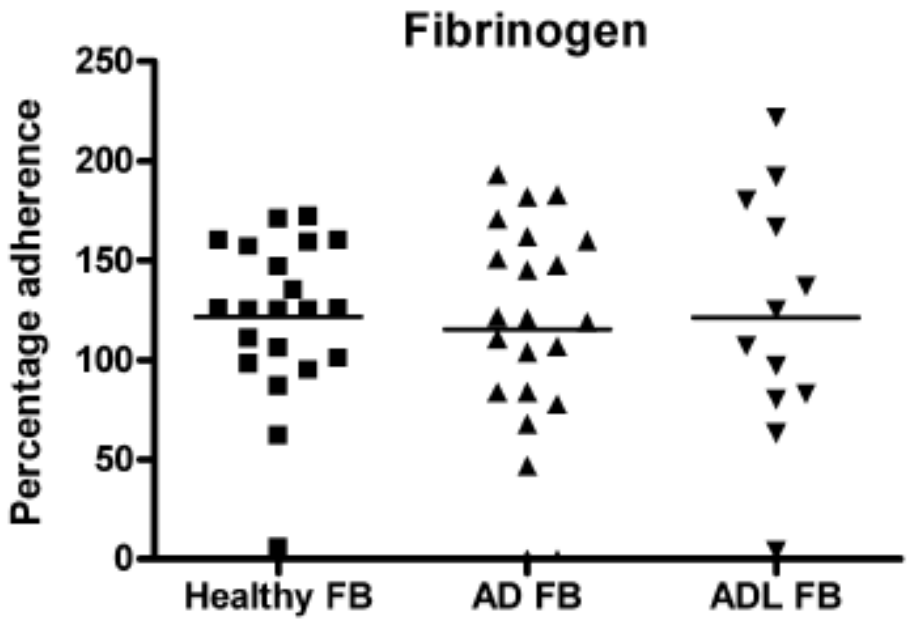
Adhere to lesional and non-lesional skin



Staphylococcal adhesion in canine AD

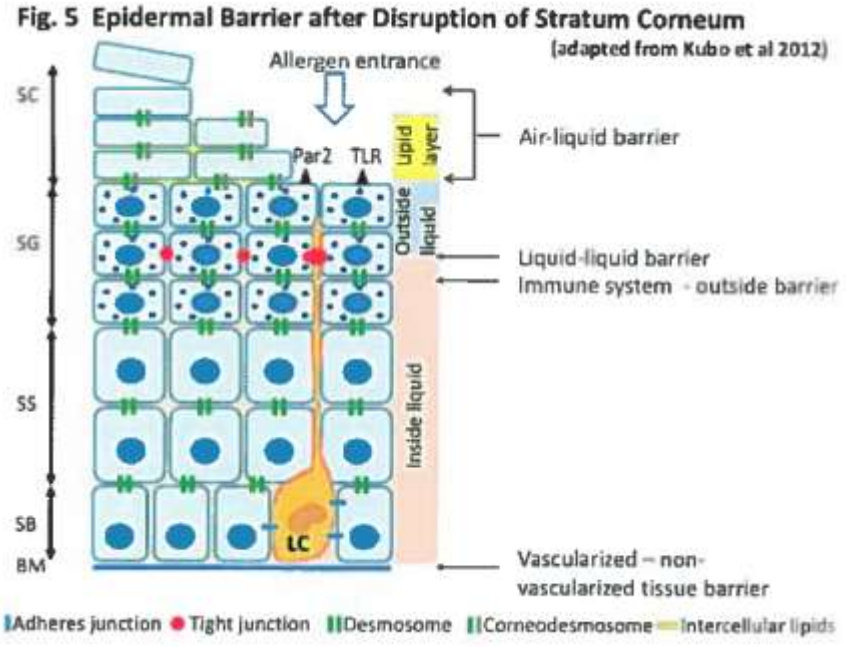
- Isolates from healthy and atopic dogs adhere equally well to fibronectin, fibrinogen and cytokeratin 10





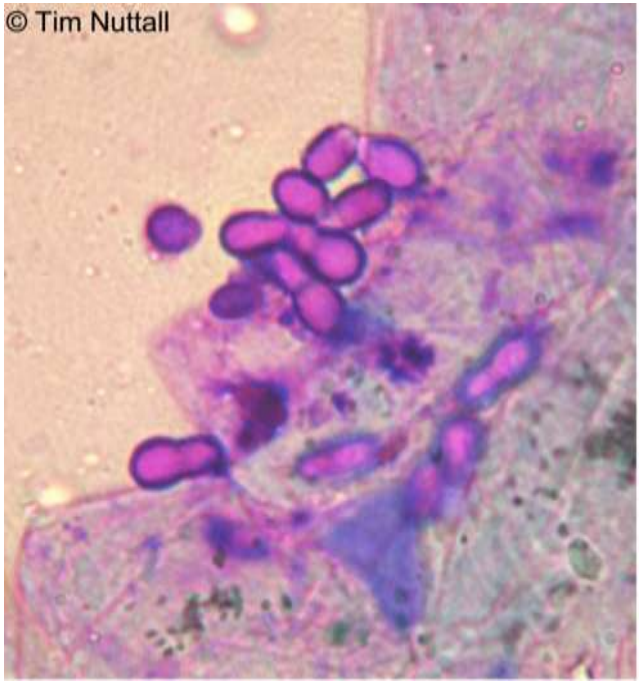
Staphylococcal colonisation in AD

- 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?



