Homology Modeling of Human Sweet Taste Receptors: T1R2-T1R3

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***Abstract*—The sweet taste perception in human is mainly due to the specific G protein- copulated heterodimeric receptors (GPCR) T1R2-T1R3 and these receptors gathered in the taste buds of the tongue. The sweet protein acts as an important rule for molecular understanding of the taste mechanisms. Therefore, the Homology modeling of the closely related sweet taste receptors (T1R2-T1R3), is crucial to provide an understanding of the interactions between the sweetens and the receptors. 3A21 and 3Q41 were selected as possible templates for T1R2 and T1R3, respectively based on the phylogenetic evaluations. The models of the target sequences were generated using the program MODELLER V9.10. From the Ramachandran plot analysis it was shown that 79% and 84% of the residues reside in the core region for T1R2 model and T1R3 model, respectively.**

***Index Terms*—homology modeling, human sweet taste receptors, MODELLER**

I. Introduction

There are five crucial taste traits able to be sensed by human being, which includes sweet, umami, bitter, salty, and sour. The G protein-coupled receptors are referred to sweet and umami taste, and the sweet state receptors (T1R2/T1R3) are heterodimeric belongs to the TR family closely related to G protein-coupled receptors (GPCR), [1] and these sweet taste receptors gathered in the taste buds of the tongue [2]. Furthermore, they are able to detect all class of sweeteners including sugars, artificial sweeteners, amino acids, and sweet-tasting proteins [3]. [4]. And they have different ligand binding sites. However, there is yet a clear study to give an insight of the binding ability of the human sweet taste receptors T1R2 and T1R3 [5].

In over 108 million protein sequences that have been experimentally determined, there is only a little number of those proteins with solved structures. Since the gap between the protein sequence and the structure is huge, the computational tools are needed to solve the protein structures [6]. The best method is Homology modeling or comparative modeling [7]. This method has been proven to successfully predict a 3D tertiary structure of unknown protein structure using known protein templates. [8].

In homology modeling, the sequence identity and similarity between the template and the target determine the accuracy of the model. High accuracy model will be produced when the sequence identity is more than 50%. If the sequence identity is less than 30%, it may produce a model with a possible error [9].

Fig. 1 shows the homology modeling process includes template selection, sequence alignment, model building and model refinement [7].

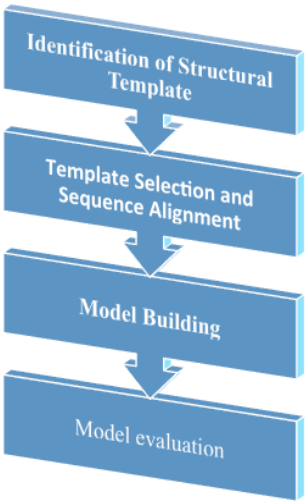

Figure 1. Flow chart of the structure prediction process of human sweet taste receptors.

II. Methodology

A. Template Selection and Sequence Alignment

The template searching was performed using Basic Local Alignment Search Tools (BLAST), which is a tool to search for sequence similarities for proteins and nucleotides [10], and subsequently using MEGA5 to construct the phylogenetic trees for both T1R2 and T1R3 to determine the closest template according to their molecular evaluation [11]. The target and the template sequences were aligned together by using the ClustalW. [12].

B. Model Building

Different models were generated using MODELLER V9.10 employing the method of satisfaction of spatial restraints [13]. The models with the lowest energy were chosen for the model evaluation.

III. Results and Discussion

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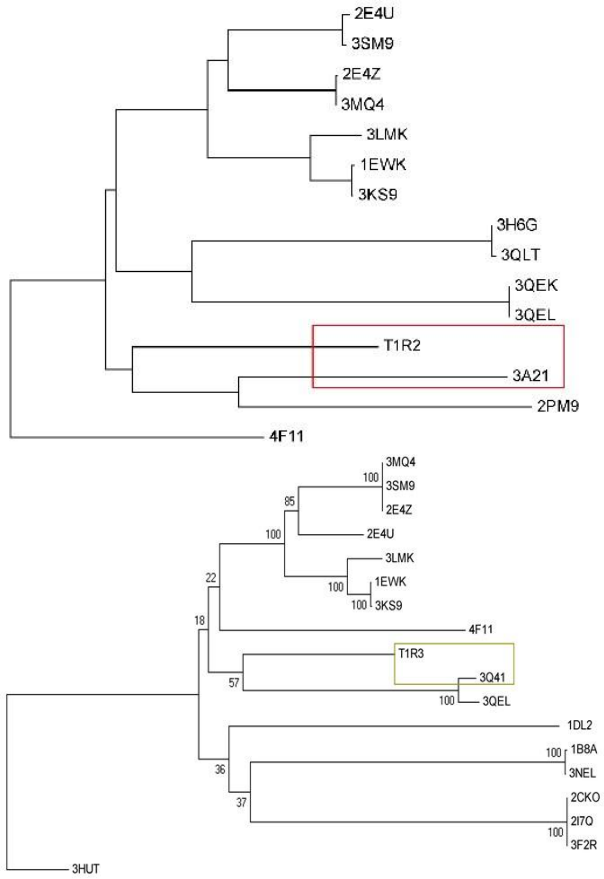
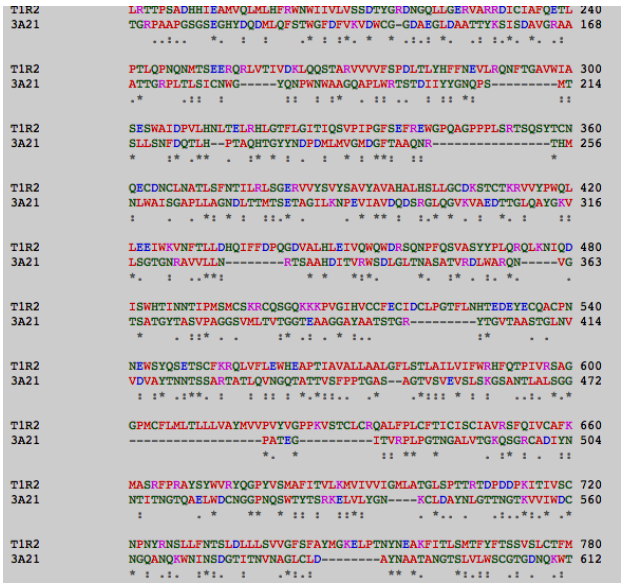


