Classification of Adrenergic Receptors using the Multi-dimensional Scaling Method

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1 Introduction

The adrenergic receptors are a family of G-protein-coupled receptors (GPCRs) that are targets of the catecholamines. Adrenergic receptors specifically bind and are activated by their endogenous ligands, the catecholamines adrenaline and noradrenaline. There are three subfamilies of adrenergic receptors, \( \alpha_1 \) (a \( G_s \) coupled receptors), \( \alpha_2 \) (\( G_i \) coupled receptors) and \( \beta \) (\( G_s \) coupled receptors). A variety of classification methods using by profile-hidden Markov models and support vector machines were proposed. Otaki and Firshtein proposed that the transmembrane topology pattern is well conserved among GPCRs that have the same function, even though the amino acid sequences are not conserved, suggesting a possibility of classifying GPCRs based on the loop lengths [4]. In this study, we propose a novel classification method for classification of adrenergic receptors based on the statistical method.

2 Materials and Method

2.1 Dataset in this study

We used only adrenergic receptor sequences with known transmembrane topology extracted from UNI-PROT/SWISS-PROT (Release 56.0) [1], of which entries with FRAGMENT are excluded, then these entries were classified according to with GPCRDB (Release 10.0) [3]. After removing the signal peptide region detected by SignalP 2.0 [2], the transmembrane topology of these adrenergic receptor was predicted by applying HMMTOP 2.0 [5]. The final dataset consists of adrenergic \( \alpha_1 \) receptor (17 sequences), \( \alpha_2 \) (23), and \( \beta \) (20) as defined by GPCRDB classification.

2.2 Statistical analysis of adrenergic receptors using the multi-dimensional scaling (MDS) method

MDS method is devised for information visualization for exploring similarities. In this study, we used the euclian distance \( ed_{ij} \) was defined as:

\[
ed_{ij} = \sqrt{\sum_{k=1}^{8} (l_{ik} - l_{jk})^2}
\]

where \( l_{ik} \) and \( l_{jk} \) were the \( k \)-th loop length of \( i \)-th and \( j \)-th adrenergic receptors.
3 Results and Discussions

Fundamental statistical (minimum, mean, median, maximum, and standard deviation) values were calculated. Standard deviation values of N-tail, intracellular 3rd, and C-tail loops were larger than intracellular 1st and 2nd, extracellular 1st and 2nd loops (Figure 1). For example, C-tail loop was distributed from 18 to 187 a.a. around the mean (79.3 a.a.) and the median (88 a.a.). Adrenergic receptors were classified three subfamilies using the MDS method (Figure 2). These results suggest a possible functional importance of adrenergic receptors.

![Figure 1: Boxplot for the lengths of N-/C- tail](image1)
![Figure 2: Scatter plot of adrenergic receptors using intracellular (icl-ic3), and extracellular (ecl-ec3) the MDS method. Black: adrenergic α1 receptors, Red: adrenergic α2 receptors, Green: adrenergic β receptors.](image2)

References


