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## Functional and clinical translation of asthma and allergy associated genetic variants in IL33 and IL1RL1

Ketelaar, Marlies

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## **“Functional and clinical translation of asthma and allergy associated genetic variants in *IL33* and *IL1RL1*”**

1. Definition of subgroups are key for understanding the potential role of phenotype-associated genetic variation at *IL33* and *IL1RL1* in molecular mechanisms and clinical pathology of asthma/allergy. (*This thesis, chapters 2, 4, 5, 8 and 9.*)
2. The asthma subgroup that the *IL33/IL1RL1* loci seem to be associated with both genetically and functionally is characterized by presence of eosinophilic inflammation either in blood or the airways, as well as associates with increased Th2 activation. (*This thesis, chapters 4, 5, 6 and 8.*)
3. Specific genetic signals at the *IL33/IL1RL1* loci that associated with asthma/allergy phenotypes regulate expression and activity of the IL-33/IL-1RL1 signalling pathway. (*This thesis, chapters 4-6.*)
4. The genetic signals that associate with eosinophilic asthma and eosinophilia (*IL33 and IL1RL1*) regulate IL-33 and IL-1RL1 expression in bronchial epithelium while the genetic signals associated with lung function and severe asthma (*IL1RL1 only*) regulate expression in lung tissue, indicating the possible involvement of other lung structural cells for the expression of the *IL1RL1* associated phenotypes. (*This thesis, chapters 4 and 5.*)
5. Clinically, the IL-33/IL-1RL1 pathway has potential as novel treatment target and as biomarker for the prediction of asthma and allergy phenotypes, identifying phenotypic subgroups such as eosinophilic asthma where the IL-33/IL-1RL1 axis might be particularly important in. (*This thesis, chapters 7-9.*)
6. Targeted treatment strategies against alarmins such as IL-33 might have benefit above targeting their receptor to respect the decoy function of the receptor's isoforms, but studies towards isoforms of IL-33 are needed to substantiate this statement. (*This thesis, chapter 10.*)
7. Novel detection methods to quantify IL-33 protein are required to enable the potential use of this alarmin as predictor of asthma/allergy and treatment response. (*This thesis, chapter 7, 10.*)
8. As there is no single way to find the best prescription for the patient as doctor and scientist, it seems better to carefully select the road of travel than to focus on the destination without seeing the joy and challenges on the way forward.
9. Translation in (bio)medical science is like learning a language; you only develop a sense for it by using it, and when you finally think you get the meaning, you find out there is yet another layer and gap to bridge...
10. Today we set the stage for the future, but do remember the past since then we were working on today.
11. Met geluk en een zuchtje wind kan een vlieger opstijgen, maar hij bereikt grote hoogtes soms alleen door tegenwind, en landt veilig door het op tijd laten vieren van de teugels.