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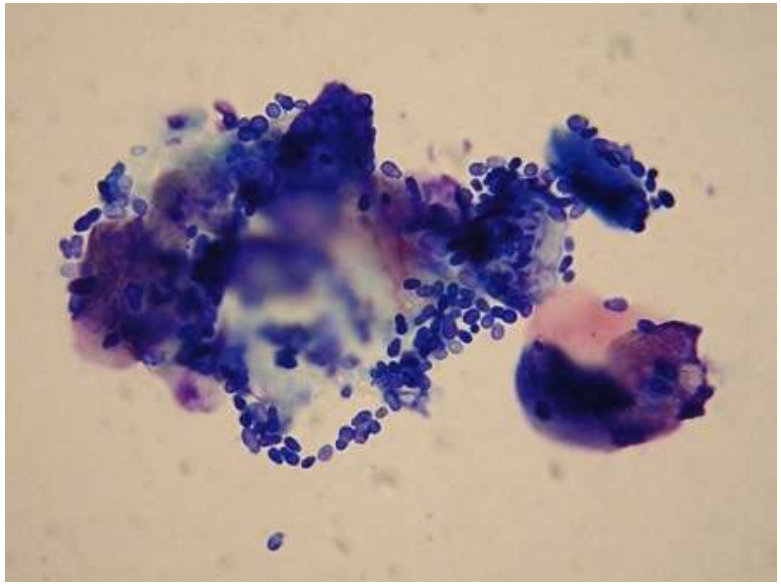
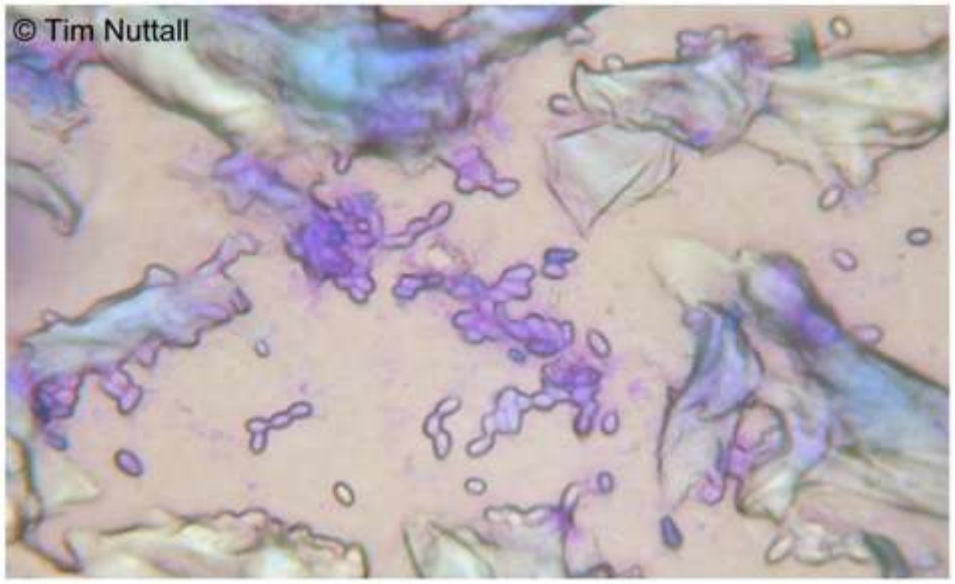
Genotyping of *Malassezia* isolates