Figure 2. The phylogenetic analysis for both T1R2 and T1R3

The results shows that the crystal structure of *Streptomyces avermitilis* beta-L- Arabinopyranosidase (3A21) and Crystal structure of the GluN1 N-terminal domain (3Q41) are the templates for T1R2 and T1R3 respectively as shown in Fig. 2. The sequence alignment between the target and the template sequences was performed using ClustalW as shown in Fig. 3. The sequence identity was 14.98% and 20.05% for T1R2 and T1R3 respectively. Fig. 4 shows the 3D structure of both T1R2 and T1R3.



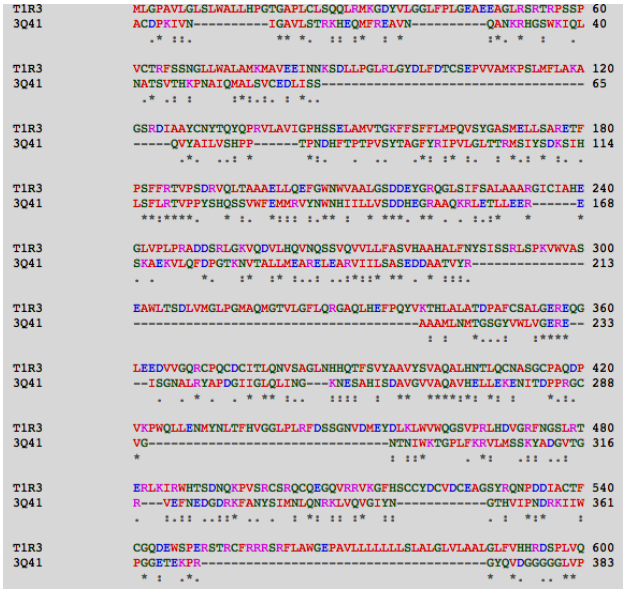


Figure 3. The ClustalW alignment for T1R2 and T1R3

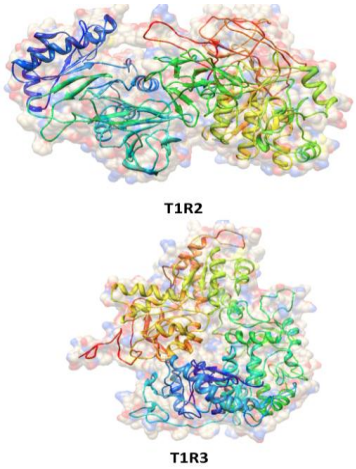


Figure 4. T1R2-3A21 and T1R3-3Q41 models.

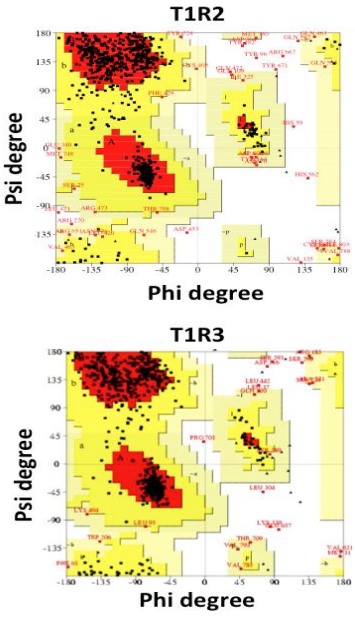


Figure 5. Ramachandran Plot of T1R2 -3A21 and T1R3- 3Q41.

The Ramachandran plot analysis was performed in order to examine the quality of the models [14], and the results for this plot shows that T1R2 model had 77.2% of the residues located in the most favoured regions, while 84.2% for the T1R3 model, correspondingly as shown in Fig. 5.

IV. Conclusion

The aim of this project was to predict the 3D structure for the human taste receptors, which are T1R2 and T1R3. This was done by identification of the template structure and performing the sequence alignment between the target sequence and the template sequence.

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