



Bitter taste in chicken – computational screening for bitter tastants



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Introduction

Bitter Taste role

Bitter taste is known for its aversiveness in vertebrates, following the hypothesis that its role is to protect from ingesting certain bitter toxics. Bitter taste receptors (Tas2Rs) have diverse crucial roles and are being expressed in tissues other than the palate, such as the respiratory system¹ and the gastric system², where the bitter receptors signals trigger physiological actions such as the secretion of antimicrobial peptides in the nasal cavity³, or relaxing of the airway smooth muscles¹.

Complexity of bitter taste perception

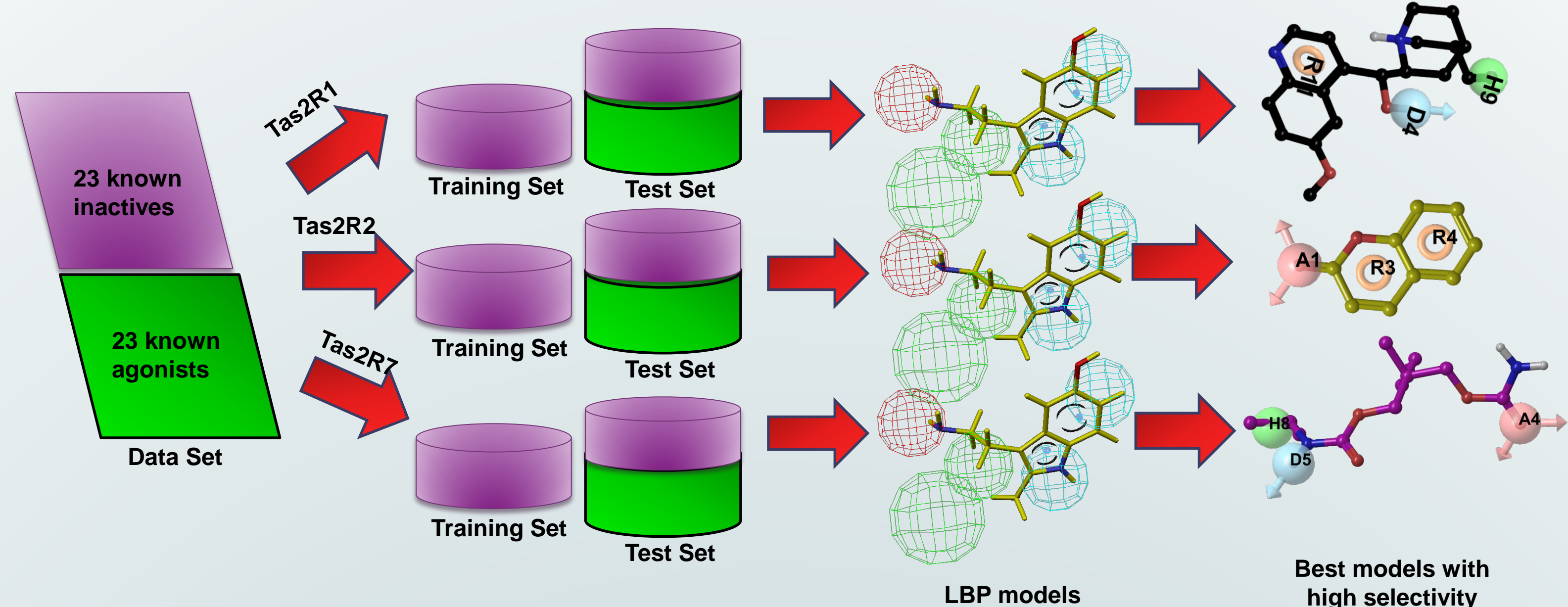
- There is no correlation between the number of Tas2R genes and the perception of bitter taste.
- Receptors can have more than one binding pocket and more than one binding mechanism.
- Many compounds binding to one receptor don't have a similar chemical structure.
- Some receptors are broadly tuned and some are narrowly tuned.