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



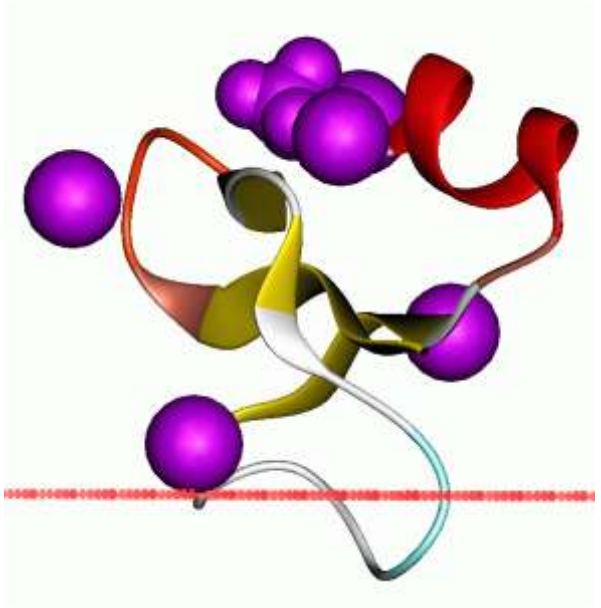
Malassezia colonisation in canine AD

- 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



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Human beta-defensins

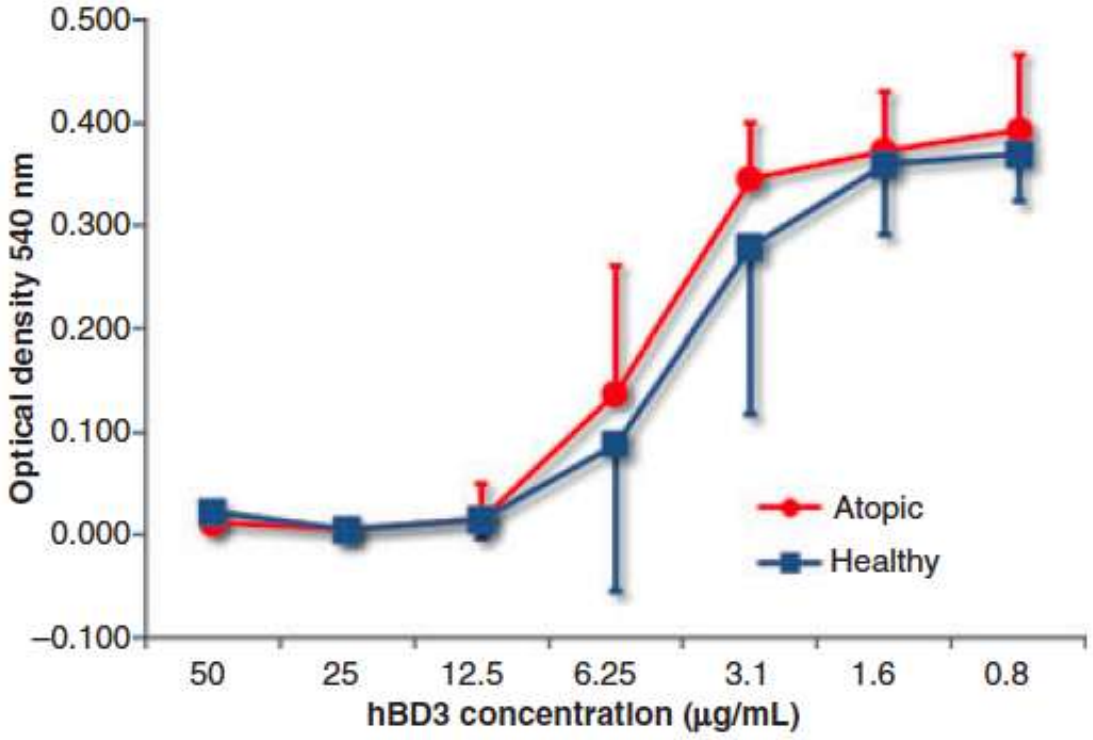
	hBD1	hBD2	hBD3
Expression	Constitutive	Induced	Induced
Inflammatory stimuli	No	TNFα, IL-1β, G-ve bacteria (also G+ve and yeasts)	TNFα, G+ve and G-ve bacteria
Antimicrobial activity	G-ve	G-ve Yeast	G+ve (esp. *S. aureus*) G-ve Yeast

