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Endotoxin level in house dust mite extract impacts the molecular phenotype of allergic airways inflammation in mice

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Background:

House dust mite (HDM) is a relevant human aero-allergen that is commonly used to induce asthma-like changes in mice. HDM contains endotoxin, the abundance of which varies widely in commercially available HDM. Endotoxin abundance in allergens is known to skew inflammatory profiles and is associated with reduced corticosteroid responsiveness in asthma. Notably, in a survey of the 250 most recent publications using HDM-challenge mouse models, only 19% state the endotoxin load in their HDM stock.

Objective:

We hypothesize that the endotoxin level in HDM significantly alters the lung transcriptome.

Methods:

Female, 8-10 week old BALB/c mice were challenged 5x/week for 2 weeks with intranasal HDM extract containing high or low levels of endotoxin; referred to here as HHDM and LHDM, respectively. The molecular phenotype of the lung was characterized by measuring the abundance of lavage cytokines and lung tissue transcriptome. Data integration was performed using Network Analyst and the mixOmics R package. Values are expressed as mean ± SEM (n=5 per group).

Results:

Differences in endotoxin levels were associated with significantly disparate molecular profiles, revealed by unique changes in the transcriptome and cytokine profile. Specifically, HHDM induced production of IL-17 in the BALF (6.3 ± 1.2 vs. 0.62 ± 0.56 pg/mL in LHDM, $p<0.05$) while LHDM caused accumulation of IL-5 in the BALF (7.6 ± 1.2 vs. 2.9 ± 0.75 pg/mL in HHDM $p<0.05$). Additionally, HHDM uniquely enriched genes involved in pathways for DNA damage repair, while LHDM uniquely enriched pathways for glucocorticoid regulation.

Conclusion:

The abundance of endotoxin in HDM plays an important role in determining the molecular phenotype of allergic airways inflammation in mice, but 81% of publications do not report this in their methods. This leads to improper interpretation of results and problems with data reproducibility all which negatively impact the success of pre-clinical work.