Why chicken?

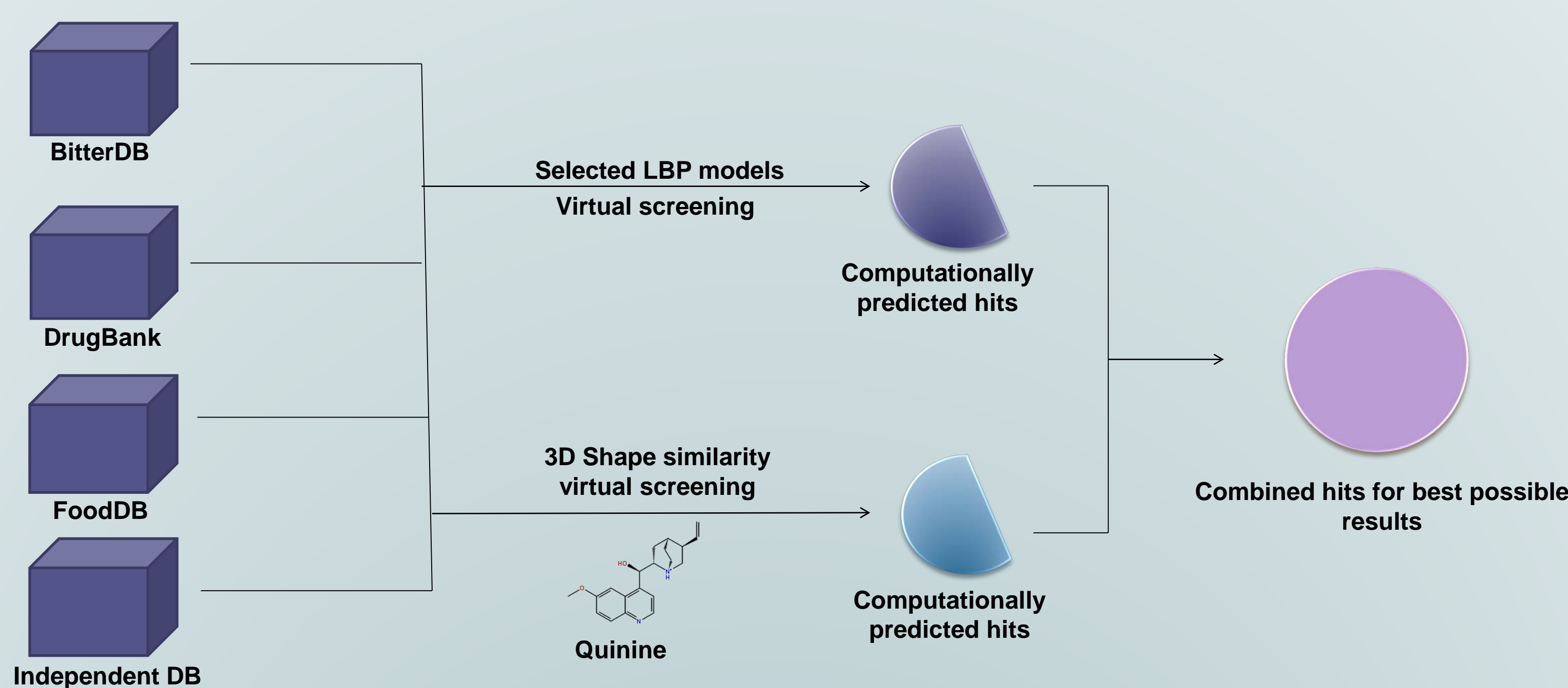
Bitter taste perception in vertebrates relies on the Tas2R genes, ranging from only 3 in chicken to over 50 in frogs. Possessing a small repertoire of Tas2Rs making the chicken a suitable candidate for a model animal in the study of different aspects regarding bitter taste. Furthermore, the agricultural importance for finding bitter tastants in chicken feedstuff is great, since their nutrition may be improved due to lack of aversiveness.