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*



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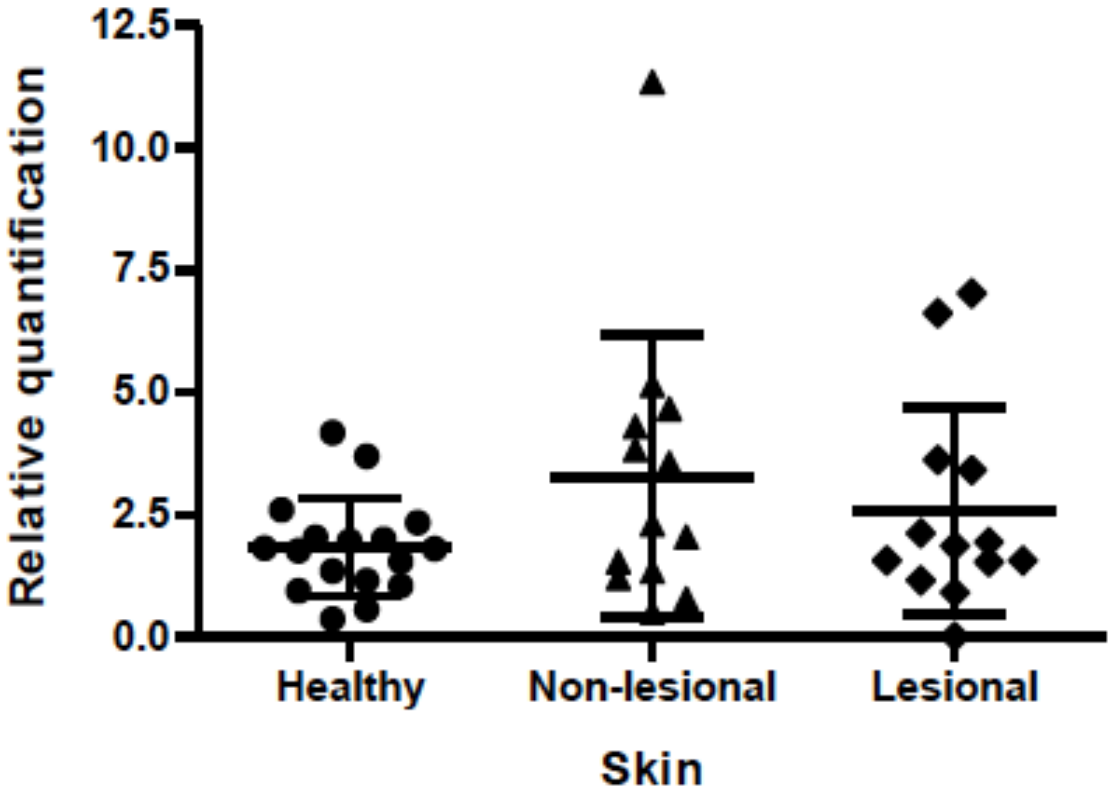
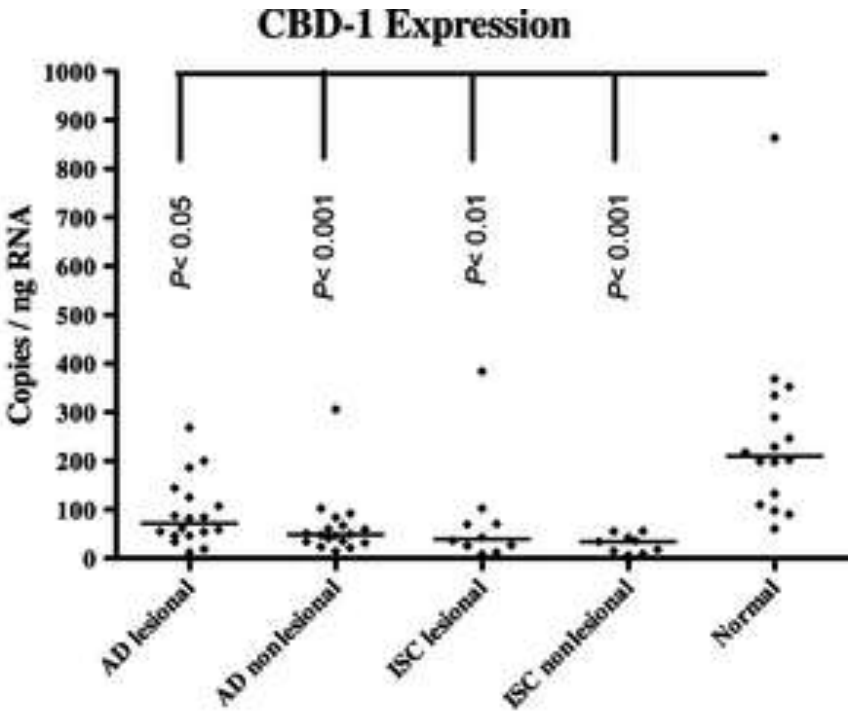
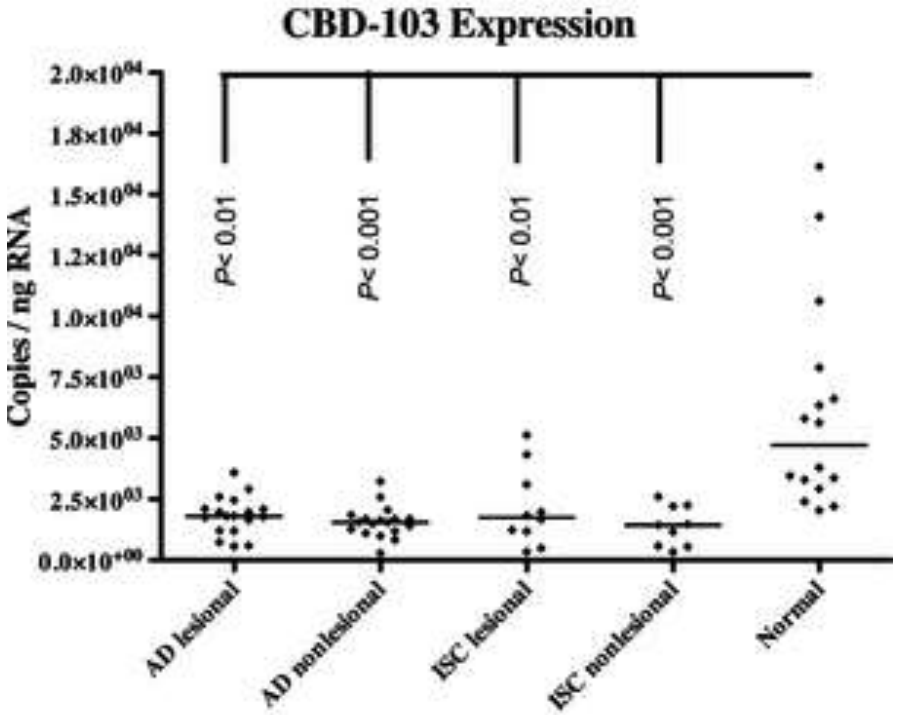
Canine beta-defensins in AD

