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1. Introduction

The odorant receptors (ORs) are located on the olfactory receptor cells, which occupy a small area on the olfactory epithelium and detect the inhaled odorant molecules. Buck and Axel identified the gene family that encoded for the human ORs [1]. These receptors belong to the family of seven transmembrane G-protein-coupled receptors (GPCRs) and constitute the largest family (family A) in the genome. Many ORs are also orphan receptors, i.e. whose endogenous ligand has not yet been identified. In the present work, the authors have investigated the structure feature analysis of the transmembrane helices (TM-helices) in human ORs.

2. Method

2.1 Reduced representation of 3D structural feature of GPCRs

In the present work, the authors have referred the database of human GPCRs. Three-dimensional structures were predicted by the computer program, TASSER [2]. It contains 322 ORs within 907 GPCRs. The program TMHMM [3] was used to identify the region of TM-helices of ORs. To describe the structural feature of ORs, each TM-helix was approximated by a point corresponding to the mid-point of residue number in membrane domain. So that, each OR structure was represented by a set of seven points and 3D coordinates of their alpha-carbons. The direction of TM-helix (i.e. from cell exterior to interior, or from interior to exterior) was also distinguished as a label of mid-point. Fig. 1 shows an illustrated example of the reduced representation of TM-helices using *Rhodopsin* (PDB-ID: 1F88).

2.2 Structural feature searching of TM-helices

Each odorant molecule may bind several odorant receptors, and each odorant receptor may accept several odorant molecules. In other words, specific odor is perceived by specific combinations of receptors [1]. These combinations of receptors are translated by the brain into diverse odor perceptions.

In the present work, we assumed that a several TM-helices play a role of the binding site for particular odorant molecule (Fig. 2). As mentioned above, structural information of OR was represented by a weighted graph of which the nodes and edges correspond to mid-point residues and the inter-atomic distances between them, respectively. The program FragSearch proposed by the authors [4] were used for comparative explore such frequent pattern of TM-helices.

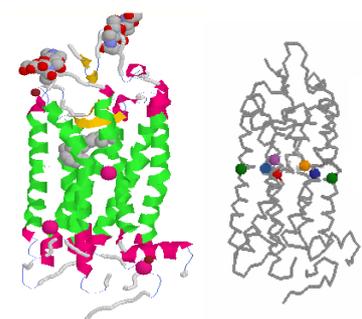


Fig.1 Reduced representation of TM-helices.

Fragment image	Olfactory Receptors	Receptors													
		1	2	3	4	5	6	7	8	9	10	11	12	13	14
	Fragments														
	OR2 TM1,2,5,6,7		●				●								
	OR1 TM1,2,6,7	●			●	●		●			●	●			
	OR5 TM4,5,6,7		●			●	●								
	OR7 TM1,2,3,4	●			●	●		●	●		●	●	●		
	OR7 TM2,3,4,6				●	●		●			●				
	OR8 TM1,3,6,7	●			●	●		●	●		●		●		●
	OR10 TM2,3,4,7				●	●		●			●		●		

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Fig.2 Basic concept of the structure feature searching in the present work.

3. Results and Discussion

To validate our representation model, three type of ORs (OR1A1 (UniProt-ID: Q9P1Q5), OR1A2 (Q9Y585), and OR10A3 (P58182)) were selected and superimposed using the mid-point of TM-helices. OR1A1 and 1A2 belong to the same OR family and their structure of seven points are quite similar. On the other hand, OR10A3 belong to the different family from them, so the pattern of seven points is different. In addition, it could be concluded that the tendency of spatial configuration of TM-helices were preserved in seven mid-points.

Subsequently, we have prepared a target dataset that contains ten ORs taken from TASSER database [2]. These ORs belong to the different OR families, respectively. Search trials were carried out under the conditions that the distance allowance is 1.5Å, and the value of frequency is 30%. As the result, four TM-helices were identified as a common structure feature between three ORs (OR12D2, 1A1, and 2B2). Graphical views of the extracted fragment are shown in Fig. 3 with their parent structures. The program identified other structural feature which consisted of four TM-helices. These results show the potential applicability of the present approach for structural feature analysis of ORs. Frequent fragment dictionary of TM-helices is also constructed for analysis of the odor-structure relationship.

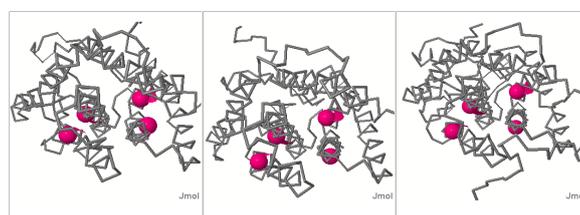


Fig.3 Graphical views of identified common structural features.

References

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