Materials and methods

1. Ligand based pharmacophore (LBP) modeling process



2. Database preparation 3. Virtual screening



4. In-Vivo testing



Figure 1. The process of building and validating LBP and shape models followed by virtual screening and in-vivo testing

Results

LBP models

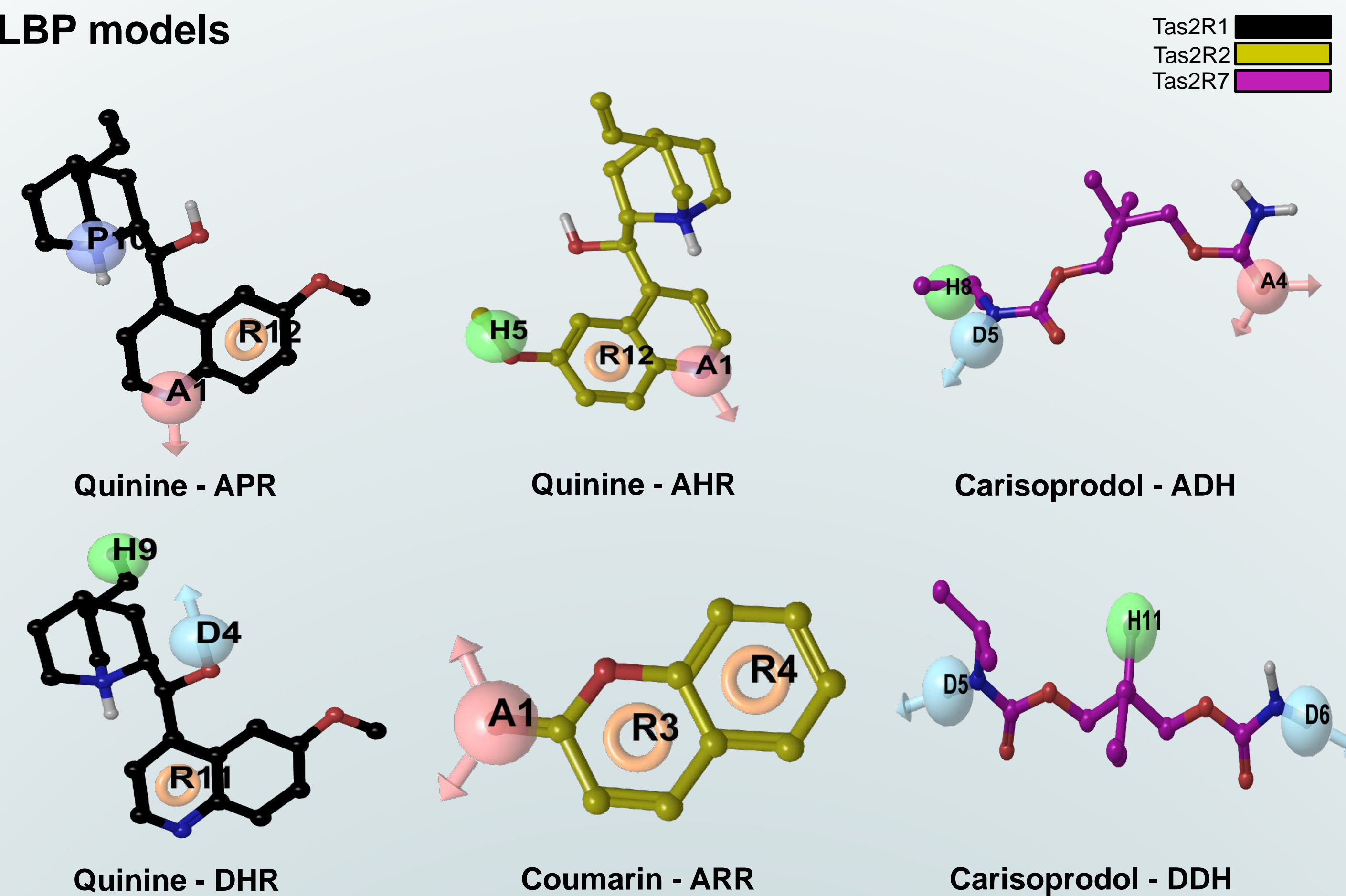


Figure 2. Selected LBP models for the three different receptors

Name	Features	Fitness	Shape similarity
Ethylhydrocupreine	APR	2.698	65%
Cinchonine	APR	2.433	58.1%
Mefloquine	APR	2.616	46.7%
Cinchonidine	DHR	2.534	55%
Hydrocinchonine	DHR	2.503	53%

Table 1. Best hits for Tas2R1, Based on LBP's with quinine as template

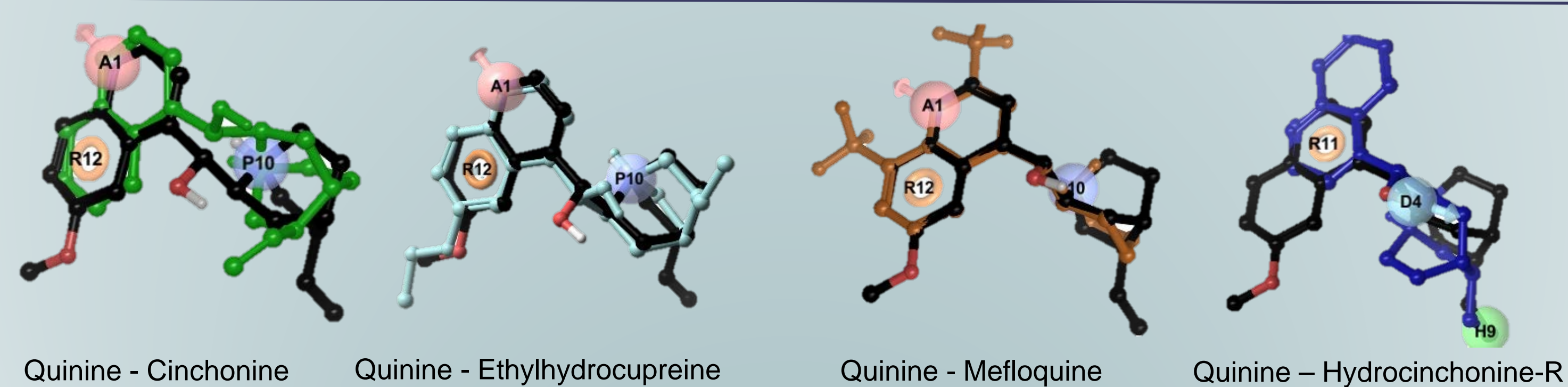


Figure 3. Alignment of Best hits for Tas2R1 with quinine

Conclusions

- Several molecules have been identified as promising candidates for agonism to Tas2R1.
- Quinine analogs can be checked for antagonism, since they derive from the quinine agonist.
- In-Vivo testing is ongoing, therefore comprehensive conclusions are still pending.
- Future direction: In-Vitro experiments will be necessary in order to prove binding to a specific receptor.

References

1. Kathryn S. Robinett et al. Bitter Taste Receptor Function in Asthmatic and Nonasthmatic Human Airway Smooth Muscle Cells. *Am J Respir Cell Mol Biol.* 2014 Apr; 50(4): 678–683.
2. Sara Janssen and Inge Depoortere. Nutrient sensing in the gut: new roads to therapeutics. 2012 Elsevier *Trends in Endocrinology and Metabolism* xx (2012) 1–9.
3. Robert J. Lee et al. Bitter and sweet taste receptors regulate human upper respiratory innate immunity. *J Clin Invest.* 2014;124(3):1393–1405.