- 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

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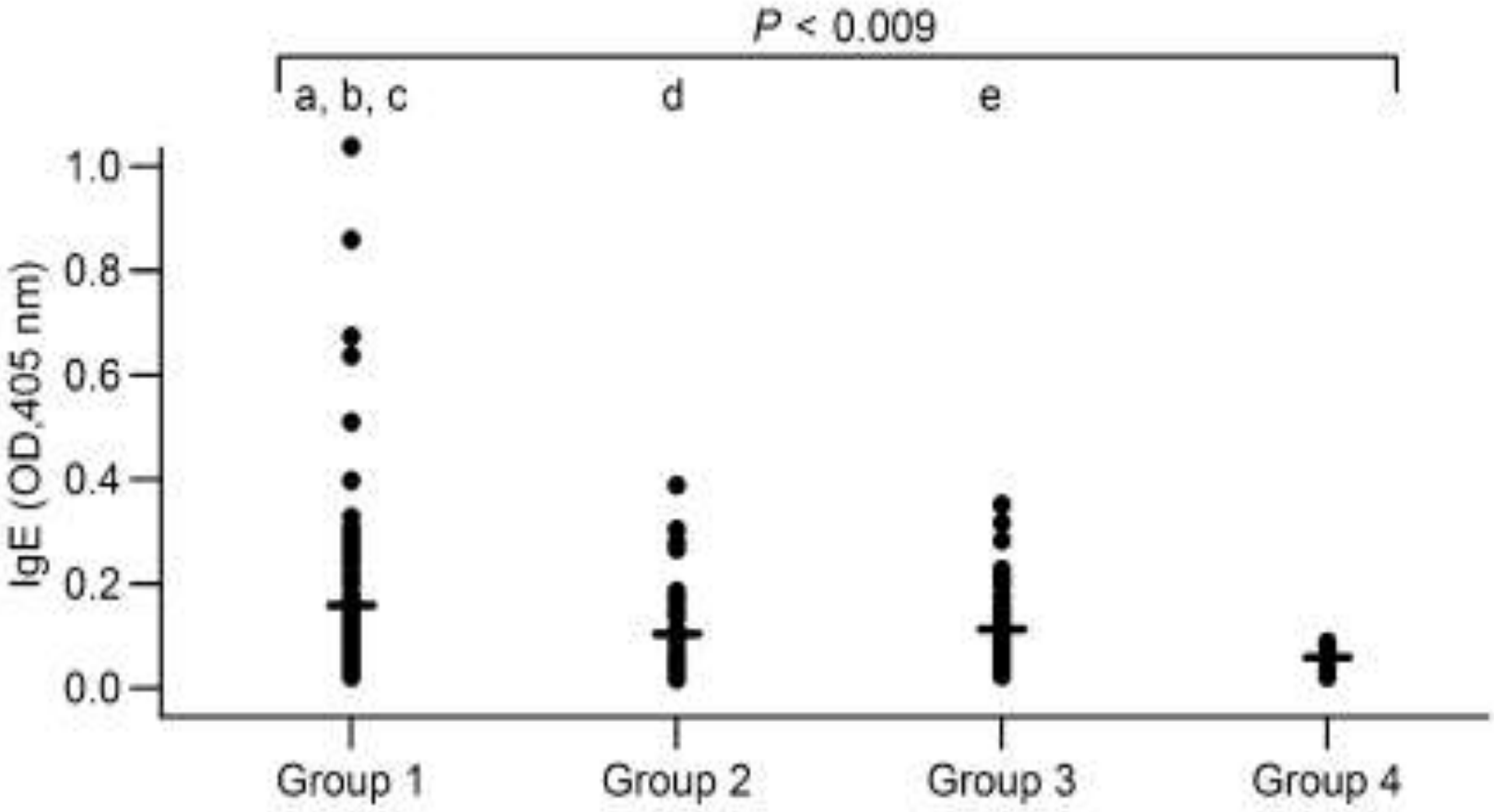
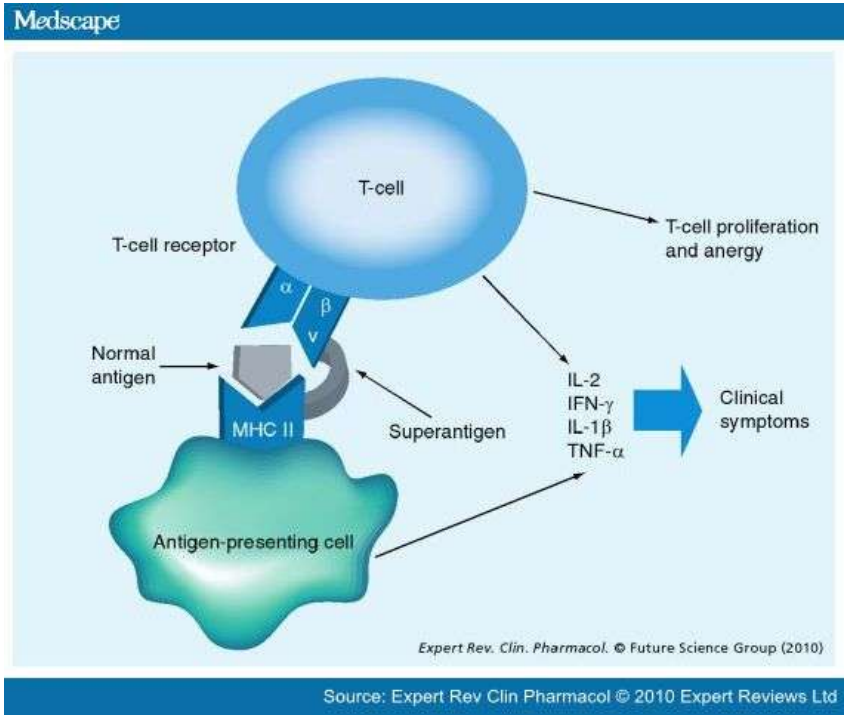
Staphylococcal exacerbation of AD



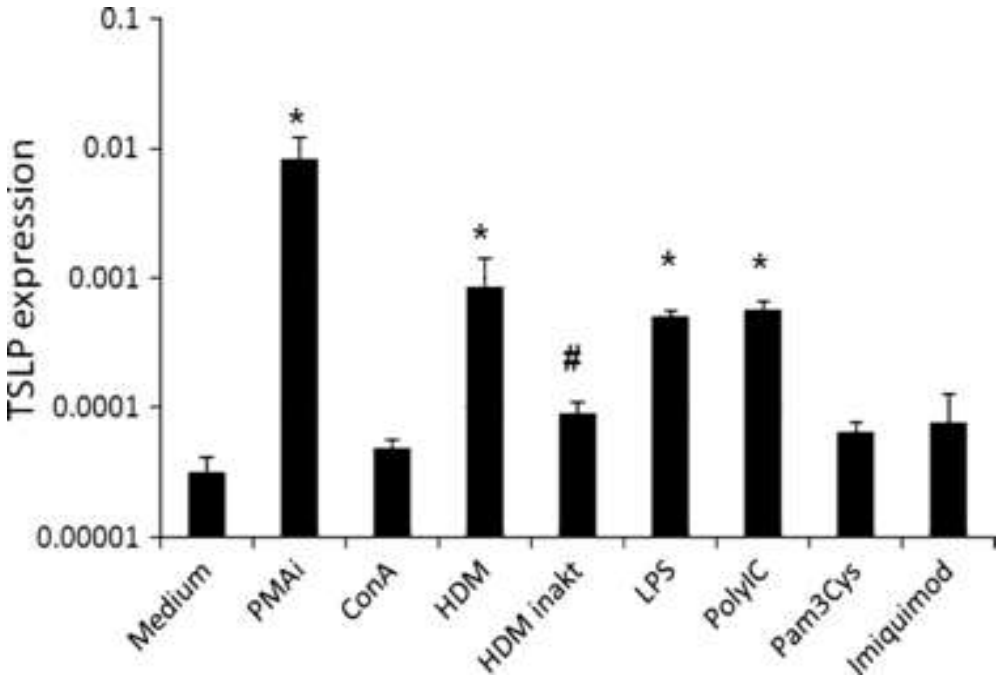
Staphylococcal SAGs in AD

- 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



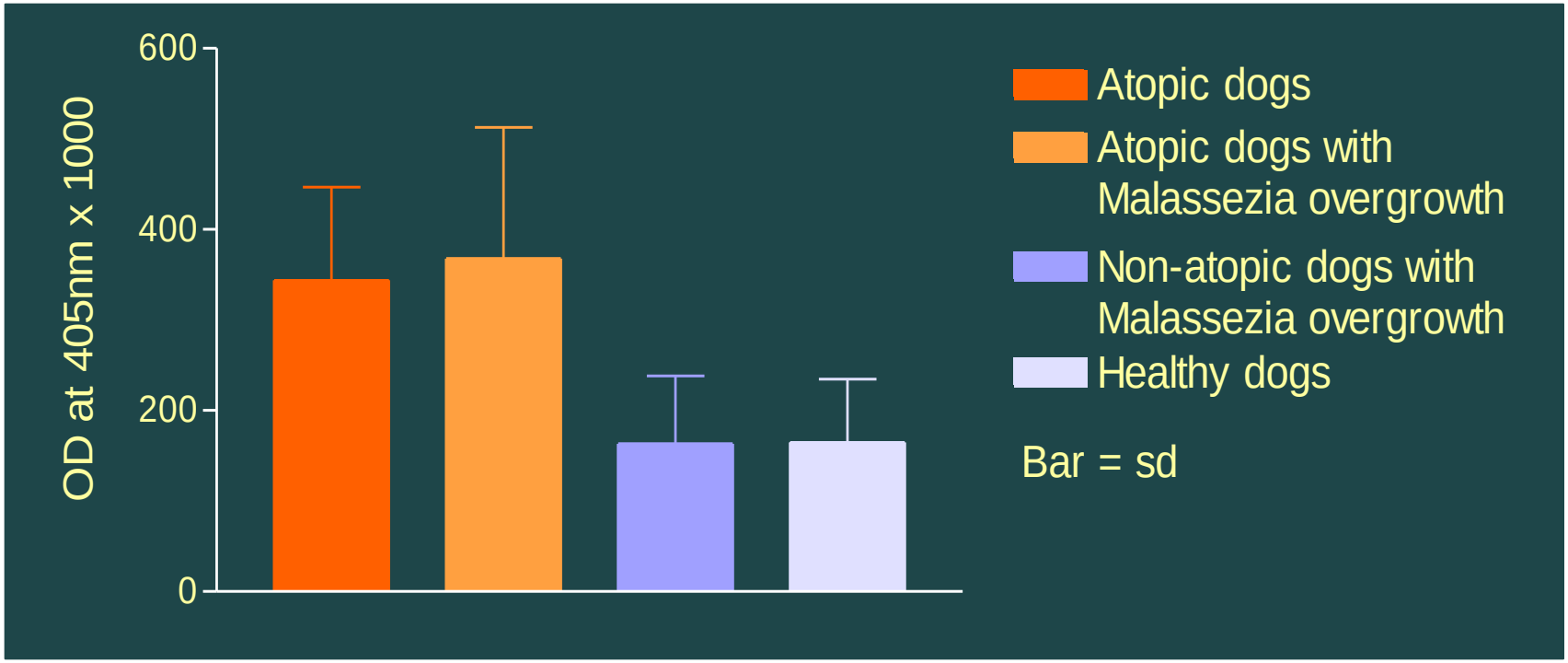
Staphylococci and TSLP

- 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



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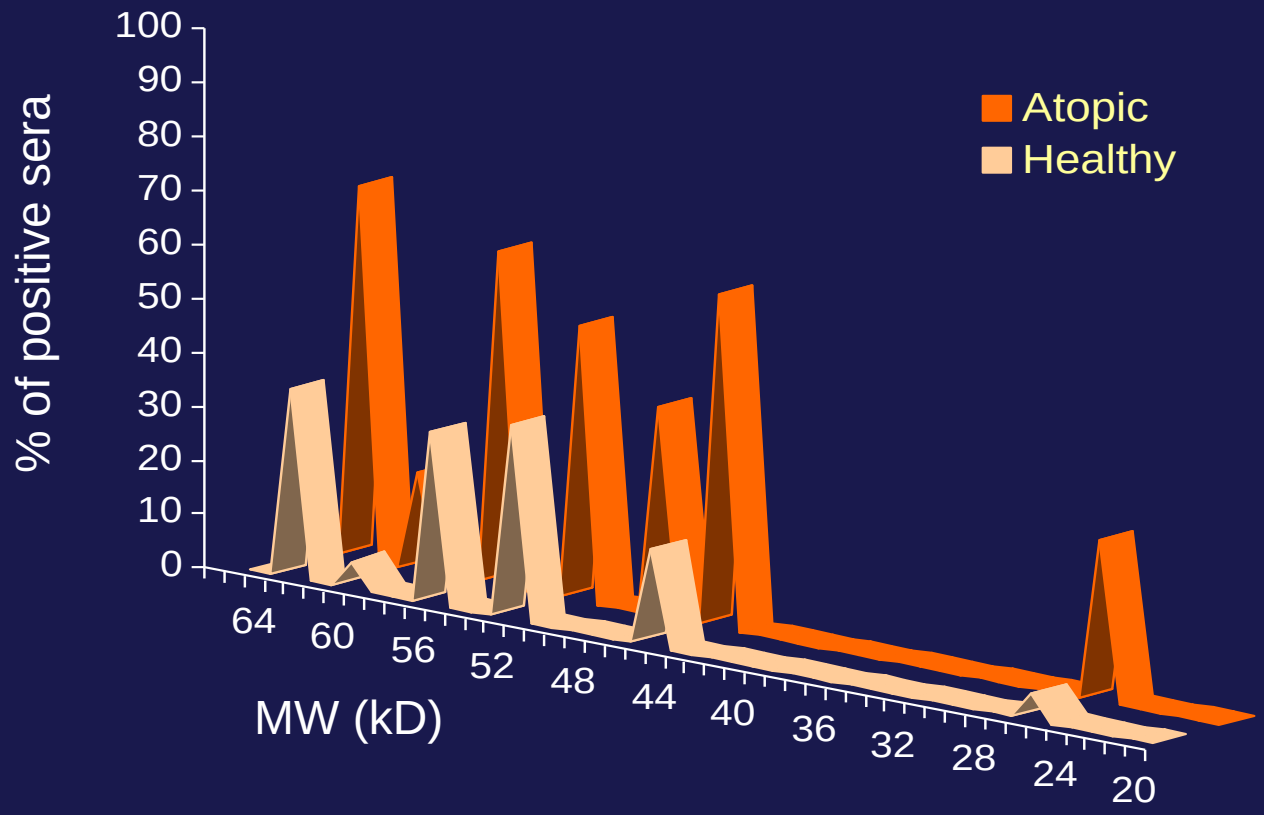
Malassezia major and minor allergens



Chen and others (2002) Veterinary Dermatology 13: 141-150

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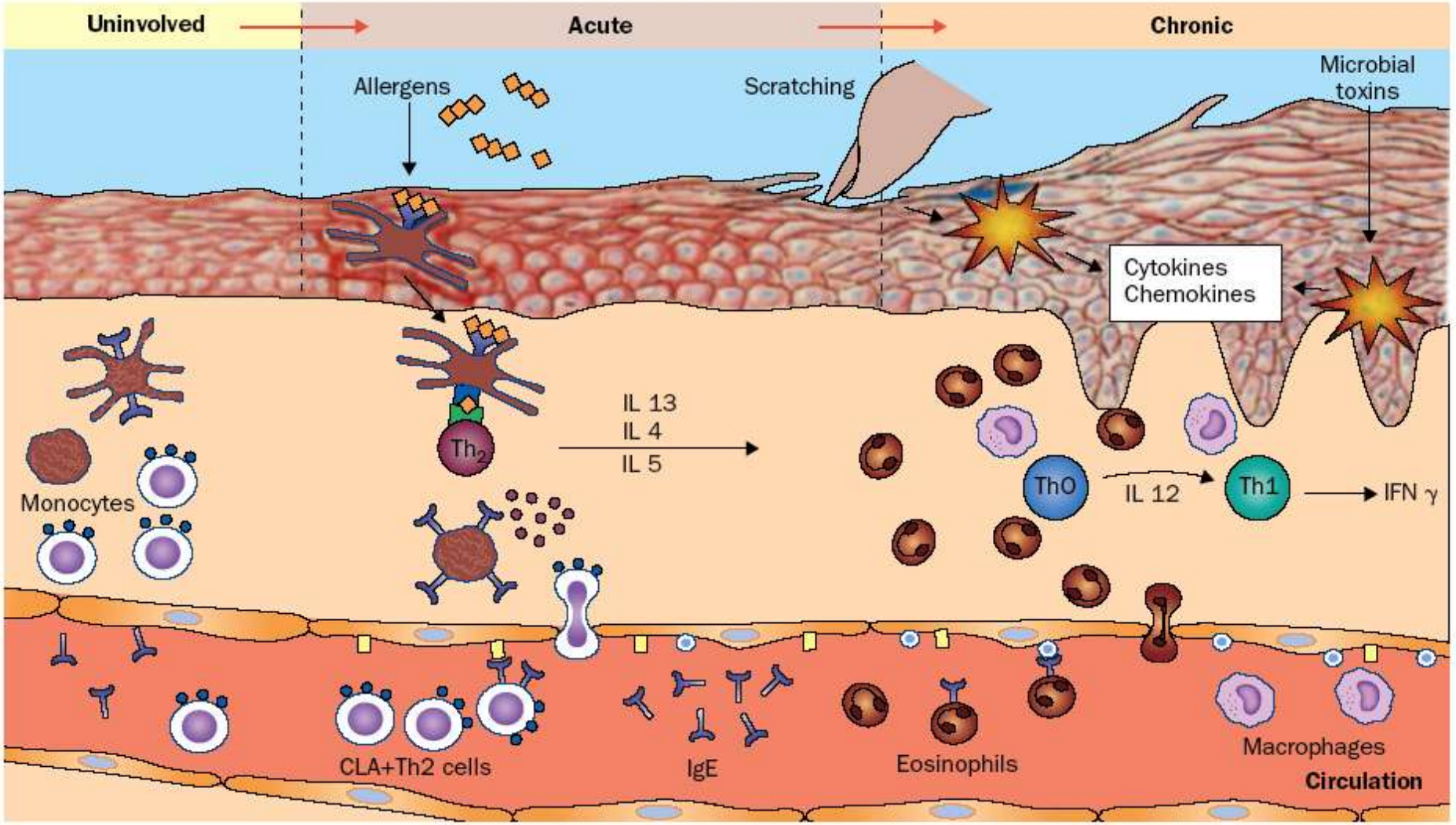
Microbial colonisation in chronic AD



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?